Aromatic Compounds from Pyrylium Salts

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Introduction

The readily obtainable substituted pyrylium salts lend themselves to the preparation of numerous, often difficultly accessible, aromatic compounds of both the heterocyclic and isocyclic series. The first known example of these reactions is the formation of pyridine and pyridinium derivatives described by Baeyer. Another reaction of this kind is the formation of thiopyrylium salts reported by Wizinger. Especially numerous are the possibilities for the preparation of isocyclic aromatic compounds, whereby known phenols and alkylated amines together with new nitrocompounds, ketones, carboxylic acids, nitriles, phenol carboxylic acids, aminonitriles, or hydrocarbons of the benzene, naphthalene, and phenanthrene series can be prepared in generally good yield. The use of pyrylium salts as the starting materials for the preparation of azulenes is also possible.

In addition to a discussion of these reactions a survey of the methods available for the preparation of pyrylium salts will be given.

Conversion of Pyrylium Salts into Heterocyclic Compounds Possessing Aromatic Character

Derivatives of Pyridine

As found by Baeyer [1], the original worker in this field, pyrylium salts can readily be converted into pyridine derivatives by warming with an aqueous ammonium carbonate solution. Following the preparation by Baeyer and Piccard [2] of collidine (2a) and 2,6-dimethyl-4-phenylpyridine (2b) from 2,4,6-trimethylpyrylium perchlorate (1a) and 2,6-dimethyl-4-phenylpyrylium perchlorate (1b) respectively, this synthesis was extended to include other 2,4,6-tri-alkyl- and aryl-substituted pyrylium salts by Dilthey [3], Gastaldi [4], and others [5]. These reactions, however, served more to elucidate the constitution of the pyrylium salts, than in the preparation of specific pyridine derivatives. Nevertheless, a large number of difficultly accessible pyridine derivatives, e.g. 2,4,6-triphenylpyridine (2c) [3a], 2,3,4,6-tetraphenylpyridine (2d) [3c], penta-phenylpyridine [3c], or 1,4-bis-[3,5-diphenylpyridino(4)1]benzene (2g)
[22], can be obtained readily in this manner. The disubstituted 2,6-di­phenylpyrylium perchlorate (1h) is also converted smoothly into 2,6­diphenylpyridine (2h) [6]; nucleophilic addition at C-2 (C-6) is pre­ferred to that at C-4.

A summary of the preparative methods for pyridine derivatives is to be found in [7].

\[
\begin{align*}
&\text{(a)} \quad R_2 = R_4 = R_6 = \text{CH}_3; \quad R_3 = H \\
&\text{(b)} \quad R_2 = R_6 = \text{CH}_3; \quad R_4 = \text{C}_6\text{H}_5; \quad R_3 = H \\
&\text{(c)} \quad R_2 = R_4 = R_6 = \text{C}_6\text{H}_5; \quad R_3 = H \\
&\text{(d)} \quad R_2 = R_4 = R_6 = \text{C}_6\text{H}_5 \\
&\text{(e)} \quad R_2 = R_6 = \text{CH}_3; \quad R_4 = \text{OCH}_3; \quad R_3 = H \\
&\text{(f)} \quad R_2 = R_6 = \text{CH}_3; \quad R_4 = \text{NHCH}_3; \quad R_3 = H; \quad \text{NCH}_3\cdot\text{ClO}_4 \text{ instead of N in (2)} \\
&\text{(g)} \quad R_2 = R_6 = \text{C}_6\text{H}_5; \quad R_3 = H; \quad R_4 = \\
&\text{(h)} \quad R_2 = R_6 = \text{C}_6\text{H}_5; \quad R_3 = R_4 = H
\end{align*}
\]

The conversion of the pyrylium salts is almost always facile and quantitative; alcoholic ammonia is sometimes better suited than aqueous ammonium carbonate. As our own experiments [8] have shown, the reaction proceeds particularly favorably when the pyrylium salt is sus­pended in absolute tert-butanol, and dry ammonia passed through; warming effects solution of the salt, and the ammonium salt of the in­organic acid constituting the anion of the pyrylium salt (ammonium perchlorate or ammonium fluoborate) separates on cooling. The pyridine derivative which remains in solution often can be precipitated practically quantitatively by the addition of a little water.

The conversion of pyrylium salts into pyridine derivatives fails when the heterocyclic oxygen atom of the pyrylium salt originates from a phenolic component. Hence neither chromylium nor xanthylium salts can be converted into quinoline or acridine derivatives. 2,4-Diphenyltetra­hydrobenzopyrylium perchlorate (3), however, gives a quantitative yield of 2,4-diphenyltetrahydroquinoline (4), by treatment with am­monia in tert-butanol [8]. The conversion of 1,3-disubstituted iso-
chromylium salts (5b and c) into 1,3-disubstituted isoquinoline derivatives (6b and c) can be accomplished similarly [8,9].

\[
\begin{align*}
&\text{(3)} & &\text{(4)} \\
&\text{H}_2\text{C} & &\text{H}_2\text{C} \\
&\text{H}_2\text{C} & &\text{H}_2\text{C} \\
&\text{C}_6\text{H}_5 & &\text{C}_6\text{H}_5 \\
&\text{ClO}_4^- & &\text{+ NH}_4\text{ClO}_4 + \text{H}_2\text{O} \\
\text{2 NH}_3 & &\text{+ NH}_4\text{ClO}_4 + \text{H}_2\text{O} \\
\end{align*}
\]

Unsubstituted isochromylium chloroferrate (5a), readily accessible from homophthalaldehyde, yields, like the aldehyde itself, isoquinoline with ammonia [10], respectively, N-substituted isoquinolinium compounds with primary aliphatic or aromatic amines [11].

\[
\begin{align*}
&\text{(5)} & &\text{(6)} \\
&\text{R}_1 & &\text{R}_3 \\
&\text{X} & &\text{R}_3 \\
&\text{H} & &\text{H} \\
&\text{CH}_3 & &\text{CH}_3 \\
&\text{C}_6\text{H}_5 & &\text{C}_6\text{H}_5 \\
\text{2 NH}_3 & &\text{+ NH}_4\text{X} + \text{H}_2\text{O} \\
\end{align*}
\]

Similarly, careful treatment of 2,6-dimethyl-4-methoxypyrylium perchlorate (1e) with aqueous ammonia yields 2,6-dimethyl-4-methoxy- pyridine (2e) [1]. According to Anker and Cook [12] the 4-methoxy, and to some extent also the 4-methylmercapto [13] group in the pyrylium salt, are sufficiently reactive to allow their replacement by other nucleophilic groups, such as alkoxy, alkylmercapto, alkylamino, or dialkylamino. The most diverse pyridine derivatives can accordingly be prepared by subsequent treatment with ammonia. If the methoxypyrylium salt (1e) is allowed to react with an excess of methylamine in methanol, both the heterocyclic oxygen atom and the methoxy group are replaced and 2,6-dimethyl-4-methylamino-N-methylpyridinium perchlorate (2f) is obtained on precipitation with perchloric acid.

**Derivatives of Pyridinium Compounds**

If 2,4,6-trisubstituted pyrylium salts (7) are allowed to react with primary aliphatic or aromatic amines instead of ammonia, the N-alkylated or N-arylated pyridinium salts (8a) are obtained. In this reaction too, the first examples were discovered by Baeyer and Piccard [1,2].
The method is exceptionally well suited to the synthesis of numerous pyridinium compounds, especially as it usually proceeds in excellent yield [14]. The only requirement is that the amine should not be too weakly basic. The simple aliphatic amines, such as methylamine, ethylamine, etc., can also be replaced by aromatic amines, such as aniline and its derivatives. Phenylhydrazine, α-methylphenylhydrazine [15], or semicarbazide [16] essentially react in similar fashion (to give 8b, c, d). Reaction with hydroxylamine yields pyridine oxides (8e), but only when the size of the α,α'-substituents is not excessive. Otherwise [e.g. with CH(CH₃)₂ and C₆H₅ in the α,α'-position] reduction occurs and the pyridine derivatives are obtained.

\[
\begin{align*}
\text{(7)} & \quad \text{R, R', R" = aliphatic and aromatic groups} \\
(a) & \quad \text{R₁ = alkyl or aryl, hydroxyaryl etc.} \\
(b) & \quad \text{R₂ = NH₅H₅} \\
(c) & \quad \text{R₁ = CH₃NC₆H₅} \\
(d) & \quad \text{R₁ = NHCONH₂} \\
(e) & \quad \text{R₁ = OH}
\end{align*}
\]

There exists thus far no other route for the preparation of the N—NH-arylpyridinium compounds (9) [17]. This class of compounds has been discovered as a result of the work of Schneider and co-workers [15], and is distinguished by a series of interesting reactions. With alkali they give strongly colored anhydro bases, which are to be regarded as \( \text{N—N betaines (10)} [18], \) i.e. the heterocyclic pyridine nitrogen carries the positive, and the anilido nitrogen the negative charge.

\[
\begin{align*}
\text{(9)} & \quad \text{R = aryl or alkyl}
\end{align*}
\]
Of especial interest are the N-hydroxyphenylpyridinium salts which are readily formed from pyrylium salts by reaction with aminophenols, and which can be converted into pyridinium-N-phenol betaines by the action of strong bases \[19\]. The compounds may also be considered phenologs of pyridine-N-oxide. By suitable substitution of the pyridine as well as the aminophenol it is possible to obtain stable betaines which have unusually large solvatochromic and thermochromic effects. They are especially useful for the measurement of the polarity of solvents \[20\]. The \(Z\) \[21\] or \(E_T\) values which are found in this way determine the polarity of the solvent much better than the dielectric constant.

The double conversion of a dipryrloeyanin dye (p. 371) into a dipyrirdiniumcyanine dyestuff is also possible. In a similar way the bis-pyrylum salt (p. 382) from terephthalaldehyde and acetophenone \[22\] with \(p\)-aminophenol and its derivatives give the bis-pyridinium-N-phenolbetaines \[23\].

Derivatives of Thiopyrylium Compounds

While the unsubstituted pyrylium salt (11) is a rather unstable compound \[24\], the corresponding thiopyrylium salt (12) \[27\] is very stable and may be prepared readily by several different routes \[25\]. Its reactions, however, in contrast to those of benzo thiopyrylium salts (13) \[26\] have hardly been investigated.

When treated with sodium sulfide in acetone, followed by precipitation with acid, 2,4,6-trisubstituted pyrylium salts (14) usually undergo replacement of the heterocyclic oxygen atom by sulfur to give the thiopyrylium salts (16) \[27\] within a few minutes. The presence of intermediates manifests itself by a blue coloration; Wizinger and Ulrich \[28\],

\[
\begin{align*}
\text{Ar} & \quad \text{Ar} \\
\text{O} & \quad \text{O} \\
\text{X} & \quad \text{X} \\
\end{align*}
\]

\(\text{(11)}\)

\[
\begin{align*}
\text{Ar} & \quad \text{Ar} \\
\text{S} & \quad \text{S} \\
\text{X} & \quad \text{X} \\
\end{align*}
\]

\(\text{(12)}\)

\[
\begin{align*}
\text{Ar} & \quad \text{Ar} \\
\text{O} & \quad \text{O} \\
\text{S} & \quad \text{S} \\
\text{X} & \quad \text{X} \\
\end{align*}
\]

\(\text{(13)}\)

\[
\begin{align*}
\text{Ar} & \quad \text{Ar} \\
\text{O} & \quad \text{O} \\
\text{S} & \quad \text{S} \\
\text{X} & \quad \text{X} \\
\end{align*}
\]

\(\text{(14)}\)

\[
\begin{align*}
\text{Ar} & \quad \text{Ar} \\
\text{O} & \quad \text{O} \\
\text{X} & \quad \text{X} \\
\end{align*}
\]

\(\text{(15)}\)

\[
\begin{align*}
\text{Ar} & \quad \text{Ar} \\
\text{S} & \quad \text{S} \\
\text{X} & \quad \text{X} \\
\end{align*}
\]

\(\text{(16)}\)

\[
\begin{align*}
\text{Ar} = \text{C}_6\text{H}_5 \text{ or CH}=\text{CH—C}_6\text{H}_5
\end{align*}
\]
the discoverers of this reaction, believe them to be the sodium salts of ketothioenols (15).

The reaction published by Suld and Price [27] between phenyl lithium and 2,4,6-triphenylthiopyrylium perchlorate (17) in ethereal solution at a low temperature and in the absence of light, gave a stable amorphous product with a purple color which was described as 1,2,4,6-tetraphenylthiobenzene (18). On passing oxygen through an ethereal solution of the compound an oxypyrylium salt (19) was formed as well as diphenyl disulfide. This salt (19) was also prepared by an independent synthesis from benzalacetophenone and ω-acetoxyacetophenone. The compound (18) was converted, in 25% yield, into the colorless 2,4,4,6-tetraphenylthiopyran (20) on being allowed to stand for a day.

Aliphatic Grignard compounds give deep-colored intermediates with (17) which are quickly converted into 2- or 4-thiopyran derivatives. An interesting rearrangement of compound (19) to 3,5,6-triphenyl-2-pyrone has recently been found [28a].

Derivatives of Pyridone and Thiopyridone from Pyrone Derivatives

4-Pyrones (21a) and, to an even greater extent, 2,6-alkyl-substituted 4-thiopyrones (21b) such as 2,6-dimethyl-4-thiopyrone, do not behave as true ketones or thiketones, but can be regarded as internal pyrylium salts (22a, b), i.e. they possess pseudoaromatic character [29]. They react in similar manner to pyrylium salts in a number of reactions.
Ost [30] already had discovered that the heterocyclic oxygen in the substituted 4-pyrones (23) (such as meconic acid) can readily be replaced with ammonia or primary amines, to give pyridones or N-substituted pyridones (24), respectively. In a similar manner Von Pechmann [31] succeeded in converting a 2-pyrone [(25): R₄=R₆=H, R₅=COOH, coumalic acid] into the 2-pyridone or 2-hydroxypyridine derivative (26).

