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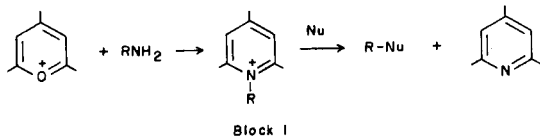
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The preparation is described of some novel pyrylium salts containing ethoxycarbonyl, anthracenyl, and adamantyl substituents.

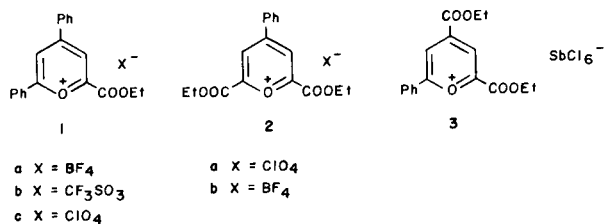
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Pyrylium salts have found extensive use in transforming primary amino groups into different functionalities (Scheme 1) [1]. The efficacy of this process is primarily determined by the ease of the nucleophilic displacement on the pyridinium salt (Step 2, Scheme 1). This, in turn, is heavily dependent on the nature of the substituents on the pyridinium ring and, hence, on those on the pyrylium ring. Especially important are the stereoelectronic effects of the alpha-substituents [1b]. In this context, we now report a study of some novel pyrylium salts.

Scheme 1. Pyrylium Mediated Transformation of Primary Amines

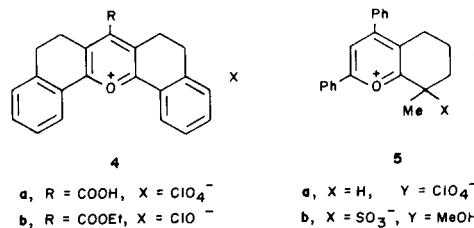


The nature of the substituents chosen here varied from the electron-withdrawing ethoxycarbonyl group (as in **1** to **4**) to the sterically demanding adamantyl and anthracenyl groups (as in **6** and **7**).



the tetrafluoroborate salt **2b**. To increase the yield, antimony pentachloride was tried as the condensing agent; surprisingly, this resulted in an isomeric compound **3** showing two different ethoxycarbonyl groups in the ¹H nmr spectrum. The unsymmetrical nature of compound **3** was also evident from the fact that it showed a pair of doublets (J = 3 Hz) at δ 7.7 and 7.4 for the two pyrylium ring protons; contrast the singlet shown by **2a** at δ 9.35. Compound **3** also shows two *O*-ethyl groups with 3H triplets at 1.33 and 1.20 ppm and 2H quartets at 4.45 and 4.16 ppm (J = 7 Hz); contrast the single *O*-ethyl shown by **2a** at 4.72 (q, 2H) and 1.50 (t, 3H, J = 8 Hz). The proposed structure **3** of this compound is also supported by elemental analysis. The mechanism of formation of **3** probably involves initial condensation between two moles of the pyruvate to give CH₃C(CO₂Et):CHCO₂Et followed by condensation of this with benzaldehyde to produce **3**. Similar reactions are well known in acylations of such compounds [5]; but, this appears to be the first example of such a reaction with an aldehyde.

α-Tetralone reacted with glyoxylic acid to give the pentacyclic acid **4a**, which was esterified to give **4b**.



Ethoxycarbonyl Substituted Pyryliums.

2-Ethoxycarbonyl-4,6-diphenyl pyrylium salts previously prepared are the tetrafluoroborate **1a** [2] and the triflate **1b** [3]. We now find that the corresponding perchlorate salt **1c** can be prepared under milder conditions and in better yields. The symmetric di(ethoxycarbonyl)pyrylium salt **2a** was readily prepared from benzaldehyde and two moles of ethyl pyruvate in presence of perchloric acid, but the yield was lower than that previously reported [4] for

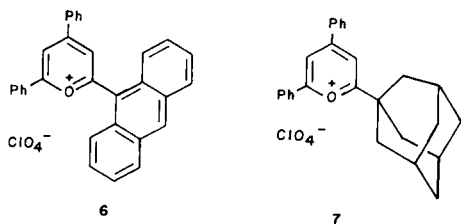
Pyryliums Derived from 2-Methylcyclohexanone.

