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# SYNTHESIS OF PYRYLIUM SALTS AND PYRIDINES CONTAINING HETEROCYCLIC SUBSTITUENTS

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A method of synthesizing pyrylium salts with heterocyclic substituents in the ring, has been investigated. The synthesis was carried out in two stages: alkaline condensation of aromatic and heterocyclic aldehydes with methyl ketones to give 1, 5-diketones, followed by cyclization to pyrylium salts by treatment with triphenylmethyl perchlorate. Pyridines containing heterocyclic substituents were obtained by treating the pyrylium salts with ammonia.

The most extensively used method for synthesizing triaryl substituted salts is straight acid condensation of carbonyl compounds (aromatic aldehydes with aliphatic-aromatic ketones) and β-dicarbonyl compounds with ketones [2]. Straight acid condensation requires quite drastic conditions, making it impossible to use acidophobic heterocyclic compounds in such reactions. As the synthesis of pyrylium salts by that method evidently proceeds via 1, 5-diketones, pyrylium salts were also prepared by cyclizing previously prepared 1, 5-diketones containing heterocyclic substituents. These latter were prepared by alkaline condensation of aromatic aldehydes with heterocyclic ones (benzaldehyde, 1-methyl-3-formylindole, 1-methyl-2-formylpyrrole, 2-thiophenealdehyde, 2-selenophenealdehyde, 1-methyl-3-indazolealdehyde) with methyl ketones (acetophenone, 2-acetothienone, 2-acetylfuran) in ethanolic solution.

Table 1

Properties of 1, 5-Diketones

| R | R' | Mp, °C | Formula | Found, % | | | Calculated, % | | | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | C | H | S | C | H | S | |
| Phenyl | 1-Methyl-3-indolyl | 140 | $C_{26}H_{23}NO_2$ | 82.36<br>82.38 | 6.63<br>6.59 | — | 81.90 | 6.09 | | 65 |
| Phenyl | 1-Methyl-2-pyrrolyl | 101.5 | $C_{22}H_{21}NO_2$ | 80.21<br>80.19 | 6.49<br>6.54 | — | 79.80 | 6.34 | | 53 |
| 2-Thienyl | 2-Thienyl | 103.5 | $C_{17}H_{14}O_2S_3$ | 58.87<br>58.94 | 4.00<br>4.23 | 27.53<br>27.44 | 58.96 | 4.07 | 27.75 | 70 |
| Phenyl | 2-Selenienyl | 101 | $C_{21}H_{18}O_2Se$ | — | — | 20.51*<br>20.44 | — | — | 20.73* | 64 |
| Phenyl | 2-Pyridyl | 162 | $C_{22}H_{19}NO_2$ | 80.29<br>80.30 | 5.95<br>6.11 | — | 80.24 | 5.77 | | 61 |

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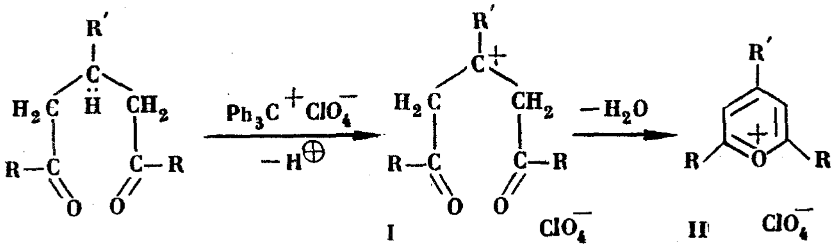
*This is the Se content.

Table 1 gives data for the 1, 5-diketones synthesized. Triphenylmethyl perchlorate was the cyclizing agent used. It is an effective hydride ion acceptor, and Siemiatycki [3], by using it, first obtained pyrylium salts containing a number of aromatic substituents. The mechanism is:



Removal of a hydride ion from the tertiary carbon atom of the diketone gives rise to the carbonium ion I, which is stabilized by splitting off a molecule of water from the enol form of the diketone to give the pyrylium salt II, in which the charge is delocalized in the ring.