Numerous syntheses of pyridones and N-substituted pyridones from pyrones and ammonia or the most varied primary aliphatic amines, respectively, have since been described [32]. The reactions are readily accomplished by the mere treatment of the pyrone derivative with aqueous ammonia or aqueous alkylamine solutions. More complicated pyrones, such as naphthopyrones, often react in another way [33].
Dehydroacetic acid (27) readily reacts both on warming with ammonia and with methylamine in an autoclave to give lutidone (28a) and N-methyllutidone (28b) [34], respectively. An analogous N-phenyl­lutidone (28c) synthesis using aniline affords a yield of over 90% when the reactants are boiled for 2 hr under reflux in the presence of a little more than the equivalent amount of hydrochloric acid. 2,6-Dimethyl-4-pyrone [(23): \( R_1 = R_2 = \text{CH}_3 \)] itself does not react with aniline under these conditions [35]. The unsubstituted 4-pyrone, on the other hand, initially reacts with aniline to give the dianilido derivative, and the action of acid on the latter results in the formation of N-phenylpyridone [36]. The reaction can also be carried out in a single operation by boiling with aniline/hydrochloric acid [35]. These reactions, unlike those with pyryl­ium salts, consequently require no protection by substituents in the 2,6- or 2,4-positions of the 4- or 2-pyrone, respectively. More conversions of this kind, of pyrones into pyridones, have recently been described by Hünig and Köbrich [35].

\[
\begin{align*}
\text{(27)} & \xrightarrow{H_2NR} \text{(28)} \\
\text{(a) } R = H & \quad \text{(b) } R = \text{CH}_3 \\
\text{(c) } R = \text{C}_6\text{H}_5
\end{align*}
\]

\[Y = \text{OR'} \text{ or halogen}\]

2,6-Diphenyl-4-pyrone (30) cannot be converted into the pyridone derivative either with aqueous ammonium acetate or with aniline acetate, even if the reaction is attempted at 0°C [37]. The conversion can, however, readily be accomplished with alcoholic ammonia. But since 2,6-diphenyl-4-pyridone is almost instantaneously reconverted into 2,6-diphenyl-4-pyrone in the presence of a trace of hydrochloric acid [38], it is possible that the previous observation was the result of inadequate precautions in the work-up.

\[
\begin{align*}
\text{(30)} & \xrightarrow{\text{alcoholic NH}_3} \text{(31)} \\
\text{\( \text{H}_2\text{Cl} \)}} & \xrightarrow{\text{aqueous HCl}} \text{(30)}
\end{align*}
\]
The N-alkyl- and N-arylpyridones constitute valuable intermediates for the preparation of numerous pyridinium compounds, since alkylation or halogenation yields reactive intermediates (29); these [cf. the methoxypyrylium salts (1e)] readily exchange the p-alkoxy group or halogen by other nucleophilic groups [38].

In the presence of alcoholic hydroxylamine, 2,6-diphenyl-4-pyrone gives N-hydroxy-2,6-diphenylpyridone [37,39]. 2,6-Dimethyl-4-pyrone (32) forms 4-hydroxylamino-2,6-dimethylpyridine-N-oxide (33) which on catalytic hydrogenation gives 2,6-dimethyl-4-aminopyridine (34) [40]. Cyanamide reacts with 4-pyrones in aqueous ethanol (1:1) to give N-cyanopyridones in 70–80% yield (34a) [41]. For the reactions of 2-pyrones with sodium cyanide which lead to ring-opening see Vogel [42].

\[
\begin{align*}
\text{H}_2\text{C} & \quad \downarrow_{\text{NH}_2\text{OH}} \quad \downarrow_{\text{Red.}} \\
\text{O} & \quad \text{NOH} & \quad \text{NH}_2 \\
\text{H}_2\text{C} & \quad \text{N} & \quad \text{NH}_2 \\
\text{O} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{O} \\
\text{O} & \quad \text{CH}_3 \\
\text{O} & \quad \text{CN} \\
\text{H}_2\text{C} & \quad \text{N} & \quad \text{NH}_2 \\
\text{CN} & \quad \text{CH}_3 \\
\text{O} & \quad \text{N} & \quad \text{O} \\
\text{H}_2\text{C} & \quad \text{N} & \quad \text{NH}_2 \\
\text{CH}_3 & \quad \text{O} \\
\end{align*}
\]

(32) (33) (34a) (34)

Pyrones can also be converted into thiapyrones by an essentially similar method [43]. The heterocyclic oxygen atom in 2,6-diphenyl-4-pyrone (35) is replaced by sulfur (albeit in traces only) to give (36) by the action of boiling alcoholic potassium hydrogen sulfide. 2,6-Diphenyl-4-thiopyrone (37), on the other hand, reacts more readily and affords 2,6-diphenyldithiopyrone (38) in approximately 50% yield [45].

The recent publication of a synthesis for the ready preparation of isocoumarin (40) by the decarboxylation of isocoumarin-3-carboxylic acid (39), obtained as a condensation product from dimethyl diglycolate and methylphthalaldehyde [46], allows a similar reaction with ammonia.
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(a) $R = H$
(b) $R = \text{alkyl or aryl}$
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and primary amines to give isoquinolones (41). With Grignard reagents and acids 1-substituted isochromylium salts (42) are formed, which with ammonia or amines can be converted into isoquinolines or isoquinolinium salts (43a and b). The reaction allows a wide range of substituted isoquinoline compounds to be formed, since both the isocoumarin and the compound which contains the nitrogen atom can carry new substituents.

DERIVATIVES OF DIHYDROPYRIDINES AND THIOPYRANS

4H-4-Dehydroionanes

The carbonyl group of the 4-pyrones (44) can react with nucleophilic reagents, though its reactivity is relatively small. Thus, from 4-pyrones and compounds which contain an acidic CH group, such as malononitrile, in toluene or glacial acetic acid and acetic anhydride solution Woods \[47\] obtained pyrylium salts (45) which with alkali readily split out the proton in the \(\alpha\)-position to the pyrylium ring to give 4H-4-dehydroionanes (46).

\[
\begin{align*}
\text{(44)} & \xrightarrow{\text{CH}_2R'R'' + \text{HX}} \text{(45)} \quad \text{OH}^- \\
\text{R'} = \text{R''} = \text{CN}
\end{align*}
\]

Similar reactions were carried out by Ohta and Kato \[48\], Eiden \[49\] and Wizinger \[50\]. Malonic ester, acetylacetone, cyclopentadiene, and nitromethane failed to give this reaction. The colored bases (48) recently obtained from a reaction between hydrindanone and 1,3-dicarbonyl compounds by Schroth and Fischer \[51\] also belong to this series of dehydroionanes; with acids they yield the indenopyrylium salts (47). The pyrancyclopentadiene compounds (48a, 48b) are very similar pyrane/pyrylium derivatives \[52\].

By the reaction of 2,6-diphenyl-4-thiopyrone (49) and diphenyl diazomethane Schönberg \[53\] obtained, by way of an intermediate product, 2,6-diphenyl-4-(\(\alpha,\alpha\)-diphenylmethylene)pyran (50). Reaction of the thiopyrone (49) with diazomethane and the subsequent removal of the sulfur with phenyl lithium leads to the very stable pyran derivative (51) \[53,54\]; this compound is also obtained if the thiopyrone is heated to 230\(^\circ\). A further method for the preparation of the dipyranilidene is
The reaction of 2,6-dimethyl-4-pyrone and diphenylketene gives 2,6-dimethyl-4-(α,α'-diphenylmethylene)pyran [55].

4-Methoxy-2,6-dimethylpyrylium perchlorate (52) can also be used as the starting material for the preparation of compounds of type (45) and (46). According to Ohta and Kato [48] the methoxyl group is so
reactive that it can enter into a reaction with the active CH group in such compounds as malononitrile, cyanoacetic ester, etc. In this method the reactants are warmed together in tert-butanol with sodium tert-butoxide, whereby the 4H-dehydro-4-pyrans (53) are formed, which with acids are converted into pyrylium salts (54).

\[
\begin{align*}
\text{OCH}_3 & \quad \text{R'\text{CH}_2R''} \quad \text{base} \\
\text{H}_3\text{C} & \quad \text{R''C'\text{R'}} \\
\text{H}_3\text{C} & \quad + \text{HX} \\
\text{x} & \quad + \text{OH} \\
\end{align*}
\]

\((52)\) \rightarrow \((53)\) \rightarrow \((54)\)

\textit{4H-Pyrans Which Still Contain a Hydrogen Atom at C-4}

4H-Pyrans which still contain a hydrogen atom at C-4 are prepared from 2,6-disubstituted pyrylium salts by the addition of nucleophilic reagents. The readily accessible 2,6-diphenylpyrylium perchlorate (see Experimental Section) always reacts at C-4. Only its reaction with ammonia is an exception to this [see structure (1h)]. In the presence of potassium tert-butoxide the anions formed from acetylacetone, cyanoacetic acid, benzoyleaceton, and nitromethane, etc., react with (55) to form the 4H-pyrans (56a–d) \([57,58]\). With Grignard reagents in ethereal solution, the pyrylium salt (55) may be substituted with a variety of aliphatic and aromatic groups to give the 4H-pyrans (56e–h) in yields of up to 80\% \([59,60]\).

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{H}_3\text{C} \\
\text{O} & \quad \text{C}_6\text{H}_{5} \quad \text{C}_6\text{H}_{5} \\
\text{x} & \quad - \text{H}^\ominus \\
\end{align*}
\]

\((55)\) \rightarrow \((56)\) \rightarrow \((57)\)

\((a)\) \(R_4 = \text{CH(COCH}_3)_2\) \hspace{1cm} \((g)\) \(R_4 = \text{CH}_2\text{C}_6\text{H}_5\)  \\
\((b)\) \(R_4 = \text{CH(CN)(CO}_2\text{H}_3\) \hspace{1cm} \((h)\) \(R_4 = \text{C}_7\text{H}_{11}\)  \\
\((c)\) \(R_4 = \text{CH(COC}_2\text{H}_5)_2\) \hspace{1cm} \((i)\) \(R_4 = \text{C(CH}_3)_3\)  \\
\((d)\) \(R_4 = \text{CH}_2\text{NO}_2\) \hspace{1cm} \((j)\) \(R_4 = \text{C}_6\text{H}_5\)  \\
\((e)\) \(R_4 = \text{CH}_3\) \hspace{1cm} \((k)\) \(R_4 = \text{CH}_2\text{–CH(CH}_3)_2\) \text{ (only 57)}

Such 4H-pyrans are also obtained from 2,4,6-trisubstituted pyrylium salts (together with a mixture of dienones) by the addition of a hydride ion from sodium borohydride to the C-4 position \([61]\).

The nonsubstituted 4H-pyran (74) is itself a sensitive compound. It
was prepared by the reaction of glutaraldehyde with hydrogen chloride to form 2,6-dichlorotetrahydroxypryn which splits out two moles of hydrogen chloride; 2-chloro-3,4-dihydro-2H-pyran was an intermediate product [62]. By rapid experimental and distillation procedures the pure pyran is obtained in 40% yield [63]. The pyrolysis of 2-acetoxy-3,4-dihydro-2H-pyran has been shown by Masamune and Castellucci [64] to give the compound, but since it was produced in only small quantities and not actually isolated, the method is not a preparative one.

Substituted 4H-pyrans of the type (56) give a series of interesting reactions.

(1) With strong acids the R₄ substituent on C-4 is replaced when it is capable of forming an enolizable and mesomeric stabilized anion; this is the case of the compounds (56a–d). Simultaneously the 2,6-diphenylpyrylium salt is formed.

(2) When the substituent is tightly held, as in compounds (56e–j), the hydrogen atom at C-4 is split off and appears to be transferred to another molecule of the pyran, solvent, or cation, etc. Although the reaction is often successful with strong acids alone (e.g., with perchloric or fluoboric acids) it goes better in the presence of ferric chloride in glacial acetic acid. In this way numerous, otherwise difficultly accessible, 2,6-diphenylpyrylium salts substituted in the 4-position with alkyl or aryl substituents can be obtained; the yields can be as high as 70% [59, 60]. The unsubstituted pyrane (74), by triphenylcarboniumfluoborate, gives pyrylium fluoborate in a very convenient manner with a yield of 90% [27].

(3) Through the dehydrogenation of 4H-pyrans (58a–e), 4-dehydro-4H-pyrans (59a–e) can be obtained. The dehydrogenation can be carried out by shaking a benzene solution of the compound with alkaline ferricyanide, together with a 5–10% molar concentration of 2,4,6-triphenylphenol as a hydrogen carrier; the yields of product are on the order of 65–85% [59].
The yield of product is poor when potassium permanganate in cold N,N-dimethylformamide is used, a reagent described by Kröhnke [58] for similar dehydrogenations in the flavene series. Spontaneous dehydrogenation of (58b) occurs on crystallization of this compound from glacial acetic acid.

All 4-dehydro-4H-pyrans (59) form pyrylium salts (60) on treatment with acids; with bases the reverse reaction occurs and it is especially easy when R' and R'' are electron-withdrawing substituents. Numerous 4-alkylated-4H-pyrans and alkyl-substituted pyrylium salts can be formed in this way.

Instead of protons, carbonium ions may be added, but in this case the reaction is not reversible: 2,6-Diphenyl-4-isopropylidene-4H-pyran (61) gives 2,6-diphenyl-4-tert-butylpyrylium iodide (62) on heating with methyl iodide [62]. This pyrylium salt (62) is also accessible from (55) and (CH₃)₃CMgCl [65] (see reaction 56i → 57i).

The course of the reaction between 2,6-diphenyl-4-benzylidene-4H-pyran (63) and 2,6-diphenylpyrylium perchlorate (55) is very similar. In methylene chloride the pyran derivative (64) is smoothly formed and undergoes dehydrogenation to give the dipyrlycyanine dyestuff (65). The yield is better if chloranil is added as a dehydrogenation agent; the yields in these latter experiments are of the order of 75% [66]. Pyrylycyanines were first prepared by Wizinger and Riester [67].
By the hydrolysis of 4H-pyrans (e.g. 66a–o) with 25% hydrochloric acid, the heterocyclic ring is opened and 1,5-diketones (67a–d) are obtained [60,66]. It is noteworthy that with the nitromethyl compound (66a) the CH₂NO₂ group is not split off under these conditions.

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{H}_2\text{C} & \quad \text{O} \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5 \\
\end{align*}
\]

(a) R = CH₂NO₂  
(b) R = CH₃  
(c) R = CH(CH₃)₂  
(d) R = CH₂–C₆H₅

2,6-Diphenylpyrone is hydrolyzed, though in alkaline solution, to give 1,3-diphenylpentan-1,3,5-trione [68].

1,5-Diketones react with alcoholic ammonia or with ammonium acetate in glacial acetic acid to give pyridine derivatives by dehydrogenation or by splitting out of an appropriate substituent [69,70]. These reactions correspond to the usual synthesis employed for the preparation of pyridine derivatives, although generally the 1,5-dicarbonyl compounds are not isolated [66].

**4,4-Disubstituted 4H-Pyrans**

Through the addition of nucleophilic reagents to 2,4,6-trisubstituted pyrylium salts (68) [in addition to the 2,2-disubstituted 2H-pyrans (70) and their series of products] 4,4-disubstituted 4H-pyrans (69) are obtained.

\[
\begin{align*}
\text{R}_4 & \quad \text{X}^{-} \\
\text{R}_6 & \quad \text{R}_2 \\
\text{O} & \quad \text{R}_2 \\
\end{align*}
\]

(68)  

\[
\begin{align*}
\text{R}_4 & \quad \text{R} \\
\text{R}_6 & \quad \text{R}_2 \\
\text{O} & \quad \text{R}_2 \\
\end{align*}
\]

(69)  

\[
\begin{align*}
\text{R}_4 & \quad \text{R} \\
\text{R}_6 & \quad \text{R}_2 \\
\text{O} & \quad \text{R} \\
\end{align*}
\]

(70)

These reactions are dealt with more fully on pages 391 and 392.