Benzylideneacetophenone and 2-methylcyclohexanone reacted in the normal way to give the perchlorate **5a** (39%): previously [6], this compound was prepared as the trifluoro-methanesulphonate in 21% yield. Analogous condensation using sulphuric acid-acetic anhydride gave unexpectedly the zwitterionic compound **5b**, the structure of which was supported analytically and spectrally.

The perchlorate **5a** shows the expected strong band at 1080 cm^{-1} (perchlorate anion) in the ir and in the ^1H nmr spectra a doublet at 1.77 ppm (8-methyl, $J = 7\text{ Hz}$) and a multiplet at 3.55 ppm corresponding to 8-CH. The sulphonate betaine **5b** absorbs at 1375 and 1150 cm^{-1} (SO_3^-) in the ir: the 8-methyl protons give a singlet at 2.23 ppm in the ^1H nmr spectrum, and a singlet appears at 4.03 ppm (methanol solvent of crystallisation). All pyrylium sulphonates which have been synthesised so far have been found to contain solvent of crystallisation [7].

Pyrylium Containing Other Bulky α -Substituents.

The preparation of 2-(9-anthracenyl)-4,6-diphenylpyrylium perchlorate from benzylideneacetophenone and 9-acetylanthracene failed at 80 - 100° but succeeded at 40° . A brown by-product was extracted out by hot chloroform. The deep blue-violet anthracenylpyrylium perchlorate **6** shows the expected ir spectrum; in the ^1H nmr spectrum the 3- and 5-pyrylium hydrogen atoms appear as doublets ($J = 1\text{ Hz}$) at 8.93 and 8.50 ppm respectively; the former proton is strongly deshielded by the anthracenyl group; the 10-anthracenyl proton appears as a singlet at 8.83 ppm.



Block 4

2-(1-Adamantyl)-4,6-diphenylpyrylium perchlorate **7** was obtained from 1-acetyladamantane and chalcone under the usual conditions (yield 31%) keeping the temperature below 80° .

EXPERIMENTAL

^1H nmr spectra were recorded with either a Varian EM 360L spectrometer or a Varian A-60A spectrometer using tetramethylsilane as internal standard. Ir spectra were run either as solutions in bromoform using sodium chloride plates on a Perkin Elmer 283B spectrophotometer or as potassium bromide pellets on a Specora 75 IR instrument. Melting points were measured on a Kofler hot stage apparatus and are uncorrected.

2-Ethoxycarbonyl-4,6-diphenylpyrylium Perchlorate (**1c**).

Benzylideneacetophenone (chalcone) [8] (8.32 g, 0.04 mole) and ethyl pyruvate (2.32 g, 0.02 mole) in acetic anhydride (4 ml) were treated dropwise with 70% aqueous perchloric acid (2 ml, 0.024 mole) at 40° . The mixture was stirred for 12 hours at 25° and ethyl acetate (75 ml) added. The precipitated perchlorate (3.3 g, 41%) crystallised from ethanol as yellow prisms; ^1H nmr (trifluoroacetic acid): 9.10 (s, 1 H), 9.00 (s, 1 H), 8.60-7.60 (m, 10 H), 4.80 (q, 2 H), 1.60 (t, 3 H).

Anal. Calcd. for $\text{C}_{20}\text{H}_{17}\text{ClO}_7$: C, 59.3; H, 4.2. Found: C, 59.3; H, 4.2.

2,6-Diethoxycarbonyl-4-phenylpyrylium Perchlorate (**2a**).