Table 2

Properties of Pyrylium Salts Synthesized

| Experiment No. | Starting 1, 5-diketone | Pyrylium salt | Mp, °C | $R_f^*$ (gypsum) | γ, cm⁻¹ | Formula | Found, % | | | | Calculated, % | | | | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | C | H | C1 | S | C | H | C1 | S | |
| 1 | 1, 3-Dibenzoyl-2-(1'-methyl-3'-indolyl) propane | 2, 6-Diphenyl-4-(1'-methyl-3'-indolyl) pyrylium perchlorate | 207—8 resinification | 0.14 | 1633<br>1584<br>1529 | $C_{26}H_{20}NO_5Cl$ | 67.97<br>68.11 | 4.32<br>4.37 | 7.07<br>7.27 | —<br>— | 67.68 | 4.33 | 7.70 | — | 82.5 |
| 2 | 1, 3-Dibenzoyl-2-(1'-methyl-2'-α-pyrryl) propane | Mixture of two salts | — | 0.06<br>0.20 | — | — | — | — | — | — | — | — | — | — | — |
| 3 | 1, 3-Dibenzoyl-2-(1'-methyl-3'-indazolyl) propane | 2, 6-Diphenyl-4-(1'-methyl-3'-indazolyl) pyrylium perchlorate | 311 | 0.07 | 1626<br>1581<br>1510 | $C_{25}H_{19}N_2O_5Cl$ | 64.56<br>64.58 | 4.24<br>4.28 | 8.18<br>8.01 | — | 64.93 | 4.11 | 7.68 | — | 83 |
| 4 | 1, 3-Dibenzoyl-2-(α-thienyl) propane | Mixture of two salts | — | 0.14<br>0.53 | 1623<br>1581<br>1511 | — | — | — | — | — | — | — | — | — | |
| 5 | 1, 3-Di(α-thenoyl)-2-phenylpropane | 2, 6-Di(α-thienyl)-4-phenylpyrylium perchlorate | 277 | 0.18 | 1618<br>1596<br>1517 | $C_{19}H_{13}O_5S_2Cl$ | 54.88<br>54.60 | 3.29<br>3.23 | 8.21<br>8.14 | 14.60<br>14.72 | 54.28 | 3.09 | 8.45 | 15.2 | 50 |
| 6 | 1, 3-Di(α-thenoyl)-2-(α-thienyl) propane | 2, 6-Di(α-thienyl)-4-(α-trityl-α'-thienyl) pyrylium perchlorate | 192 | 0.40 | 1618<br>1526 | $C_{36}H_{25}ClO_5S_3$ | 64.88<br>64.97 | 4.06<br>4.02 | 4.91<br>4.78 | 13.90<br>13.81 | 64.67 | 3.74 | 5.31 | 14.36 | Низк. |
| 7 | 1, 3-Di(α-furoyl)-2-phenylpropane | 2, 6-Di(α-furyl)-4-phenylpyrylium perchlorate | 250 | 0.36 | 1643<br>1595<br>1511 | $C_{19}H_{13}O_7Cl$ | 58.92<br>59.04 | 3.61<br>3.70 | 8.69<br>8.81 | — | 58.76 | 3.35 | 9.13 | — | 31.7 |
| 8 | 1, 3-Dibenzoyl-2-(α-selenienyl) propane | Mixture of two salts | — | 0.16<br>0.44 | 1622<br>1580<br>1512 | — | — | — | — | — | — | — | — | — | |

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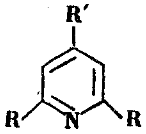
* Solvent benzene: chloroform = 5 : 6

Almost always, brief boiling of 1, 5-diketones with slight excess of triphenylmethyl perchlorate in acetic acid gave the corresponding pyrylium salt. Only the diketone prepared by condensing acetophenone with picolinaldehyde is not cyclized to a pyrylium salt, apparently because of the formation of a salt at the nitrogen of the pyridine ring (Table 2).

Table 3

Characteristics of the Pyridines Synthesized



| Expt. No. | R | R′ | Mp, °C | Formula | Found, % | | Calculated,% | |
|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | C | H |
| 1 | Phenyl | 1-Methyl-3-indolyl | 144.5 | $C_{26}H_{20}N_2$ | 86.88<br>87.03 | 5.78<br>5.72 | 86.66 | 5.56 |
| 2 | Phenyl | 1-Methyl-2-pyrrolyl | 138 | $C_{22}H_{18}N_2$ | 85.66<br>85.42 | 6.06<br>6.19 | 85.16 | 5.80 |
| 3 | Phenyl | 5-Trityl-2-thienyl | 212.5 | $C_{40}H_{30}NS$ | 85.67<br>85.70 | 5.33<br>5.40 | 86.03 | 5.51 |
| 4 | 2-Thienyl | Phenyl | 116.5 | $C_{19}H_{13}NS_2$ | 71.49<br>71.30 | 4.08<br>4.01 | 71.42 | 4.07 |
| 5 | 2-Furyl | Phenyl | 128 | $C_{19}H_{13}NO_2$ | 79.72<br>79.64 | 4.72<br>4.65 | 79.45 | 4.53 |