Although these pyrans generally react differently from the mono-substituted 4H-pyran (66), they also are hydrolyzed to 1,5-diketones with aqueous alcoholic hydrochloric acid [69,66]. In this way 2,6-diphenyl-4-phenyl-4-benzyl-4H-pyran (69, R₂ = R₄ = R₆ = C₆H₅, R = CH₃–C₆H₅)
is smoothly converted into 3-benzyl-1,3,5-triphenylpentan-1,5-dione.

By the acid hydrolysis of the addition product formed from benzyl magnesium chloride and 2,4,6-trimethylpyrylium perchlorate (71), we obtained the doubly unsaturated ketone (72) but no 1,5-diketone [68]. The addition product of benzyl magnesium chloride and 2,4-diphenyl-6-tert-butylpyrylium perchlorate behaved similarly; on reaction with an ethereal solution of hydrogen chloride it gave the pyrylium salt (2,4-diphenyl-6-tert-butylpyrylium chloride) together with 10% of an unsaturated ketone [65]. By the careful reaction of Grignard compounds such as phenyl magnesium bromide with 2,4,6-trimethyl and other aliphatically substituted pyrylium salts (71), Köbrich [71] isolated compounds of the type (73) which he considered were valence tautomers of the unsaturated ketones of type (72).

From the final products obtained in these experiments it is not possible to say with certainty whether the initial product is a 2H- or a 4H-pyran or an unsaturated ketone of the type (72), since it is not inconceivable that during the course of the reaction, hydrolysis followed by rearrangement occurs. The situation is similar to the reaction products of Grignard compounds with 2-pyrones according to Gompper [72].

The reactions of 4-mono- and disubstituted 4H-pyrans with dihalogenocarbenes by the addition of CCl₂ or CBr₂ to the double bond are now considered. The 4H-pyran (74) adds one molecule of the dihalogenocarbene to give (75) and with an excess of the dichlorocarbene two CCl₂ radicals add to give (76). In addition, compound (77) is formed through
an insertion mechanism from compound (74). By careful thermal catalytic dehydrohalogenation of (77) instead of the rather unstable chloroxepin (78) 4-chloromethylenepyran was formed [73].

\[
\begin{align*}
(75) & \quad + \quad (76) \quad + \quad (77) \\
\text{H\textsubscript{2}C\textsubscript{Cl}2} & \quad \text{CCl}_2 & \quad \text{HCHCl}_2 \\
(74) & \quad (78)
\end{align*}
\]

**Pyridine Derivatives from 4H-Pyrans**

4-Dehydro-4H-pyrans (79) react with primary amines to form N-alkyl-4-methylenedihydropyridine derivatives (80).

\[
\begin{align*}
(79) & \quad \xrightarrow{\text{H}_2\text{N}-\text{R}_1} \quad (80) \\
\text{R'} \quad \text{or} \quad \text{R''} & = \text{CN, COR, CO}_2\text{R, NO}_2, \text{etc.} \\
\text{R}_2 & = \text{R}_0 = \text{C}_6\text{H}_5 \text{ or } \text{CH}_3 \\
\text{R}_1 & = \text{alkyl, aryl, NH}_2, \text{and H}
\end{align*}
\]

This reaction to prepare 4-alkylidene-1,4-dihydropyridine derivatives was discovered at almost the same time by Wolf [59], Kato and his co-workers [74], and Eiden [49]. It is of importance since, in contrast to 4-pyrones, 4-pyridones fail to condense with compounds which contain an acidic CH group. Reactions take place with aliphatic and aromatic primary amines and also with hydrazine or with formamide: in the last case the reaction gives the pyridine derivative (82) and not the N-substituted pyridinium salt.
For all these reactions the 4-dehydro-4H-pyrans (79) have to be substituted with electron-withdrawing groups (R' and R''); alkyl-substituted compounds on treatment with primary amines remain unchanged. The reactions of 4H-pyrans which still have one or two hydrogens present at C-4 do not seem to have been investigated. Although it has yet to be proved it seems possible that the heterocyclic ring is also formed by the reaction of the amines either with a 1,5-diketone (67) or with a doubly unsaturated ketone of type (72).

**Thiopyrans**

The 4H-thiopyran which is obtained by the action of H₂S and HCl on glutaraldehyde in methylene chloride seem considerably more stable than the 4H-pyran. 4H- and 2H-thiopyrans also are formed by the action of Grignard reagents on thiopyrylium salts [75]; in these reactions it is difficult to predict whether the addition will take place at C-2 or C-4.

**Derivatives of Furfurans**

Dilthey [76] observed that 2,3,4,6-tetraphenylpyrylium perbromide (83) gave 2,3,4-triphenyl-5-benzoylfuran on hydrolysis and that this compound formed 2,3,4-triphenylfuran (84) in the presence of alkali. The course of the reaction can be illustrated as follows:
In a similar way, pentaphenylpyrylium salt with alkali gives, by way of the pseudobase or similar products, tetraphenylfuran [77].

According to Balaban and Nenitzescu [78] alkyl-substituted pyrylium salts form furan derivatives on reaction with hydrogen peroxide. The reaction is assumed by them to take place by the following path*:

\[
\begin{align*}
\text{R}_4 & \quad \text{R}_4 \\
\begin{array}{c}
\text{Furane} \\
\text{Pseudobase}
\end{array}
\end{align*}
\]

Examples of Furans (86)

<table>
<thead>
<tr>
<th>R₂ = R₅</th>
<th>R₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) CH₃</td>
<td>CH₃</td>
</tr>
<tr>
<td>(b) CH₃</td>
<td>C₂H₅</td>
</tr>
<tr>
<td>(c) C₂H₅</td>
<td>CH₃</td>
</tr>
<tr>
<td>(d) CH₃</td>
<td>CH(CH₃)₂</td>
</tr>
<tr>
<td>(e) CH(CH₃)₂</td>
<td>CH₃</td>
</tr>
</tbody>
</table>

The reaction takes place with pyrylium salts having different groups present (85a–e); with (85a) the yield is approximately 45%. In the light of these investigations the reactions of aryl-substituted pyrylium salts which Dilthey [79] has described may well stand further examination.

Pyrones can also be converted into furan derivatives. The investigations by F. Feist [80] of the conversion of bromocoumalic acid (87) into furan-2,4-dicarboxylic acid (88) by alkali have long been known.

* A further possible mechanism is discussed on pages 404 and 405.
In a similar manner the rearrangement of a C-5-substituted 4,6-diphenyl-2-pyrone (89) with bromine and alcoholic alkali gives a 4-substituted 3,5-diphenylfuran carboxylic acid (90) [81].

The thermal rearrangement of 3,4,5,6-tetrachloro-2H-pyrone into 3,4,5-trichlorofuran-1-carboxylic acid chloride [82] has been described by Roedig and Märkl [83].

Also of interest in this connection is the photochemical conversion, in quite dilute solution (0.02% aqueous solution), of 2,6-dimethyl-4H-pyran (91) into both the four-membered ring dimer and 2,3-dimethylfuran-5-aldehyde (92) in a 1% yield [84].

The reverse reaction in which furan-2-acyl derivatives are converted into pyridine derivatives is also known. An example of this is the con-
version of 2,4-dimethyl-5-acetylfuran (93, R=CH₃), with aqueous ammonia at 180°C in an autoclave, into 2,4,6-trimethyl-3-hydroxypyridine [85] (94, R=CH₃); the yield for the reaction is 75%.

**Conversion of Pyrylium Salts into Benzene Derivatives**

**Phenols**

2,4,6-Trisubstituted pyrylium salts containing a methyl group in the 2- or 4-positions yield 3,5-substituted phenols on boiling with 10% sodium hydroxide solution. The reaction was discovered by Baeyer and Piccard [2], who obtained sym-xylenol (98a) from 2,4,6-trimethylpyrylium perchlorate (95a). The pseudobase (96) may be formed first, and undergoes an irreversible phenol ring closure via the tautomeric ketone (97) to give (98). 2,6-Dimethyl-4-phenylpyrylium perchlorate (95b) yields 3-methyl-5-phenylphenol (98b); the 2,6-dimethyl-4-ethylpyrylium salt gives 3-methyl-5-ethylphenol, and so on. 2,6-Diethyl-4-methylpyrylium perchlorate yields 2,5-dimethyl-3-ethylphenol [16].

\[
\begin{align*}
\text{(95)} & \quad \xrightarrow{\text{NaOH}} \quad \text{(96)} \\
\text{(98a)} & \quad \xrightarrow{\downarrow} \quad \xrightarrow{\uparrow} \quad \text{(98b)} \\
\text{(96)} & \quad \xrightarrow{\downarrow} \quad \xrightarrow{\uparrow} \quad \text{(97)}
\end{align*}
\]

(a) \( R_4 = R_6 = \text{CH}_3 \)
(b) \( R_4 = \text{C}_6\text{H}_5; \quad R_6 = \text{CH}_3 \)

This reaction is of interest in relation to the synthesis of \( m \) - and higher substituted phenols. Pyrylium salts with a phenyl group in the 6-position however, cannot be converted into phenyl-substituted phenols in this manner; they decompose in aqueous alkali and the benzoic acid fragment is eliminated [16].
AROMATIC COMPOUNDS FROM PYRYLIUM SALTS

Alkylated Amines

Diels and Alder [86] allowed an ethereal solution of secondary amines such as dimethylamine or piperidine to react in the cold with an ethereal suspension of 2,4,6-trimethylpyrylium perchlorate (95a) and other 2-methyl-substituted pyrylium salts (95c and d). A vigorous reaction ensues, and N-dimethyl-sym-m-xylidine (100a) and other m-substituted N-dimethyl- or N-pentamethyleneanilines (100c and d) are obtained via intermediates, (99), which are not isolated. The yields amount to approximately 65%. Scarcely any attention has thus far been paid to this reaction, though it may be of considerable interest with respect to the synthesis of certain aromatic tertiary amines.

Nitro Compounds

A reaction capable of widespread application was discovered in our laboratory in 1956 by Bräuniger and Neubauer [87]; it consists in the conversion of 2,4,6-trisubstituted pyrylium salts (101) into 2,4,6-trisubstituted nitrobenzene derivatives (102) by the action of nitromethane in the presence of alkoxide, and gives yields of 45–90%. The simplest procedure consists in suspending the pyrylium salt together with 1 mole of nitromethane in tert-butanol, adding 2 equivalents of potassium tert-butoxide, and warming for some time.
TABLE 1  
NITRO COMPOUNDS (104) FROM PYRYLIUM SALTS (103)