Ethyl pyruvate (4.64 g, 0.04 mole) and benzaldehyde (2.12 g, 0.02 mole) in acetic anhydride (4 ml) were treated dropwise with 70% aqueous perchloric acid (2 ml, 0.024 mole) over 2 minutes so that gentle reflux was maintained. After refluxing for 10 minutes followed by 12 hours at 25° , the reaction mixture was poured into ether (200 ml) with vigorous stirring. The pyrylium perchlorate precipitated out (0.9 g, 11%); it crystallised from ethyl acetate:ethanol (4:1) as yellow prisms, mp 167 - 169° ; ir (bromoform): 1745, 1630, 1590, 1400, 1380, 1360, 1080, 770 cm^{-1} ; ^1H nmr (trifluoroacetic acid): 9.35 (s, 2 H), 8.45 (m, 2 H), 7.80 (m, 3 H), 4.72 (q, 4 H), 1.50 (t, 6 H).

Anal. Calcd. for $\text{C}_{17}\text{H}_{11}\text{ClO}_7$: C, 50.9; H, 4.3. Found: C, 50.9; H, 4.3.

2,4-Diethoxycarbonyl-6-phenylpyrylium Hexachloroantimonate (**3b**).

Ethyl pyruvate (4.64 g, 0.04 mole) and benzaldehyde (2.12 g, 0.02 mole) in acetic anhydride (5 ml) were treated dropwise with antimony pentachloride (9 g, 0.03 mole), so that reflux was maintained. The mixture was stirred at 25° for 3 hours. Ether (100 ml) was then added to precipitate the product which was extracted with boiling chloroform (250 ml), filtered off (3.6 g, 28%), and recrystallised from ethyl acetate, to afford large yellow prisms, mp 215 - 217° ; ir (bromoform): 1740, 1620, 1575, 1450, 1340, 1230, 990, 840, 760 cm^{-1} ; ^1H nmr (trifluoroacetic acid): 7.8-6.8 (m, 7 H), 4.7-3.9 (m, 4 H), 1.6-0.9 (m, 6 H).

Anal. Calcd. for $\text{C}_{17}\text{H}_{17}\text{Cl}_6\text{O}_5\text{Sb}$: C, 32.1; H, 2.7; Cl, 3.35. Found: C, 32.1; H, 2.7; Cl, 3.34.

5,6,8,9-Tetrahydro-7-carboxydibenzo[*c,h*]xanthylium Perchlorate (**4a**).

α -Tetralone (10.2 g, 0.07 mole) and glyoxylic acid monohydrate (3.2 g, 0.035 mole) in acetic anhydride (4 ml) was treated dropwise with 70% aqueous perchloric acid (3 ml, 0.036 mole) so that reflux was maintained. After 0.5 hour more refluxing and 3 hours at 25° , the precipitate was filtered off (3 g). Pouring the mother liquor into ether (200 ml) gave further product (total yield 40%). Recrystallisation from acetic acid afforded orange prisms, mp 263 - 265° ; ir (bromoform): 1740, 1700, 1600, 1530, 1470, 1400, 1270, 1000-1200, 750 cm^{-1} ; ^1H nmr (trifluoroacetic acid): 8.35 (m, 3 H), 7.60 (m, 5 H), 3.30 (broad s, 8 H).

Anal. Calcd. for $\text{C}_{22}\text{H}_{17}\text{ClO}_7$: C, 61.6; H, 4.0. Found: C, 61.4; H, 4.2.

5,6,8,9-Tetrahydro-7-ethoxycarbonyldibenzo[*c,h*]xanthylium Perchlorate (**4b**).

The acid **4a** (2.14 g, 0.005 mole), ethanol (200 ml), and 70% aqueous perchloric acid (0.1 ml) was refluxed for 10 hours. Charcoal (0.5 g) was added and after filtration, the clear filtrate was concentrated at $50^\circ/15\text{ mm Hg}$ to 30 ml and poured into ether (200 ml). The product (1.75 g, 76%) crystallised from 2-propanol, as orange plates, mp 175 - 177° ; ir (bromoform): 1730, 1590, 1470, 1380, 1080, 740 cm^{-1} ; ^1H nmr (trifluoroacetic acid): 8.40-7.20 (m, 8 H), 4.20 (q, 2 H), 3.30 (s, 8 H), 1.10 (t, 3 H).