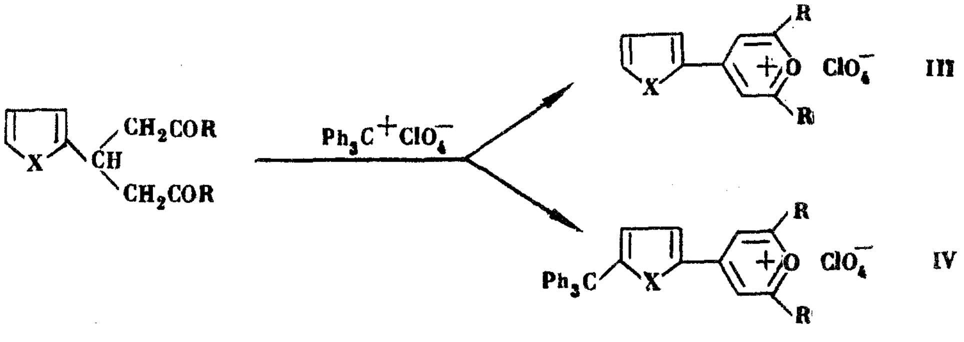
The pyrylium salts synthesized were treated with aqueous ammonia, to give high yields of the corresponding pyridines containing heterocyclic substituents, whose synthesis was quite difficult by other methods. Table 3 gives their properties and analyses.

Cyclization of 1, 5-diketones with a thiophene, pyrrole, or selenophene group in the meso position gave mixtures which thin-layer chromatography on gypsym showed to contain two products. It was quite difficult to separate such mixtures. Only in one case (Table 2, 6) did it prove possible to isolate an individual substance, and the elementary analysis of this corresponded to the tritylation product of the expected pyrylium salt.

The cyclization of diketones containing analogous heterocyclic rings at the 1, 5 position (5 and 7 in Table 2) took place without their being tritylated. This can be ascribed to the deactivating effect of the carbonyl group linked to an α carbon atom of the heterocyclic ring. Hence it is most probable that the trityl substituent is at the free α position of the heterocyclic ring, and situated at the fourth carbon atom of the pyrylium ring of III.

Further treatment of the mixed cyclization products from the diketones with ammonia led to formation of mixed pyridines, in one case an individual tritylated pyridine (Table 3, 3, fractional crystallization) was isolated, in another, an untritylated one (Table 3, 2, chromatography on an $Al_2O_3$ column).

From these results, and also from IR spectra (Table 2) it can be concluded that when such ketones are cyclized with triphenylmethyl perchlorate there is partial tritylation to a mixture of pyrylium salts, one of which is the ordinary cyclization product III, the other a tritylated one IV:



X = NH, S, Se

The alkylating action of triphenylmethyl perchlorate was previously described for a number of active aromatic compounds (aniline, phenol, anisole) [4], but this is the first time that it has been observed with heterocyclic compounds.

To show that the products belonged to the pyrylium salt class, their IR spectra were investigated. It is known that the characteristic absorption maxima in the spectra of pyrylium salts occur in the range 1650-1400 $cm^{-1}$, where there is a group of pyrylium ring and aromatic substituent valence vibrations. In all the present cases there is an intense absorption band at 1643-1622 $cm^{-1}$, belonging to the valence vibrations of C=C bonds of the pyrylium cation [5], while for salts containing phenyl substituents, there are intense absorption bands at 1595-1580 $cm^{-1}$, characteristic of the C=C bonds of the aromatic ring.

## Experimental

Preparation of 1, 5-diketones. A solution of 2 g NaOH in 3 ml water was added to a solution of 0.02 mole aldehyde and 0.06 mole methyl ketone in 25 ml ethanol and the mixture heated for 40 min on a water bath. The precipitate which separated on cooling was filtered off with suction, and recrystallized from ethanol.

1, 3-Dibenzoyl-2-(1-methyl-3-indazolyl) propane was first synthesized by B. A. Tertovyi and M. A. Kazanbieva, who kindly made it available to the authors.

Syntheses of pyrylium salts. A solution of 0.005 mole diketone and 0.006 mole trityl perchlorate in 15-20 ml glacial acetic acid was refluxed for 7-15 min. After cooling, ether was added until the product was completely precipitated. The impure product was filtered off and recrystallized from glacial acetic acid containing one drop of 70% perchloric acid.

Product homogeneity was shown by thin-layer chromatography on gypsum, and structures were found by elementary analysis plus IR spectra. An IKS-14 spectrophotometer with a NaCl prism was used to measure the IR spectra of the compounds synthesized, which were made into a paste with vaseline.

Conversion of pyrylium salts to pyridines. The pyrylium salt was shaken for a few minutes with aqueous ammonia, and the reaction product extracted with ether. The ether extract was evaporated to give an impure product which was recrystallized from ethanol and petrol ether.

The homogeneities of the pyridines were shown by thin-layer chromatography on alumina, and their structures by elementary analysis. 2, 6-Diphenyl-4-(1-methyl-α-pyrryl) pyridine was isolated by column chromatography on $Al_2O_3$.

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