<table>
<thead>
<tr>
<th>R_2</th>
<th>R_3</th>
<th>R_4</th>
<th>M.p. (°C)</th>
<th>M.p. (°C)</th>
<th>Yield (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH_3</td>
<td>H</td>
<td>CH_3</td>
<td>242 (dec.)</td>
<td>41-42</td>
<td>72</td>
<td>[87]</td>
</tr>
<tr>
<td>CH_3</td>
<td>H</td>
<td>C_6H_5</td>
<td>175^a</td>
<td>96-97</td>
<td>48</td>
<td>[87]</td>
</tr>
<tr>
<td>C(CH_3)_2</td>
<td>H</td>
<td>C_6H_5</td>
<td>253-256</td>
<td>96-97</td>
<td>44</td>
<td>[87]</td>
</tr>
<tr>
<td>C_6H_5</td>
<td>H</td>
<td>C_6H_5</td>
<td>214-215</td>
<td>144-145</td>
<td>85</td>
<td>[87]</td>
</tr>
<tr>
<td>CH(CH_3)_2</td>
<td>H</td>
<td>C_6H_5</td>
<td>247-257^c</td>
<td>91.5-92</td>
<td>57</td>
<td>[60]</td>
</tr>
<tr>
<td>C_6H_6</td>
<td>H</td>
<td>CH_2—CH(CH_3)_2</td>
<td>204-206^c</td>
<td>126-127</td>
<td>38</td>
<td>[60]</td>
</tr>
<tr>
<td>C_6H_6</td>
<td>H</td>
<td>C(CH_3)_2</td>
<td>231-234^e</td>
<td>190-191</td>
<td>87</td>
<td>[65]</td>
</tr>
<tr>
<td>C_6H_6</td>
<td>H</td>
<td>C_6H_11</td>
<td>219-223^a</td>
<td>202-204</td>
<td>25</td>
<td>[60]</td>
</tr>
<tr>
<td>C_6H_6</td>
<td>H</td>
<td>R^b</td>
<td>298-302^c</td>
<td>222-225</td>
<td>73</td>
<td>[66]</td>
</tr>
<tr>
<td>C_6H_6</td>
<td>H</td>
<td>C_6H_6NO_2(4)</td>
<td>296-298^c</td>
<td>166-167</td>
<td>55</td>
<td>[60]</td>
</tr>
<tr>
<td>C_6H_6</td>
<td>H</td>
<td>C_6H_5</td>
<td>C_6H_6CH_6(4)</td>
<td>215-218</td>
<td>126-127</td>
<td>58</td>
</tr>
<tr>
<td>C_6H_6CH_6(4)</td>
<td>H</td>
<td>C_6H_5</td>
<td>C_6H_6CH_6(4)</td>
<td>228-233</td>
<td>140-141.5</td>
<td>56</td>
</tr>
<tr>
<td>C_6H_6Cl(4)</td>
<td>H</td>
<td>C_6H_5</td>
<td>C_6H_6Cl(4)</td>
<td>219-221</td>
<td>164-164.5</td>
<td>72</td>
</tr>
<tr>
<td>C_6H_6Br(4)</td>
<td>H</td>
<td>C_6H_5</td>
<td>C_6H_6Br(4)</td>
<td>220-225</td>
<td>157-157.5</td>
<td>64</td>
</tr>
<tr>
<td>C_6H_6Br(3)</td>
<td>H</td>
<td>C_6H_5</td>
<td>C_6H_6Br(3)</td>
<td>211-226</td>
<td>136-137</td>
<td>80</td>
</tr>
<tr>
<td>C_6H_6Br(2)</td>
<td>H</td>
<td>C_6H_5</td>
<td>C_6H_6</td>
<td>190-195</td>
<td>110-112(82)</td>
<td>—</td>
</tr>
<tr>
<td>Compound</td>
<td>Functional Group</td>
<td>Additional Info</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>----------</td>
<td>-----------------</td>
<td>-----------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C₆H₆</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C₆H₅</td>
<td>H</td>
<td>C₆H₅Br(4)</td>
<td>H</td>
<td>C₆H₃</td>
<td>270-275</td>
<td>142</td>
</tr>
<tr>
<td>C₆H₅</td>
<td>H</td>
<td>C₆H₅Br(3)</td>
<td>H</td>
<td>C₆H₅</td>
<td>205-217</td>
<td>155-156</td>
</tr>
<tr>
<td>C₆H₆</td>
<td>H</td>
<td>C₆H₅Br(2)</td>
<td>H</td>
<td>C₆H₅</td>
<td>182-208</td>
<td>243-243.5</td>
</tr>
<tr>
<td>C₂H₄Cl(4)</td>
<td>H</td>
<td>C₂H₄Cl(4)</td>
<td>H</td>
<td>C₂H₄Cl(4)</td>
<td>257-275</td>
<td>179</td>
</tr>
<tr>
<td>C₂H₄CH₃(4)</td>
<td>H</td>
<td>C₂H₄CH₃(4)</td>
<td>H</td>
<td>C₂H₄CH₃(4)</td>
<td>~200</td>
<td>136-138</td>
</tr>
<tr>
<td>C₂H₄Cl(4)</td>
<td>H</td>
<td>C₂H₄Cl(4)</td>
<td>H</td>
<td>C₂H₄Cl(4)</td>
<td>190-210</td>
<td>205-207</td>
</tr>
<tr>
<td>C₂H₅</td>
<td>H</td>
<td>C₂H₅OCH₂(4)</td>
<td>H</td>
<td>C₂H₅</td>
<td>235-236</td>
<td>120-122</td>
</tr>
<tr>
<td>C₂H₅</td>
<td>H</td>
<td>C₂H₅N(CH₃)₂(4)</td>
<td>H</td>
<td>C₂H₅</td>
<td>Over 300°</td>
<td>160-161</td>
</tr>
<tr>
<td>C₂H₅OCH₂(4)</td>
<td>H</td>
<td>C₂H₅OCH₂(4)</td>
<td>H</td>
<td>C₂H₅</td>
<td>207-209</td>
<td>119-120</td>
</tr>
<tr>
<td>C₂H₅OCH₂(4)</td>
<td>H</td>
<td>C₂H₅OCH₂(4)</td>
<td>H</td>
<td>C₂H₅</td>
<td>243-245</td>
<td>115-116</td>
</tr>
<tr>
<td>C₂H₅OCH₃(4)</td>
<td>H</td>
<td>C₂H₅OCH₃(4)</td>
<td>H</td>
<td>C₂H₅OCH₃(4)</td>
<td>262-263</td>
<td>150</td>
</tr>
<tr>
<td>C₂H₅OCH₄(4)</td>
<td>H</td>
<td>C₂H₅OCH₄(4)</td>
<td>H</td>
<td>C₂H₅OCH₄(4)</td>
<td>303-305</td>
<td>124-126</td>
</tr>
<tr>
<td>CH₃</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>CH₃</td>
<td>217-220&lt;sup&gt;c&lt;/sup&gt;</td>
<td>49</td>
</tr>
<tr>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>H</td>
<td>C₆H₅</td>
<td>230-233</td>
<td>221</td>
</tr>
<tr>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>278-281</td>
<td>292</td>
</tr>
<tr>
<td>C₆H₅</td>
<td>H</td>
<td>C₆H₅</td>
<td>CH₂—CH₂</td>
<td>CH₂—CH₂</td>
<td>207-208</td>
<td>165</td>
</tr>
<tr>
<td>CH₄</td>
<td>H</td>
<td>OCH₃</td>
<td>H</td>
<td>CH₄</td>
<td>195-196&lt;sup&gt;c&lt;/sup&gt;</td>
<td>50</td>
</tr>
<tr>
<td>CH₃</td>
<td>H</td>
<td>SCH₃</td>
<td>H</td>
<td>CH₃</td>
<td>174-175&lt;sup&gt;c&lt;/sup&gt;</td>
<td>62</td>
</tr>
<tr>
<td>C₆H₅—C₆H₄</td>
<td>H</td>
<td>C₆H₅</td>
<td>H</td>
<td>C₆H₅</td>
<td>225-238</td>
<td>189-190</td>
</tr>
<tr>
<td>C₆H₅—C₆H₄</td>
<td>H</td>
<td>C₆H₅</td>
<td>H</td>
<td>C₆H₅—C₆H₄</td>
<td>240-252</td>
<td>264-265</td>
</tr>
<tr>
<td>C₆H₅—C₆H₄</td>
<td>H</td>
<td>C₆H₅</td>
<td>H</td>
<td>C₆H₅—C₆H₄</td>
<td>175-190</td>
<td>138-140</td>
</tr>
<tr>
<td>α-C₆H₅H₇</td>
<td>H</td>
<td>C₆H₆</td>
<td>H</td>
<td>C₆H₆</td>
<td>215-234</td>
<td>164-165</td>
</tr>
<tr>
<td>C₆H₆</td>
<td>H</td>
<td>C₆H₆(NO₂)</td>
<td>H</td>
<td>C₆H₆</td>
<td>—</td>
<td>342-344</td>
</tr>
</tbody>
</table>

<sup>a</sup>Pyrilium chloroferrate

<sup>b</sup>R = C(C₆H₅)=O

<sup>c</sup>Pyrilium perchlorate
Both alkyl- and aryl-substituted pyrylium salts can successfully be subjected to this reaction; the latter can also be extended to pyrylium salts with other substituents, as illustrated by the facile preparation of 2,6-dimethyl-4-methoxynitrobenzene from 2,6-dimethyl-4-methoxypyrylium perchlorate and nitromethane [88]. 4-Thioalkyl-substituted pyrylium salts also undergo this reaction [48]. More highly substituted nitro compounds can, of course, also be obtained by this reaction. A selection of nitro compounds which we have prepared is given in Table 1.

The dipyrylium salt [22] reacts twice with nitromethane to give 4,4"-dinitro-3,5,3",5"-tetraphenyl-1,1',4',1"'-terphenyl [95].

As in their failure to react with ammonia to give quinolines, chromylium salts also fail to react with nitromethane.

Isochromylium salts, e.g. 1,3-dimethyl- or 1,3-diphenylisochromylium fluoborate could not be converted into 2-nitronaphthalene derivatives in this manner, even though they readily give isoquinoline derivatives with ammonia and amines [8]. The conversion of 2,4-diphenyl-5,6,7,8-tetrahydrochromylium fluoborate (105) into 1-nitro-2,4-diphenyltetrahydro-1-naphthylamine, dehydrogenated to give 2,4-diphenyl-1-naphthylamine (107), and converted into 2,4-diphenyl-1-naphthol [8].
The condensation of nitromethane and 2,6-diphenyl-4-methylpyrylium fluoborate (108) [60] fails to give the nitro compound (111) as was thought [87] at first and instead the 4-pyran (109) is obtained exclusively. It seems probable that the influence of the small methyl group favors the addition on C-4 so strongly that no addition at C-2 takes place. The subsequent reaction to give the 2-pyran (110) and the final formation of the aromatic nitrocompounds, therefore, is not possible.

That the reaction does not occur for steric reasons has been proved by the reaction of 2,4-diphenyl-6-tert-butylpyrylium salt with nitromethane to give 2,4-diphenyl-6-tert-butylnitrobenzene [60]. Further evidence is supplied by the fact that 2,6-diphenyl-4-isobutylpyrylium fluoborate with nitromethane and tert-butoxide is smoothly converted into 2,6-diphenyl-4-isobutynitrobenzene [60].

Pyrylium salts which have a hydrogen atom in the α-position on C-4 to the pyrylium ring which is capable of being split out as a proton, do not react with nitromethane to give aromatic compounds since the removal of the hydrogen atom to give 4-dehydro-4H-pyrans as a concurrent reaction proceeds much faster. The compounds (60a–c), (60d), and also (60e) failed to give nitrobenzene derivatives but formed instead their respective 4-dehydro-4H-pyrans (59).

2,6-Diphenyl-4-cyclohexylpyrylium fluoborate (112) reacts in two different directions. In addition to the formation of alkylidenpyran (113),
2,6-diphenyl-4-cyclohexylnitrobenzene (114) in a 25% yield is also formed. This evidently is favored because of the greater steric hindrance of the cyclohexyl portion opposite the isopropyl group in (60e).

![Diagram](image.png)

The condensation reaction compared with the addition reaction is favored by working at a higher temperature and by the addition of the pyrylium salt to a preformed mixture of nitromethane and potassium tert-butoxide (see the Experimental section).

Finally the nitromethane condensation with 2,6-disubstituted pyrylium salts such as (55) also failed to work. Here, the 4-addition compound (56d) was formed exclusively; this was dehydrogenated with triphenylphenol to give the alkylidene pyran (59c) [59] (see page 383), but could not be transformed to the aromatic nitro compound. With methylamine (59c) condenses without difficulty to give N-methyl-4-nitromethylene-1,4-dihydropyridine (80, R = H, R'' = NO₂, R₂ = R₆ = C₆H₅, R₁ = CH₃) [59].

Since aromatic nitro compounds are key substances for numerous other aromatic compounds (amines, phenols, halides, nitriles, etc.), this reaction offers very many preparative possibilities [96]. Moreover, starting from the pyrylium salt, it proceeds unambiguously, so that it is eminently suitable for structure determinations. This is of particular importance in the case of aryl-substituted derivatives of benzene, since these give no useful data with regard to structure by degradative methods. The synthesis of all seven isomeric monobrominated 2,4,6-triphenylnitrobenzenes (or phenols) becomes simple with the aid of the pyrylium salt/nitromethane method; the course of the reaction between triphenylphenoxy and bromine, for example, could thus rapidly be elucidated [91].

The synthesis of the nitro compounds from pyrylium compounds could also be used to elucidate the substitution of the nitrobenzoic acids [97]. 2,4,6-Triphenylnitrobenzene (115) is oxidized to 3,5-diphenyl-4-nitrobenzoic acid (116) which can also be prepared from 2,6-diphenyl-4-cyclohexyl- (or 4-isobutyl-) nitrobenzene (117) by oxidation.
AROMATIC COMPOUNDS FROM PYRYLIUM SALTS

A synthesis of phenyl-substituted nitrobenzoic acids of definite constitution is also possible by the following route. The pyrylium salts are prepared with anisyl (instead of phenyl) groups (e.g., 119) and converted into the corresponding nitrobenzene derivatives which are then oxidized with chromic oxide in glacial acetic acid. The anisyl groups are in this way, preferential to the phenyl groups, oxidized to carboxylic acid groups.

By this route 3,5-diphenyl-4-nitrobenzoic acid (116) has been prepared from 4-anisyl-2,6-diphenylnitrobenzene (118), and 3,5-diphenyl-2-nitrobenzoic acid (121) from 2-anisyl-4,6-diphenylnitrobenzene (120) [97].

KETONES, CARBOXYLIC ACIDS, NITRILES

It was found in the case of 2,4,6-triphenylpyrylium fluoborate (122) that the pyrylium salt will also react with other compounds containing
an active methylene group, e.g. acetoacetic ester, acetylacetone, or cyanoacetic ester, in the presence of 2 moles of tert-butoxide \[\text{[98]}\]. Elimination of the acetyl group

\[
\begin{align*}
\text{CH}_3\text{CO-CH}_2\text{CO}_2R + 2 \text{(OR)} \rightarrow \\
\text{H}_5\text{C}_6\text{C}_6\text{H}_3\text{CO}_2R
\end{align*}
\]

(123)

in the first two cases and the carboxyl group in the last results in the formation of 2,4,6-triphenylbenzoic ester (123), 2,4,6-triphenylacetophenone (124), and 2,4,6-triphenylbenzonitrile (125), respectively.

If the pyrylium salt (122) is allowed to react with acetyl acetone in the presence of only 1 mole of potassium tert-butoxide, then the primary addition product in the form of lemon-yellow crystals is isolated \[\text{[65]}\]. Its constitution is either that of a 2-pyran (126) or the isomeric ketone (127). With a hot potassium hydroxide solution it gives a 70% yield of red 2,4,6-triphenylacetophenone (124). The addition product of acetylacetone and 2,3,4,5,6-pentaphenylpyrylium perchlorate behaves similarly

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CO-CH}_2\text{CO}_2R + 2 \text{(OR)} \rightarrow \\
\text{H}_5\text{C}_6\text{C}_6\text{H}_3\text{COCH}_3
\end{align*}
\]

(124)

\[
\begin{align*}
\text{NC-CH}_2\text{CO}_2R + 2 \text{(OR)} \rightarrow \\
\text{H}_5\text{C}_6\text{C}_6\text{H}_3\text{CN}
\end{align*}
\]

(125)
and on heating with aqueous alcoholic base gives pentaphenylacetophene in 63% yield. It is noteworthy that the addition product of acetylacetone and 2-tert-butyl-4,6-diphenylpyrylium fluoborate, which is an analog of (126) or (127), splits out both acetyl substituents with base and gives an 82% yield of a hydrocarbon, C_{22}H_{22}, 2-tert-butyl-4,6-diphenylbenzene (128) [65].

The degree to which this reaction can be applied to other pyrylium salts, and the extent to which other compounds with active methylene groups are usable have thus far not been systematically investigated.* But since 2,4,6-triphenylpyrylium salts by no means represent the most reactive pyrylium salts, it is not improbable that a large number of alkyl- and aryl-substituted pyrylium salts will react with similar success. Isochromylium salts react just as poorly as with nitromethane.

**Phenolic Acids**

The reaction between 2,4,6-triphenylpyrylium fluoborate (122) and diethyl malonate in the presence of tert-butoxide proceeds quite differently from its reaction with the active methylene groups of the compounds mentioned above: Condensation to a phenolic ester, namely 2-hydroxy-3-carbethoxy-4,6-diphenylbenzophenone (130), takes place without elimination of a carboxyl group. Compound (129) may be an intermediate product [99]. The degree to which this reaction may be extended to other pyrylium salts has not yet been investigated.

The reaction of 2,4,6-triphenylpyrylium fluoborate (131) and diethylacetonedicarboxylate in the presence of potassium tert-butoxide gives a

*Recently, we found that 2,4,6-triphenylpyrylium fluoborate and phenylnitromethane give an addition product which rearranges by heating to 1,2,3,5-tetraphenylnitrobenzene and in the presence of alkali to 2,3,4,6-tetraphenylphenol [100].
58% yield of the initial addition product [2H-pyran (132) or isomeric ketone] as yellow crystals [100]. With a further mole of the alcoholate the compound splits out the malonic ester and gives ethyl-2,4,6-triphenylbenzoate (123). A higher membered ring compound is not isolated.

\[
\begin{align*}
\text{\begin{align*}
\text{H}_5\text{C}_6 & \text{BF}_4^- \quad + \quad \text{CH}_2-\text{CO}_2\text{C}_2\text{H}_5 \\
\end{align*}}
\end{align*}
\]

\[\text{KOBu-}t \rightarrow \]

\[
\begin{align*}
\text{\begin{align*}
\text{H}_5\text{C}_6 & \quad \text{C}_6\text{H}_5 \\
\text{CO}_2\text{C}_2\text{H}_5 & \quad \text{CO} \\
\end{align*}}
\end{align*}
\]

\[\text{(131)} \quad \text{(132)} \quad \text{(123)}\]

**Aminonitriles**

The reaction between 2,4,6-triphenylpyrylium fluoborate (131) and malononitrile proceeds in similar manner to that with malonic ester. No elimination of the fragment containing the active methylene group occurs in this instance either. The aromatic ring is formed by incorporation of two C atoms of the active methylene-containing reagent, without participation of the C-6 or C-2 atom of the pyrylium salt. 2-Amino-3-cyano-4,6-diphenylbenzophenone (133) is formed in yields exceeding 75% [99]. Nor has it thus far been investigated whether alkyl-substituted pyrylium salts will undergo this reaction sequence.

\[
\begin{align*}
\text{\begin{align*}
\text{H}_5\text{C}_6 & \text{BF}_4^- \quad + \quad \text{CH}_2\text{(CN)}_2 \quad K\text{OBu-}t \\
\end{align*}}
\end{align*}
\]

\[\text{(131)} \quad \text{(133)}\]
**HYDROCARBONS**

![Chemical structure](image)

**Derivatives of Benzene**

Derivatives of 2H-pyran (134) which have in the 2-position a methyl group or a reactive methylene group can, under the influence of basic reagents, form benzene derivatives (135); the reaction is analogous to the Baeyer phenol synthesis described above.

There are more possibilities for carrying out this reaction, depending upon the way the 2H-pyran derivatives (134) are formed; it is not necessary in every case to isolate the 2H-pyran. Gompper and Christmann [72,101] used 2-pyrones as the starting materials. If the 2-pyrone is allowed to drop into an excess of Grignard reagent, the aromatic hydrocarbon is formed in one step. The assumption is that either the 2-pyrone or the Grignard reagent used in the reaction contains a methyl group necessary for the formation of the aromatic ring. Thus 3,5-di-phenyltoluene (137) is obtained from either 2,4-dimethyl-6-pyrone (136a) with 2 moles of phenyl magnesium bromide, or in a similar fashion from 2,4-diphenyl-6-pyrone (136b) with 2 moles of methyl magnesium iodide.

![Chemical reactions](image)

In a similar way trimethylpyrylium perchlorate (138) can react with Grignard reagents or compounds with an acidic CH in the presence of triethylamine to give derivatives of 3,5-dimethylbenzene (140a–c) [72]; the yields for the reaction vary between 27 and 81%.

Köbrich [71] successfully isolated an intermediate product for the reaction which he considered to be the doubly unsaturated ketone (139a); it cannot be ruled out that the compound was a 2H-pyran of the structure (139b).
This reaction has a close similarity to the one used by Dimroth and Neubauer [98] for the preparation of hydrocarbons from 2,4,6-triphenylpyrylium perchlorate (141) and benzyl lithium or benzyl magnesium chloride.
AROMATIC COMPOUNDS FROM PYRYLIUM SALTS

chloride. Here a crystalline addition product of the 4,4-disubstituted 4H-pyran was formed (142) [102]. On heating this compound with calcium oxide, or better, with sodium diethylene glycolate at 240°C, 1,2,3,5-tetraphenylbenzene (144) was obtained in 50% yield; the 2H-pyran (143) must be formed in an intermediate step.

It is possible, by the irradiation of the 4H-pyran (142), to isolate the intermediate 2H-pyran (143) [102]. This compound is converted with extreme ease into the hydrocarbon (144) either with base or weak acid.

The reaction of 2,3,4,5,6-pentaphenylpyrylium fluoborate with benzyl magnesium chloride gives the 2H-pyran and not the 4H compound. This compound cleaves at once to give the unsaturated ketone (145), which upon heating with sodium diethylene glycolate, gives the hexaphenylbenzene (146) by ring closure.

\[
\text{C}_6\text{H}_5\text{OCH}_2\text{C}_6\text{H}_5\quad \text{C}_6\text{H}_5\text{CH}_2\text{C}_6\text{H}_5
\]

The synthesis is only successful if the 2H-pyran is formed, directly or as an intermediate product, by an allylic rearrangement from the 4H-pyran.

The 4,4-disubstituted 4H-pyrans of the type (142) are easily distinguished from the 2H-pyrans of the type (143) by their physical and chemical properties. The 4H-pyrans absorb at 248 m\(\mu\) (see also reference [72]). With dilute acids they form diketones, but with strong acids naphthalene derivatives (see next section). The 2H-pyran (143), on the other hand, is a yellow crystalline compound which absorbs at 335 m\(\mu\), and with dilute acids in ethanol gives a quantitative yield of 1,2,3,5-tetraphenylbenzene [102]. The deep yellow color of the acidic solution formed is probably due to the valence tautomerism of 1,3,5,6-tetraphenylhexa-2,4-dien-1-one.

A further hydrocarbon synthesis of a different type has been described by Märkl [103] and other workers [66, 104]. In this synthesis, methylene triphenylphosphorane reacts with the pyrylium salt to give the benzene derivative (149) in generally good yield. In some cases the intermediate product (148) was isolated by Märkl. Since the reaction could not be applied to alkoxymethylene triphenylphosphorane, phenol
ethers could not be prepared and the reaction has not been followed further. The formation of azulenes, on the other hand, is interesting and is described in a later section (p. 397).

**Derivatives of the Naphthalenes and Phenanthrenes**

Tetrasubstituted 4H-pyrans of the type (150) with a benzyl or an α-methylnaphthyl group at C-4 undergo a surprisingly smooth reaction with 70% perchloric acid to give naphthalene or phenanthrene derivatives (151) [105] in 80-90% yields. At the same time 1 mole of methyl ketone is split out.

The 4H-pyrans are easily accessible from 2,4,6-trisubstituted pyrylium perchlorates and benzyl- or α-methylnaphthyl magnesium chloride, and give yields of product in the region of 50-70% (see Table 2).

The naphthalene system can only be formed from the 4H-pyrans. It can be concluded from this that the pyran (150c) gives 1-methyl-3-phenynaphthalene (151c) and not the 1-phenyl-3-methylnaphthalene (154) expected from the 2H-pyrans (153) [102].
TABLE 2
4,4-Disubstituted 4H-Pyrans (152) from 2,4,6-Trisubstituted Pyrylium Salts

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₄'</th>
<th>R₄</th>
<th>M.p. (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃</td>
<td>H</td>
<td>CH₃</td>
<td>CH₂C₆H₅</td>
<td>H</td>
<td>130-131/11</td>
<td>78</td>
</tr>
<tr>
<td>CH₃</td>
<td>CH₃</td>
<td>CH₃</td>
<td>CH₂C₆H₅</td>
<td>CH₃</td>
<td>95-97/11</td>
<td>72</td>
</tr>
<tr>
<td>CH₃</td>
<td>H</td>
<td>C₆H₅</td>
<td>CH₂C₆H₅</td>
<td>H</td>
<td>120/3</td>
<td>61</td>
</tr>
<tr>
<td>C₆H₄</td>
<td>H</td>
<td>C₆H₅</td>
<td>CH₂C₆H₅</td>
<td>H</td>
<td>143-144</td>
<td>70</td>
</tr>
<tr>
<td>C₆H₄</td>
<td>H</td>
<td>C₆H₅</td>
<td>CH₂C₆H₂OCH₃(4)</td>
<td>H</td>
<td>140-141</td>
<td>72</td>
</tr>
<tr>
<td>C₆H₄-C₆H₂(4)</td>
<td>H</td>
<td>C₆H₂OCH₂(4)</td>
<td>CH₂C₆H₅</td>
<td>H</td>
<td>123-124</td>
<td>51</td>
</tr>
<tr>
<td>C₆H₆</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>CH₂C₆H₄</td>
<td>H</td>
<td>149-150</td>
<td>54</td>
</tr>
<tr>
<td>C₆H₄</td>
<td>H</td>
<td>C₆H₅</td>
<td>α-CH₂C₆H₅</td>
<td>H</td>
<td>146-147</td>
<td>57</td>
</tr>
<tr>
<td>C₆H₆</td>
<td>H</td>
<td>C₆H₅</td>
<td>α-CH₂C₆H₅</td>
<td>H</td>
<td>169-170</td>
<td>68</td>
</tr>
</tbody>
</table>

* Taken from [105].
Moreover, the 2H-pyrans, which can be obtained from the 4H-pyrans by UV irradiation, fail to form naphthalenes but give hydrocarbons of the type (135) in the presence of acids and bases [102]. If the 4H-pyran (150) contains dissimilar substituents in the 2- and 6-positions, one of the substituents can be exclusively split out. This is the case with the pyran (150d), when only 1,3-diphenylnaphthalene and no 1-tert-butyl-3-phenylnaphthalene is obtained as a product. The tert-butyl residue is removed as methyl tert-butyl ketone, and not the phenyl group as aceto-phenone.

Substituents at C-4 in ring A of the Grignard reagent are present at C-7 in the naphthalene ring after ring closure. From α-naphthylmethyl magnesium chloride and triphenylpyrylium perchlorate the pyran (155) is formed, from which 1,3-diphenylphenanthrene (156) is obtained on ring closure.

A summary of the different methods of preparing naphthalene derivatives is given in Table 3.

The hydrolysis of the pyrans (152) with aqueous alcoholic hydrochloric acid gives the 1,5-diketones which, as well as the unsaturated
**TABLE 3**

**Naphthalene Derivatives (157) from Tetrasubstituted 4H-Pyrans**

![Chemical Structure](Image)

<table>
<thead>
<tr>
<th></th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>R&lt;sub&gt;2&lt;/sub&gt;</th>
<th>R&lt;sub&gt;3&lt;/sub&gt;</th>
<th>R&lt;sub&gt;4&lt;/sub&gt;</th>
<th>R&lt;sub&gt;5&lt;/sub&gt;</th>
<th>R&lt;sub&gt;6&lt;/sub&gt;</th>
<th>M.p. (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>H</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>Picrat, 115-116</td>
<td>70</td>
</tr>
<tr>
<td>(b)</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>Picrat, 142-143</td>
<td>52</td>
</tr>
<tr>
<td>(c)</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>H</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>67-68</td>
<td>89</td>
</tr>
<tr>
<td>(d + f)</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>H</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>77-78</td>
<td>84 + 93</td>
</tr>
<tr>
<td>(e)</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>C(CH&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;3&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>Liquid, b.p. 135/5mm</td>
<td>71</td>
</tr>
<tr>
<td>(g)</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>H</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>117-118</td>
<td>91</td>
</tr>
<tr>
<td>(h)</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;-OCH&lt;sub&gt;3&lt;/sub&gt;(4)</td>
<td>H</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;-OCH&lt;sub&gt;3&lt;/sub&gt;(4)</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>98-99</td>
<td>45</td>
</tr>
<tr>
<td>(i)</td>
<td>CeH&lt;sub&gt;8&lt;/sub&gt;</td>
<td>H</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>Oily&lt;sup&gt;a&lt;/sup&gt;</td>
<td>—</td>
</tr>
<tr>
<td>(j)</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>H</td>
<td>CeH&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;3&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>H</td>
<td></td>
<td>154-155</td>
<td>94</td>
</tr>
</tbody>
</table>

<sup>a</sup> Gives the known 9-phenylphenanthrene by dehydrogenation with palladium.
ketone obtained from (152d), also give good yields of the corresponding naphthalene derivatives when treated with 70% perchloric acid.

The method, as (155) \rightarrow (156) show, also allows the formation of phenanthrene derivatives of definite constitution. The method may hold an important position in the preparation of both naphthalene and phenanthrene derivatives of unambiguous structure. The reaction of 2,4,6-triphenyl-4(3-thionaphthylmethyl)-4H-pyran (158) with perchloric acid gives an 88% yield of 2,4-diphenyldibenzothiophene (159), which with Raney nickel gives 1,3,5-triphenylbenzene (160) [102].

\[
\begin{align*}
\text{H}_5\text{C}_6 & \quad \text{CH}_2 \\
\text{H}_5\text{C}_6 & \quad \text{C}_6\text{H}_5 \\
\text{H}_5\text{C}_6 & \quad \text{C}_6\text{H}_5 \\
\end{align*}
\]

\[\text{H}_5\text{C}_6 \quad \text{C}_6\text{H}_5\]

(158) \quad H\text{ClO}_4 \quad \text{Ni}

(159)

(160)

\textbf{Conversion of Pyrylium Salts into Azulene Derivatives}

According to Hafner and Kaiser [106], 2,4,6-trimethylpyrylium perchlorate (161) will react with the sodium derivative of cyclopentadiene in tetrahydrofuran to give 4,6,8-trimethylazulene (162); the reaction proceeds at room temperature and affords yields of over 60%.

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \\
\text{ClO}_4 & \quad \text{Na} \quad \text{Na} \quad \text{H}_2\text{O} \\
\end{align*}
\]

(161) \quad - \text{NaClO}_4 \quad - \text{H}_2\text{O}

(162)

This elegant azulene synthesis is closely related to earlier syntheses devised by Hafner and co-workers [107], in which the pyrylium salt is
AROMATIC COMPOUNDS FROM PYRYLIUM SALTS

replaced by pyridine derivatives; these are initially converted into derivatives of glutaconaldehyde by opening of the pyridine ring.

The azulene synthesis from trimethylpyrylium salt can be extended to other pyrylium salts. It is essential, however, that all three reactive positions (2,4,6) are occupied and that at least one 2-group is not too large. 2,4,6-Triphenylpyrylium perchlorate no longer yields an azulene derivative, though 2,6-dimethyl-4-phenylpyrylium perchlorate and 2,4-diphenyl-6-methylpyrylium perchlorate will do so (87 and 25%, respectively). 2,6-Dimethyl-4-methoxypyrylium salt also reacts readily with the sodium derivative of cyclopentadiene to give 4,8-dimethyl-6-methoxyazulene (55%). Further variations in the synthesis are possible by modification of the cyclopentadiene constituent.

The reaction of 2,4,6-triaryl-substituted pyrylium salts (163) and methylene triphenylphosphorane [105] constitutes a quite different type of azulene synthesis. An excess of an ethereal solution of methylene triphenylphosphorane solution is added to a solution of the pyrylium salt in acetonitrile, whereupon the deep blue aryl-substituted azulene (165) is obtained in approximately 30% yield.

\[
\begin{align*}
\text{2} & \quad \text{H}_5\text{C}_6 \quad \text{O} \quad \text{C}_6\text{H}_5 \\
& \quad \text{H}_5\text{C}_6 \quad \text{BF}_4^- \\
\text{(163)}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2\text{P(C}_6\text{H}_5)_3 & \quad \oplus \quad \text{CH}_2\text{P(C}_6\text{H}_5)_3 \\
\text{H}_5\text{C}_6 & \quad \text{O} \quad \text{C}_6\text{H}_5 \\
& \quad \text{H}_5\text{C}_6 \quad \text{CHP(C}_6\text{H}_5)_3 \\
\text{(164)}
\end{align*}
\]

\[
\begin{align*}
\text{H}_5\text{C}_6 & \quad \text{O} \quad \text{C}_6\text{H}_5 \\
& \quad \text{H}_5\text{C}_6 \quad \text{H}_5\text{C}_6 \\
& \quad \text{P(C}_6\text{H}_5)_3 \\
\text{(165)}
\end{align*}
\]

The reaction must proceed by way of an intermediate (164) in which two molecules of the pyrylium salt are in combination with one molecule.
of the phosphorane. By a transannular reaction, triphenylphosphine is split out and the azulene results.

The Reaction Mechanism

The Primary Reaction

The pyrylium cation (166a) is a cation stabilized by aromatization, whose carbon atoms 2,6, and 4 (formulas 166b–d, respectively) readily add nucleophilic reagents. The question of whether the addition will be preferred at C-2 and C-6 to that at C-4 cannot be answered generally. The calculation of the electron density indeed shows that positions C-2 and C-6 (166b and c) [108] are the favored ones for nucleophilic addition, although experimental evidence—as in the series of thiopyrylium salts [27]—shows that no definite conclusions can be drawn. The reaction conditions must be closely investigated to determine how far the kinetic and thermodynamic considerations govern the formation of the initial addition product.

It is, however, known with certainty that bulky (lipophilic?) substituents decisively influence whether the C-4 or the C-2 positions will be favored [60].

The primary addition products are either the 2H- or the 4H-pyrans; in some cases either one or the other could be isolated [102]. Theoretically these compounds should be interconverted by an allylic rearrangement.

Exhaustive recent investigations have shown that the 2H-pyrans formed initially cannot generally be isolated since, through opening of the six-membered ring, they form doubly unsaturated ketones (170) and (171), respectively (if $X = OH$, the enol ketone and the 1,5-diketone) [71]. If the pyrylium salt is unsymmetrically substituted then two different structural isomers for (167) and (170), respectively, and (168) and (171) could be formed.

Moreover stereoisomers (geometrical isomers) are possible:

(a) The nucleophile can be added cis ($R_2$ and H on the same side of the double bond $\equiv C_2=C_3 \equiv$) or trans ($R_2$ and H on different sides of the double bond).
During, or after the addition, the second double bond can also undergo cis-trans rearrangement.

The addition products from hydroxyl ions \[109,110\], cyanide ions \[111\], and phenylhydrazine \[112,113\] were carefully investigated.

While the careful hydrolysis of 2,3,5,6-tetraphenylpyrylium salts \(173\) gave two isomers which were distinguished as the enol-ketone \(175\) and the cis-diketone \(176\) \[110a\], the isolation of enol-ketones or cyclic hemiacetals of the structure \(174\) was not successful in other cases.

Two different diketones \(179\) and \(180\) were isolated from 2,3,4,6-tetraphenylpyrylium salt \(177\) \[110\]. Light brings about an intercon-
version of the two ketones, and an equilibrium mixture is formed. With hydroxyl or methylate ions only the *trans* diketone (180) is formed.

Finally, from 3-methyl-2,4,6-triphenylpyrylium salt (181) by careful hydrolysis, the diketone (184) is formed; it undergoes rearrangement with further hydroxyl ions to give a mixture of the structural isomers, *cis*- and *trans*-diketones (185) and (186) [110b]. From this it can be concluded that the initial attack of the hydroxyl ions takes place on C-6,
and that the reaction products (182) and (183) are rapidly produced. Similar results are obtained for the reaction of cyanide ions with alkyl-substituted pyrylium salts (187). Here, Balaban and Nenitzescu [111] established that initially cyano-cis-alkyldienone (189) was formed which with acid was converted into the trans isomer. The steric position of the two substituents on the double bond in (190) is not certain.

\[
\text{CN}^{-} + \text{R}_{2}C_{6}H_{4}OC_{6}H_{4}C_{6}H_{4} \rightarrow \text{R}_{2}C_{6}H_{4}OC_{6}H_{4}C_{6}H_{4}CN
\]

\[
\text{R}_{2}C_{6}H_{4}OC_{6}H_{4}C_{6}H_{4}CN \rightarrow \text{R}_{2}C_{6}H_{4}OC_{6}H_{4}C_{6}H_{4}CN
\]

\[
\text{Ar}_{2}OC_{6}H_{4}Ar \rightarrow \text{Ar}_{2}OC_{6}H_{4}Ar
\]

\[
\text{Ar}_{2}OC_{6}H_{4}Ar \rightarrow \text{Ar}_{2}OC_{6}H_{4}Ar
\]

\[
\beta\text{-Phenylhydrazide} \quad \alpha\text{-Phenylhydrazide}
\]
The reactions of aryl-substituted pyrylium salts with phenylhydrazine have long been known to give two isomers. Only the so-called α-phenylhydrazides are transformed to the pyridine compounds [15]. Once again it is a matter of geometrical isomers [112, 113]:

The primary product of the addition of a nucleophile to a pyrylium salt is, in the case of neutral nucleophiles (e.g. H₂O, NH₃, NH₂R, etc.), a cation, and in the case of nucleophilic anions (e.g. OH⁻, SH⁻, CH₂R⁻, etc.), a neutral compound.

THE SECONDARY REACTIONS

Addition Products at C-4

The most important secondary reactions are:

1. The splitting out again of the added nucleophile X to give the original pyrylium salts.
2. The splitting out of the group R₄ or of the hydrogen atom as an

\[ \text{Addition Products} \]

\[ \text{Reaction Equations} \]

\[ \text{Structural Representation} \]
anion (hydride ion) with the formation of a new pyrylium salt. An example of this type of reaction is the formation of pyrylium salts from 4-pyrones with organometallic compounds, which in acid solution split out the OH group.

(3) The hydrolytic splitting of the pyran ring to give 1,5-diketones.

(4) The allylic rearrangement of a 4H-pyran into a 2H-pyran by alkali, light, etc.

(5) In the case of \( X = \text{CH}_2\)-Aryl (\( \text{CH}_2\)-naphthyl, \( \text{CH}_2\)-thienyl, etc.) and \( R_4 = \text{alkyl or aryl}, \) \( R_2\text{-CO-CH}_3 \) can be split out and a derivative of naphthalene, phenanthrene, thi anthrene, etc., is formed.

(6) In the case of \( X = \text{CH}_2R'R'' \) and \( R_4 = \text{H} \), dehydrogenation can take place and a 4H-4-dehydropyran is formed.

For each of these possibilities we have given examples

Addition Products at C-2

The important secondary reactions are:

(1) The splitting out of the added nucleophile X or the \( R_2 \) substituent already present as an anion to give the original or a new pyrylium salt. The formation of pyrylium salts from 2-pyrones is an example of this type of reaction.

(2) The opening of the pyran ring with the formation of a doubly unsaturated ketone. The reaction can occur with or without steric rearrangement at either one, or both of the double bonds. With \( X = \text{OH} \) ("pseudobase") enol ketones or simple unsaturated 1,5-diketones of different structure and exhibiting geometrical isomerism are formed.

(3) Allylic rearrangement to give a 4H-pyran (unknown).

(4) In the case of a nucleophile added at C-2 which also contains a hydrogen atom or a substituent which is capable of being split off to give an electrophile, an aldol-type condensation can take place between the carbonyl group at C-6 to give heterocyclic or isocyclic six-membered aromatic ring systems (through splitting out of \( \text{OH}^- \) from C-6 or \( \text{HOH}, \text{HOR}, \text{etc.}, \) from C-6 and X).

(5) An analogous reaction to (4) can also occur with the group \( R_2 \) already present at C-2 if this possesses a suitable constitution (\( \text{CH}_3, \text{CH}_2\cdot\text{CH}_3, \text{etc.} \)). With \( X = \text{OH}, \text{NR}_2', \text{3,5-disubstituted phenols and NR}_2' \) anilines are produced.

(6) If the reaction takes place with a cyclopentadienyl substituent, the aldol condensation which follows is between the carbonyl group at C-6 and the neighboring atom to C-2 and not C-2 itself. In this way the triply unsaturated seven-membered ring of the azulenes is produced (synthesis of Hafner).
The secondary reactions of 2H-pyrans are still not exhausted. In addition to the reactions by which structural or steric changes can occur at the double bond and those in which the substituent on the C-5 atom is split into fragments, the C-5 atom adjoining the carbonyl group of C-6 can react nucleophilically with the electrophilic substituent at C-2. Three examples are given.

(7) The reactions of pyrylium salts with malonic ester and malondi-nitrile to give phenols and amines:

(8) The reaction of pyrylium salts with hydrogen peroxide to give furan derivatives:
(9) The reaction of 2 moles of pyrylium salt and methylene triphenylphosphorane to give an unsaturated ten-membered ring, which is stabilized by the formation of an azulene:

Methods of Preparation of Pyrylium Salts

The formation of pyrylium salts frequently proceeds astonishingly readily. The more important and versatile syntheses are mentioned below.

Conversion of Pyrones into Pyrylium Salts

Disubstituted 2- or 4-pyrones will react with nucleophilic agents in acid solution, to give pyrylium salts. This method is useful when suitably substituted pyrones are readily accessible. This is true particularly for 2,6-dimethyl-4-pyrone, which is formed in almost quantitative yield from dehydroacetic acid by boiling with hydrochloric acid [114], as well as for 2,6-diphenyl-4-pyrone [115], 4,6-dimethyl-2-pyrone [116], and 4,6-diphenyl-2-pyrone [117]. An interesting synthesis of 3,5-dibenzyl-4-pyrone should also be noted [118].

Many 2,4,6-trisubstituted pyrylium salts with almost any substituent can be prepared in this way by the use of Grignard reagents, dimethyl aniline [119], and other compounds. Altogether, pyrones are accessible by several methods and by acylation at C-3 [120], or condensation with aldehydes at the methyl group at C-2 [121], even further modifications can be made.

4-Pyrones condense with malononitrile or cyanoacetic ester [47],
and diphenylketone also produces a pyrylium salt [56]. Thiapyrones form thiopyrylium salts [28].

In a similar way, 3-phenylisocoumarin reacts with phenyl magnesium bromide to give the 1,3-diphenylisochromylium salt [122].

4-Alkoxypyrylium salts are obtained by the reaction of 4-pyrones with alkylating agents such as methyl iodide or dimethyl sulfate [2]. In a similar way 4-thiopyrones form 4-thioalkylpyrylium salts [128]. On the other hand, the 2-ethoxypyrylium salt is only obtained by the action of triethylxonium fluoborate on the 2-pyrone. The compound is unstable and decomposes rapidly in damp air to give the original 4-pyrones [124]. The 2-thiopyrones are essentially much easier to alkylate and react readily with methyl iodide and dimethyl sulfate.

**The Synthesis of Pyrylium Salts from 1,5-Dicarbonyl Compounds, from Ketones and α,β-Unsaturated Ketones, or from 2 Moles of Ketone and 1 Mole of Aldehyde**

According to Dilthey and co-workers [125], 1,5-diketones are converted into 2,4,6-trisubstituted pyrylium salts in yields usually exceeding 50%, by the action of dehydrating complexing agents such as FeCl₃, SbCl₅, POCl₃, concentrated H₂SO₄ and triphenylcarbonium fluoborate which can act as acceptors for hydride ions [126]. Homophthalaldehyde and perchloric acid yield isochozum perchlorate [10, 11], whereas glutacnaldehyde gives the unsubstituted pyrylium perchlorate in a very poor yield [24]. A much better way for getting pyrylium fluoborate is by dehydrating 4H-pyran (74) with triphenylcarbonium fluoborate [127]. The 1,5-diketones can be replaced by α,β-unsaturated aromatic ketones (chalcones) which will condense with methyl ketones (acetophenone and its derivatives) [128]. Numerous pyrylium salts are accessible by this route. Chalcone reacts with acetophenone, deoxybenzoin, and cyclohexanone to give 2,4,6-triphenylpyrylium salt, 2,3,4,6-tetraphenylpyrylium salt [129], and 2,4-diphenyl-5,6,7,8-tetrahydrochromylium salt [130], respectively.

Finally, 2 moles of aryl methyl ketone react with 1 mole of aryl aldehyde to give pyrylium salts [3a], e.g., acetophenone and benzaldehyde yield triphenylpyrylium salt. Even 3 moles of acetophenone, however, give 2,4,6-triphenylpyrylium salt; the mechanism was elucidated by Elderfield [131].

Dienones, e.g. cinnamylideneacetophenone, can also be condensed to give pyrylium salts (2,6-diphenylpyrylium salt), though the yields are rather lower (20%) [132]. We could improve this synthesis to give a 45% yield, as described in the Experimental section. Stetter obtained
the same compound in 60% yield from the difficulty accessible 1,5-di-
diphenylpent-1-yn-3-en-5-one [133].

In the absence of another reactant of high reactivity chalcone alone
forms the pyrylium salt (191) [93].

Pyrylium Salts from \( \alpha,\beta \)-Unsaturated Methyl Ketones
and Carboxylic Acid Derivatives

Another very frequently used synthesis was also devised by Dilthey
and his collaborators [134]; this involves the condensation of
\( \alpha,\beta \)-unsaturated methyl ketones such as, \textit{inter alia}, dypnone or mesityl oxide,
and carboxylic acid anhydrides, chlorides, or other carboxylic acid
derivatives in the presence of complex acids to give 2,4,6-substituted
pyrylium salts. Schneider [135] used "sulfoacetic acid" in the preparation of α-methyl-substituted pyrylium salts. The synthesis of 2,4,6-trimethylpyrylium perchlorate from glacial acetic acid/perchloric acid and mesityl oxide according to the method of Diels and Alder [86] proceeds particularly readily. Numerous carboxylic acids have been utilized in the synthesis of pyrylium salts containing various α-substituents [136]. Instead of the α,β-unsaturated methyl ketones, 2 moles of methyl ketone (acetophenone) can be made to react with the carboxylic acid derivative [137]. This reaction takes place without dehydrogenation.

\[
\begin{align*}
\text{R}_1 & \quad + \text{HX} \\
\text{R}_2 & \quad - 2 \text{H}_2\text{O} \\
\text{R}_3 & \\
\text{R}_4 & \\
\text{O} & \\
\text{C} & \\
\text{H} & \\
\text{H}_2\text{C} & \\
\text{C} & \\
\text{Cl} & \\
\text{Cl} & \\
\text{R}_5 & \\
\text{O} & \\
\text{C} & \\
\text{R}_6 & \\
\text{R}_7 & \\
\text{R}_8 & \\
\text{R}_9 & \\
\text{R}_{10} & \\
\text{X} & \\
\end{align*}
\]

\[
\begin{align*}
\text{R}_1 & \quad + \text{HX} \\
\text{R}_2 & \quad - 3 \text{H}_2\text{O} \\
\text{R}_3 & \\
\text{R}_4 & \\
\text{O} & \\
\text{C} & \\
\text{H}_2\text{C} & \\
\text{C} & \\
\text{CH}_3 & \\
\text{R}_5 & \\
\text{O} & \\
\text{C} & \\
\text{R}_6 & \\
\text{R}_7 & \\
\text{R}_8 & \\
\text{R}_9 & \\
\text{R}_{10} & \\
\text{X} & \\
\end{align*}
\]

SYNTHESIS FROM OLEFINS AND ACID CHLORIDES

According to Balaban and Nenitzescu [16], olefins react with 2 moles of acid chloride in the presence of complexing agents such as aluminum trichloride to give 2,4,6-substituted pyrylium salts; the yields usually amount to 20–40%. Many pyrylium salts, especially those containing branched aliphatic groups in positions 2 and 6 have been prepared via this recently discovered synthesis:

\[
\begin{align*}
\text{R}_1 & \quad + \text{AlCl}_3 \\
\text{R}_2 & \quad - \text{HCl}, - \text{H}_2\text{O} \\
\text{R}_3 & \\
\text{R}_4 & \\
\text{O} & \\
\text{C} & \\
\text{R}_5 & \\
\text{O} & \\
\text{C} & \\
\text{R}_6 & \\
\text{R}_7 & \\
\text{R}_8 & \\
\text{R}_9 & \\
\text{R}_{10} & \\
\text{AlCl}_4 & \\
\end{align*}
\]

Extensive work has been carried out on this method, especially on the use of different Lewis acids for the preparation of different pyrylium salts; a detailed review of this work has already been published [138].

CONVERSION OF PYRYLIUM SALTS INTO DIFFERENT PYRYLIUM SALTS

2,4,6-Substituted pyrylium salts containing a 4-alkoxy or thioalkyl substituent readily exchange that alkoxy (or thioalkyl) group for other nucleophilic groups. Thus secondary amines yield the 4-dialkylamino derivatives [13], while malononitrile or cyanoacetic ester give methylene-4H-pyrans [48], which are converted into pyrylium salts by the action of acid.

2,6-Substituted pyrylium salts unsubstituted in the 4-position readily
AROMATIC COMPOUNDS FROM PYRYLIUM SALTS

add nucleophilic groups at that position; with compounds such as acetylacetone and nitromethane, which contain an acidic CH group, 4H-pyrans are formed which can be dehydrogenated to give 4-alkyl-4H-pyrans. These on treatment with acid form the 4-alkylpyrylium salts [58, 59]. With Grignard reagents 4H-pyrans are formed which on oxidation with ferric chloride in glacial acetic acid directly form new 4-substituted pyrylium salts [59, 60]. 2,6-Diphenyl-4-methylpyrylium salt [66] is formed in 25% yield from the reaction between 2,6-diphenylpyrylium salt and diazomethane.

The condensation of aldehydes or ketones with 2- or 4-methyl-substituted pyrylium salts gives rise to the formation of new pyrylium salts which contain unsaturated side chains [139]. Numerous condensations of this type have been carried out by Wizinger [119].

By the nitration of 2,4,6-triphenylpyrylium perchlorate, Le Fevre [140] succeeded in obtaining trinitrottriphenylypyrylium perchlorate in which the 2- and 6-phenyl groups were nitrated in the meta, and the 4-phenyl group in the para position.

Experimental

Pyrylium Salts

2,4,6-Trimethylpyrylium perchlorate [141]. Perchloric acid (15 gm, 70%) is added dropwise to acetic anhydride (30 gm) cooled in ice. Freshly distilled mesityl oxide (10 gm) is then added, followed by more acetic anhydride (20 gm) and the mixture heated on a boiling water bath for 15 min. On cooling the crystalline mass is filtered and washed with glacial acetic acid, alcohol, and finally ether, yielding an almost colorless product (14-16 gm, 64-72%), m.p. 245-247°C. These directions also allow the preparation of larger quantities (500 gm, yield 67%), but the perchlorate should not be stored dry; it should be utilized immediately in the form of a suspension in a little solvent. Recrystallization of larger quantities from glacial acetic acid also demands care.

The fluoborate, m.p. 206-208°C, is obtained from an aqueous solution of the perchlorate and hydrofluoboric acid in glacial acetic acid.

2,6-Diphenylpyrylium perchlorate [66]. A boiling solution of freshly sublimed ferric chloride (100 gm) in glacial acetic acid (300 ml) is added slowly to a boiling solution of cinnamylideneacetophenone (20 gm) in glacial acetic acid (450 ml). The mixture froths and darkens. The mixture is heated for 2-3 min and then quickly cooled, whereupon the diphenylpyrylium chloroferrate separates as deep blue crystals. The compound is dissolved in a solution of tartaric acid and immediately filtered
into 40–50% perchloric acid (200 ml). If necessary, the precipitate which remains on the filter is washed through with more aqueous tartaric acid. The perchlorate is precipitated from the filtrate (13.0 gm, 45%), m.p. 220–225°C.

2,6-Diphenyl-4-isopropylpyrylium chloroferrate [97]. (a) 2,6-Diphenyl-4-isopropyl-4H-pyran. A Grignard compound prepared from isopropyl chloride (5.0 gm) and magnesium (1.5 gm) in ether (45 ml) is added rather quickly to a suspension of 2,6-diphenylpyrylium perchlorate (5.2 gm) (see above) in dry ether (60 ml) until the pyrylium salt is in solution. The resulting mixture is stirred for 20 min at room temperature and the yellow slightly turbid solution is then cooled in an ice bath and decomposed with cold aqueous ammonium chloride. The ether layer is washed once with 1 N sodium carbonate solution, and three times with water, and finally dried overnight with calcium chloride. The ether is removed under vacuum at 40°C to leave an orange oil which slowly crystallizes. By careful crystallization of the product from isopropanol in the absence of light, colorless crystals are obtained (3.5–3.7 gm, 80–85%), m.p. 58–59°C.

(b) 2,6-Diphenyl-4-isopropylpyrylium chloroferrate. Sublimed ferric chloride (25 gm) is added portionwise to a refluxing solution of 2,6-diphenyl-4-isopropyl-4H-pyran in glacial acetic acid (120 ml). The heating is continued for 1 min under reflux and then the mixture is cooled. The pyrylium salt is obtained as dark-yellow crystals which are crystallized from glacial acetic acid (18.5 gm, 90%), m.p. 156–157°C.

2,4,6-Triphenylpyrylium chloroferrate [142]. Acetophenone (12 gm) is added to benzaldehyde (10.6 gm) and the mixture treated with a solution of sodium methoxide (6 ml, 10%). The mixture is allowed to stand in the refrigerator overnight, and the solid mass triturated with a little glacial acetic acid. Crystalline benzalacetophenone (19 gm, 89%) is obtained, m.p. 57.5–58°C after recrystallization from methanol.

Benzalacetophenone (62.4 gm) and acetophenone (36 gm) are dissolved in carbon disulfide (450 ml) contained in a three-necked flask fitted with stirrer, reflux condenser, and dropping funnel, and sublimed ferric chloride (146 gm) added to the well-stirred and cooled solution. Acetic anhydride (25 ml) is then slowly run in through the condenser and, as soon as the reaction has subsided, the mixture is warmed on a water bath. More acetic anhydride (65 ml) is added in small portions. The reaction mixture is boiled for 2 hr and stored for 1–2 days in the refrigerator. The dark-brown mass is thoroughly triturated several times with ether–glacial acetic acid (9:1), filtered, and washed with ether, yielding pyrylium salt (93 gm, 55%), m.p. 276–278°C.

Conversion into the fluoborate is effected as follows: The 2,4,6-tri-
phenylpyrylium chloroferrate (80 gm) is dissolved by stirring into boiling water (3.5 liters) to which a few ml of glacial acetic acid are added. On addition of hydrofluoroboric acid (125 ml, 40%), a thick yellow precipitate separates. This can be purified by bringing to the boil portionwise, and adding glacial acetic acid (total quantity 550 ml) to the boiling solution. The solution is filtered hot and on cooling 2,4,6-triphenylpyrylium fluoroborate (39 gm, 62%), crystallizes as yellow needles, m.p. 214–215°C.

For conversion into the iodide, the chloroferrate is dissolved in slightly acidified water at 70–80°C and sodium bisulfite and a saturated solution of potassium iodide are added. The red iodide, m.p. 221°C, is obtained in quantitative yield.

2-Methyl-4,6-diphenylpyrylium salts [15]. Acetic anhydride (100 ml) is slowly mixed with conc. sulfuric acid (30 ml), external cooling being applied throughout. When the reaction has subsided, the mixture is warmed for 2–3 hr on a water bath maintained at 75–80°C; the internal temperature must not be allowed to exceed 80°C. Free sulfuric acid can then only be detected in traces. Acetic anhydride (10–20 ml) and acetophenone (30 ml) are added to the mixture at room temperature, followed by heating for 24 hr at 45–50°C. The initially red-brown mixture becomes dark green after one-half hour. After addition of an equal volume of ethanol and cooling, the sulfoacetate of the pyrylium salt separates as a thick crystalline mass. This is filtered, washed with alcohol containing a little ether and dried; yields amount to approximately 50%. Addition of ether to the mother liquors affords a second crop. The preparation can be carried out without modification on ten times this scale, but the over-all yield is then lower. The sulfoacetate can be purified by recrystallization from ethanol, to give a product of m.p. 204°C. It is rather insoluble in pure water, and undergoes hydrolysis and decomposition, especially on warming. It is readily soluble without decomposition in acidified water.

Addition of a saturated solution of sodium chloride or potassium iodide to a warm, acidified solution of the sulfoacetate yields the chloride, m.p. 125–126°C, or the iodide, m.p. 222°C, respectively.

2-tert-Butyl-4,6-diphenylpyrylium chloroferrate [18]. Benzalpinacolone (4 gm) (m.p. 41°C, b.p. 154°C/25 mm), prepared in quantitative yield from pinacolone and benzaldehyde in aqueous-alcoholic sodium hydroxide by the method of Organic Syntheses [142a], is mixed with acetophenone (2 ml) and acetic anhydride (5 ml); sublimed ferric chloride (5 gm) is added in small portions, causing the mixture to become warm. It is allowed to stand overnight, filtered, and washed with glacial acetic acid and ether, yielding yellow needles (2.6 gm), m.p. 171–172°C; m.p. of iodide 249–250°C.
2,6-Diisobutyl-4-methylpyrylium chloroaluminate \([16]\). Aluminum chloride (14 gm) is slowly added from a large stock bottle to stirred isovaleryl chloride (27 gm) cooled to 0–10°C, care being taken to exclude moisture. The aluminum chloride largely goes into solution. If the mass becomes too viscous, this is remedied by the addition of a small quantity of tert-butyl chloride. After the tert-butyl chloride (total quantity 9.5 gm) has gradually been added, the cooling bath is removed and stirring is continued at room temperature until the mass liquefies and the evolution of HCl subsides, which requires 3–4 hr.

On the following day, the reaction mass is poured on to some crushed ice. Starting materials or by-products are removed by steam distillation or extraction with ether. The chloroaluminate is obtained from the concentrated aqueous solution by salting out; more pyrylium salt is obtained from the mother liquors by precipitation with HClO₄, HBF₄, H₂PtCl₆, or picric acid; yield 40%, m.p. of the perchlorate 106°C.

1,3-Diphenylisochromylium perchlorate \([8,122]\). (a) A mixture of o-carboxydeoxybenzoin (7.5 gm) and benzene (100 ml) is distilled until the distillate is clear and free from water. The mixture is then heated at 200°C in an open dish, cooled, carefully treated with water (150 ml), acidified with hydrochloric acid (10 ml) and the hot suspension filtered. The precipitate which separates is washed with warm 3 N hydrochloric acid and the washings combined with the filtrate. Yield of 3-phenylisocoumarin 7.2 gm (almost quantitative), m.p. 88–89°C.

(b) Phenylmagnesium bromide \((0.09\) mole) in ether (75 ml) is added to a stirred solution of 3-phenylisocoumarin (7.4 gm, 0.03 mole) in ether (75 ml) cooled to 0.5°C. Stirring is continued for 5 hr, followed by hydrolysis with ammonium chloride (42 gm) in water (250 ml). The ethereal layer is separated, washed, and dried over magnesium sulfate; addition of a solution of perchloric acid \((6.35\) ml) in acetic anhydride \((25\) ml) and absolute ether \((20\) ml) at 0°C causes the separation of an orange-red precipitate. A further crop is obtained from the filtrate. The salt is recrystallized from glacial acetic acid to which one drop of perchloric acid has been added, to give a 45% yield of pale orange crystals, m.p. 245–256°C. On combustion the salt decomposes explosively. Addition at 0°C of ferric chloride dissolved in a small quantity of hydrochloric acid to the stable carbinol (obtained from the perchlorate by the addition of alkali) in ether–acetic anhydride yields the chloroferrate.

2,6-Dimethyl-4-tert-butylpyrylium perchlorate \([141]\). Following the directions given by Baeyer and Piccard \([2]\) for the preparation of 2,6-dimethyl-4-phenylpyrylium perchlorate, 10 ml of a solution of tert-butyl chloride \((80\) gm, 0.87 mole) in ether \((120\) ml) are poured on to magnesium \((22\) gm, 0.92 mole) activated by a little iodine. As soon as the
reaction has set in, ether (100 ml) and the remainder of the butyl chloride solution are added dropwise with gentle warming.

The Grignard solution thus prepared is stirred into 2,6-dimethyl-4-pyrone (50 gm, 0.4 mole) dissolved in dry anisole (1 liter), and the temperature rises to 25°C. The red solution is then stirred into 20% perchloric acid (1 liter) cooled to −10°C, and allowed to stand for 2 hr. The crystals are filtered and washed with alcohol and ether, yielding the perchlorate (52 gm, 49%), m.p. 220–221°C.

2,6-Dimethyl-4-ethoxypyrylium perchlorate [143]. 2,6-Dimethyl-4-pyrone (6.6 gm) dissolved in methylene dichloride (22 ml) is added to a solution of triethyloxonium fluoborate (10.1 gm) in methylene dichloride (3 ml), care being taken to exclude moisture. The solution is allowed to stand for 3 days and the methylene dichloride distilled off in vacuo; the residual crystalline mass is purified by solution in methylene dichloride and precipitation with ether. Yield, 90%; m.p. 90–91°C. Addition of a concentrated sodium perchlorate solution to an aqueous solution of the fluoborate precipitates the perchlorate, m.p. 126–128°C.

Heterocyclic Aromatic Compounds from Pyrpylium Salts

2,4,6-Trimethylpyridine [2]. An aqueous solution of 2,4,6-trimethylpyrylium perchlorate is added to an excess of aqueous ammonia and the mixture gently warmed. Extraction with ether and evaporation of the solvent afford an almost quantitative yield of 2,4,6-trimethylpyridine in the form of an oil, from which the picrate, m.p. 155–156.5°C is readily precipitated by addition of aqueous picric acid.

2,4,6-Triphenylpyridine [3a, 4, 8]. 2,4,6-Triphenylpyrylium fluoborate (10 gm) is suspended in absolute tert-butanol (100 ml) and the suspension heated to boiling. A rapid stream of dry ammonia is passed in, and the pyrylium salt goes into solution. After 30 min the precipitated ammonium fluoborate is filtered off, and a little water added to the filtrate until a turbidity appears. The solution is allowed to stand for some time in the refrigerator, yielding colorless flakes (8 gm, 90%), m.p. 138°C.

N-Anilido-2-methyl-4,6-diphenylpyridinium iodide [15, 18]. 2-Methyl-4,6-diphenylpyrylium iodide (0.8 gm) is suspended in boiling benzene, and a solution of phenylhydrazine (0.3 gm) in benzene is added dropwise. After a few moments the red iodide vanishes and is replaced by a microcrystalline yellow salt (0.9 gm), m.p. 200°C after recrystallization from alcohol. It is almost insoluble in water and rapidly turns brown on exposure to light.

Addition of NaOH to a solution in alcohol-water precipitates dark-blue needles of the anhydro base (N–N–betaine), m.p. 108°C.

1,2,6-Trimethyl-4-methoxypyridinium iodide [13]. Aqueous methyl-
amine (25%, 4.4 ml) in methanol (30 ml) is slowly added to an ice-cooled solution of 2,6-dimethyl-4-methoxypyrylium iodide (9.1 gm) in methanol (50 ml). The solution is refluxed for 30 min and the solvent evaporated; addition of a small quantity of acetone causes the immediate crystallization of the pyridinium salt (4 gm, 42%), m.p. 204–205°C after recrystallization from ethanol.

2,4,6-Triphenylthiopyrylium perchlorate [28]. Crystalline sodium sulfide (1 gm) in water (10 ml) is added to a solution of 2,4,6-triphenylpyrylium perchlorate (0.82 gm) in acetone (40 ml) and the mixture, shaken at frequent intervals, is allowed to stand for half an hour, when the color changes to an intense bluish red. The solution is acidified with perchloric acid (20%, 10 ml) and diluted with water (40 ml); after 2 hr the mixture is filtered to give yellow needles, m.p. 210–211°C.

2,6-Diphenyl-4-nitromethylene-4H-pyran [59]. 2,6-Diphenyl-4-nitromethyl-4H-pyran (0.5 gm) and triphenylphenol (10 mg) are dissolved in carbon tetrachloride (30 ml). The colorless solution is shaken for 2 hr with a solution of potassium ferricyanide (3.5 gm) in 2N sodium hydroxide solution. Yellow needles of 2,6-diphenyl-4-nitromethylene-4H-pyran separate (0.43 gm), and are crystallized from ethanol to give a product with a m.p. of 170–171°C.

N-Methyl-2,6-diphenyl-4-nitromethylene-1,4-dihydropyridine [66]. Aqueous methylamine (40%, 60 ml) is added to a boiling solution of 2,6-diphenyl-4-nitromethylene-4H-pyran (0.7 gm) in ethanol (80 ml). The initially pale-red solution rapidly darkens to a deep red color, which later reverts to a pale red. The solution is allowed to cool slowly, and after approximately 2 hr water (200 ml) is added. Light brown crystals (0.6 gm, 82%), m.p. 243–245°C (dec.) separate, and can be recrystallized from ethanol-water. A further crop may be isolated from the mother liquors. Total yield, 90%.

4-[Dicyanomethylene)-2,6-dimethyl-1,4-dihydropyridine [74]. 4-Dicyanomethylene-2,6-dimethyl-4H-pyran (5 gm) is heated at 150°C for 1 hr in formamide (5 gm). On cooling, the crude product (1.7 gm) separates and is crystallized from formic acid to give a product of m.p. 330–331°C.

Benzene Derivatives from Pyrylium Salts

3,5-Dimethylphenol [2,16]. A mixture of 2,4,6-trimethylpyrylium perchlorate (11 gm) and sodium hydroxide solution (10%, 16 ml, 4 moles) is boiled for 1 hr. Nonphenolic material is extracted with ether, and the residue acidified and again extracted with ether. Evaporation of the solvent affords 3,5-xyleneol (15–35%), m.p. 65°C, which can be characterized as its tribromide, m.p. 164–167°C.
3,5-Dimethyl-N,N-dimethylaniline [86]. A solution of dimethylamine (10 gm) in ether (10 ml) is slowly added to 2,4,6-trimethylpyrylium perchlorate (22 gm) suspended in ether (50 ml). The suspended perchlorate coagulates during the course of the reaction, and white crystals of dimethylamine perchlorate can be observed in the liquid. These subsequently redissolve in the water formed. When the reaction is complete all solid particles have disappeared, and the reaction mixture consists of two liquid layers. The ethereal layer is separated, dried with alkali, and evaporated; the oily residue yields N-dimethyl-sym-m-xylidine, which distils almost completely at 222-224°C. The nearly colorless base (10 gm) is obtained on drying and distilling a second time.

2,4,6-Triphenylnitrobenzene [87]. A warm solution of the potassium derivative of nitromethane in tert-butanol [freshly prepared from tert-butanol (60 ml) and potassium (1.6 gm) followed by the addition of nitromethane (24.4 gm)] is added to a well-stirred suspension of 2,4,6-triphenylpyrylium fluoborate (11.5 gm) in absolute tert-butanol (60 ml). The reaction mixture becomes deep red and flakes of potassium fluoborate are precipitated. A further solution of potassium (1.6 gm) in tert-butanol (60 ml) is added, the mixture boiled under reflux for 45 min, filtered hot to free from potassium fluoborate, and treated with a little water. On cooling, the nitro compound separates, m.p. 144-145°C; yield, 87%.

2,6-Dimethyl-4-methoxynitrobenzene [88]. A solution of potassium (5 gm) in absolute tert-butanol (190 ml) is added dropwise to a stirred suspension of 2,6-dimethyl-4-methoxypyrylium perchlorate (15 gm) in nitromethane (160 ml). The mixture is boiled for 45 min, filtered free from precipitated potassium fluoborate, and evaporated under vacuum; the residual red oil gradually solidifies. Recrystallization from methanol/water (and purification with animal charcoal if necessary) yields pale yellow-green crystals (7 gm, 62%), m.p. 49.5-50.5°C.

2,6-Diphenyl-4-isobutylnitrobenzene [97]. Dry nitromethane (45 ml) and a solution of potassium tert-butoxide (40 ml, 1 M) are mixed with stirring in a dry atmosphere to give a thick white viscous suspension which is heated on a water bath at ca. 50°C. 2,6-Diphenyl-4-isobutylpyrylium perchlorate (7.5 gm) is added rapidly through a powder funnel with continued stirring, and the reaction mixture is then heated to reflux point. The mixture, which rapidly becomes intensely red, is heated for a further 20-30 min under reflux. The precipitated potassium perchlorate is filtered off while still hot and the filtrate is evaporated under vacuum with the temperature kept below 50°C. The addition of a little absolute ethanol to the oily residue gives the nitro compound in the form of fine small yellow needles (2.4 gm, 35%). Crystallization of these from alcohol gives a colorless product of m.p. 126-127°C.
2,4,6-Triphenylacetophenone [98]. Dry 2,4,6-triphenylpyrylium fluoborate (40 gm) is suspended in absolute tert butanol (150 ml) contained in a three-necked 1 liter flask, care being taken to exclude moisture. A mixture consisting of potassium (8 gm) in absolute tert-butanol (250 ml) and freshly distilled acetylacetone (10 gm) in tert-butanol (200 ml) is added to the stirred suspension from a wide-stemmed dropping funnel, and the contents of the flask acquire a transient red-violet color. The mixture is refluxed for 1 hr, filtered hot, and allowed to cool. A portion of the triphenylacetophenone (m.p. 125-126°C) separates out, and the remainder is obtained on concentration and extraction with ether. After recrystallization from alcohol, the total yield amounts to 24.4 gm (70%).

Ethyl 2,4,6-triphenylbenzoate [98]. The condensation is carried out exactly as above, the only difference being that ethyl acetoacetate is used instead of acetylacetone. Yield of ester, 32%; m.p. 93-94°C.

2,4-Diphenyl-5-benzoyl-6-aminobenzonitrile [99]. Malononitrile (6.6 gm) is added dropwise to a well-stirred solution of potassium (8 gm) in absolute tert-butanol (250 ml). The mixture is warmed for a brief period, and added to a suspension of dry 2,4,6-triphenylpyrylium fluoborate (39.6 gm) in absolute tert-butanol (150 ml). This is then heated under reflux for several hours until the deep violet color has disappeared; hot water (300 ml) is added to the hot mixture, and the latter is allowed to cool overnight. Pale yellow crystals (24 gm) separate, m.p. 175°C after recrystallization from methanol (1500 ml) and glacial acetic acid. A further crop (3.3 gm) is obtained from the mother liquors. Total yield is 73%.

3,5-Diphenyltoluene [72]. (a) An ethereal solution of 4,6-dimethyl-2-pyrone is added, in less than 1 min and with vigorous stirring, to the Grignard compound formed from bromobenzene (23.6 gm) and magnesium (3.7 gm) in ether (100 ml). The resulting mixture is heated under reflux for 8 hr. After cooling, the mixture is decomposed with ice acidified with 15% hydrochloric acid. The reaction mixture is repeatedly extracted with ether and the extracts are dried over anhydrous sodium acetate and magnesium carbonate. The ethereal residue distils at 128°C/0.001 mm and melts at 130°C. The yield of product is 5.0 gm (41%).

(b) The Grignard compound formed from methyl iodide (21.3 gm) and magnesium (3.7 gm) in ether (100 ml) is added dropwise over 1 hr to a refluxing solution of 4,6-diphenyl-2-pyrone (12.4 gm) in anisole (100 ml), the temperature being maintained at 100-120°C. The resulting mixture is warmed for a further 4 hr at 40°C and then allowed to stand for 12 hr. The reaction mixture is worked up as described in procedure (a) to give the product (6.5 gm, 53%).
1,2,3,5-Tetraphenylbenzene \([102]\). (a) 2,4,6-Triphenyl-4-benzyl-4H-pyran. The Grignard compound formed from benzyl chloride (15.5 gm) and magnesium (3.0 gm) in ether (80 ml) is added dropwise to a stirred suspension of 2,4,6-triphenylpyrylium perchlorate (25 gm) in ether (600 ml). The pyrylium salt goes into solution (if it fails to do this a further quantity of the ethereal solution of the Grignard compound is added). A brownish precipitate forms, and the reaction mixture is stirred for a further 4–5 hr. The precipitate is filtered off and the ethereal solution is washed once with an approximately 1 \(N\) solution of hydrochloric acid and two to three times with water. The ether is removed by evaporation from the reaction mixture and the product crystallized from ethanol. Colorless crystals of the pyran (17.4 gm, 71\%), m.p. 142–144°C are obtained.

(b) 1,2,3,5-Tetraphenylbenzene. 2,4,6-Triphenyl-4-benzyl-4H-pyran (1.0 gm) is added to a solution of sodium (1.25 gm) in diethylene glycol (25 ml) and the mixture is heated for \(\sqrt{2}\) hr on an oil bath at 240°C. On cooling most of the 1,2,3,5-tetraphenylbenzene separates out. The cooled mixture is treated with two or three aliquots of water and then extracted with benzene. The combined benzene extracts are washed with 2 \(N\) hydrochloric acid and water, and finally dried. After the evaporation of the solvent, 1,2,3,5-tetraphenylbenzene remains (0.49 gm, 51\%), m.p. 219–220°C; this is crystallized from isopropanol (ca. 500 ml).

1,3-Diphenylnaphthalene \([102]\). 2,4,6-Triphenyl-4-benzyl-4H-pyran (see above) and 70\% perchloric acid (60 ml) are vigorously shaken and slowly heated to 90°C, whereupon a brown oil separates. After 5–10 min, the yellow-brown mixture is cooled and the oil is separated and dissolved in a little warm alcohol. On slowly cooling the solution, 1,3-diphenylnaphthalene crystallizes as colorless needles (3.25 gm, 87\%), m.p. 77–78°C.

Azulene Derivatives from Pyrylium Salts

4,6,8-Trimethylazulene \([106]\). (a) Sodium derivative of cyclopentadiene. Sodium (69 gm, 3 gm atoms) is finely suspended in boiling absolute toluene (500 ml) by means of a vibromixer (Bopp and Reuther, Mannheim). When the suspension is cool the toluene is decanted off, and the sodium dust is washed with absolute tetrahydrofuran and suspended in absolute tetrahydrofuran (750 ml). Freshly distilled cyclopentadiene (198 gm, 3 moles) is slowly added dropwise to this vigorously stirred, ice-cooled sodium suspension kept under absolutely pure nitrogen, at such a rate that the temperature does not exceed 25–30°C. When the reaction is complete, a pale pink solution of the sodium derivative of cyclopen-
tadiene (approximately 3 M) is obtained; this solution is stable indefinitely in the absence of air and moisture, but rapidly turns dark brown when exposed to the atmosphere.

(b) 4,6,8-Trimethylazulene. 2,4,6-Trimethylpyrylium perchlorate (60 gm, 0.27 mole) is added in small portions to a vigorously stirred solution of the sodium derivative of cyclpentadiene in tetrahydrofuran (300 ml, 1.9 moles). The addition is carried out under pure nitrogen and at such a rate that the temperature does not exceed 45–50°C. Stirring is continued for a further 15 min, and 2/3 of the tetrahydrofuran is distilled off. The residue is diluted with water and the azulene formed is repeatedly extracted with petroleum ether (b.p. 60–70°C). The combined petroleum ether extracts are washed with water and dried over CaCl₂. The solvent is evaporated, and the residue, a deep violet oil, is distilled under high vacuum. After a small first fraction, the azulene comes over between 90° and 100°C and solidifies in the receiver. Recrystallization from ethanol yields 4,6,8-trimethylazulene (28.5 gm, 62% as violet-black crystals, m.p. 81–82°C.

4,8-Dimethyl-6-ethoxyazulene [106]. 2,6-Dimethyl-4-ethoxypyrylium perchlorate (23.6 gm) is suspended in vigorously stirred absolute tetrahydrofuran (100 ml), the operation being carried out in an atmosphere of pure nitrogen. A solution of the sodium derivative of cyclpentadiene in tetrahydrofuran (53 ml, 1.9 moles) is added dropwise to this suspension cooled to —18°C, at such a rate that the temperature does not exceed —15°C. The mixture, initially strongly colored, becomes almost colorless towards the end of the addition. The mixture is treated with a solution of potassium tert-butoxide in tert-butanol (250 ml, 1 M) at —10°C, slowly allowed to warm up with stirring, and finally refluxed for 3 hr. The working up is identical to that described under 4,6,8-Trimethylozulane. Red crystals (45%), m.p. 88–89°C, are obtained, which are recrystallized from alcohol.

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