Anal. Calcd. for $\text{C}_{22}\text{H}_{22}\text{ClO}_7$: C, 63.1; H, 4.6. Found: C, 62.8; H, 4.9.

2,4-Diphenyl-8-methyl-5,6,7,8-tetrahydrochromenylium Perchlorate (**5a**).

Chalcone (8.32 g, 0.04 mole) and 2-methylcyclohexanone (2.25 g, 0.02 mole) in acetic anhydride (4 ml) were treated dropwise with 70% aqueous perchloric acid (2 ml, 0.024 mole) so that a reflux was maintained. After refluxing for 1 hour, the reaction mixture was stirred for 3 hours at 25° .

2-Propanol (25 ml) was added and, after 30 minutes, it was added to ether (100 ml). The product (3.2 g, 39%) crystallised from ethanol:acetone (2:1), as yellow prisms, mp 210 - 212° ; ir (bromoform): 1610, 1495, 1460, 1080, 740 cm^{-1} ; ^1H nmr (trifluoroacetic acid): 8.32 (m, 3 H), 7.74 (m, 8 H), 3.55 (m, 1 H), 3.02-2.00 (m, 6 H), 1.77 (d, 3 H).

Anal. Calcd. for $\text{C}_{22}\text{H}_{21}\text{ClO}_5$: C, 65.9; H, 5.3; Cl, 8.8. Found: C, 66.0; H, 5.3; Cl, 8.9.

2,4-Diphenyl-8-methyl-5,6,7,8-tetrahydrochromenylium-8-sulphonate (**5b**).

Chalcone (8.32 g, 0.04 mole) and 2-methylcyclohexanone (2.25 g, 0.02 mole) in acetic anhydride (4 ml) was treated dropwise with 100%

sulphuric acid (1.6 ml, 0.03 mole). After refluxing for 2 hours, the mixture was stirred overnight at 25° and the product was precipitated with acetone. Recrystallisation from methanol gave yellow prisms of the *zwitterion methanolate* (2.15 g, 26%), mp 231-233°; ir (bromoform): 1600, 1475, 1420, 1375, 1215, 1150, 1020, 890, 760 cm^{-1} ; ^1H nmr (trifluoroacetic acid): 8.47 (m, 3 H), 7.75 (m, 8 H), 4.03 (s, 3 H), 3.12-2.48 (m, 6 H), 2.23 (s, 3 H).

Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{O}_3\text{SCH}_3\text{OH}$: C, 66.9; H, 5.8; S, 7.8. Found: C, 67.0; H, 5.9; S, 7.8.

2-(9-Anthracenyl)-4,6-diphenylpyrylium Perchlorate (6).

Perchloric acid (70%, 1 ml) was added dropwise to a mixture of 9-acetylanthracene (3 g, 0.01 mole), chalcone (5 g, 0.02 mole) and acetic anhydride (10 ml), so that the temperature did not exceed 40°. The reaction mixture was stirred overnight at room temperature and poured into ether (200 ml). The crude product (3.45 g, 50%) which precipitated was suspended in chloroform (200 ml) and refluxed for 30 minutes. After cooling, the blue-violet perchlorate separated, it was recrystallised from acetic acid as prisms; mp 293-295°; ir (potassium bromide): 1620, 1590, 1510, 1470, 1270, 1080, 740, 680 cm^{-1} ; ^1H nmr (trifluoroacetic acid) 8.93 (d, 1 H), 8.83 (s, 1 H), 8.50 (d, 1 H), 8.4-7.5 (m, 18 H).

Anal. Calcd. for $\text{C}_{31}\text{H}_{21}\text{ClO}_5$: C, 73.1; H, 4.1. Found: C, 72.9; H, 3.9.

2-(1-Adamanty)-4,6-diphenylpyrylium Perchlorate (7).

Perchloric acid (70%, 1.5 ml) was added dropwise to a mixture of 1-acetyladamantane (2.5 g, 0.014 mole), chalcone (6 g, 0.028 mole) and acetic anhydride (10 ml) so that the temperature did not exceed 80°. The

reaction mixture was stirred overnight at room temperature, filtered off, washed with acetic acid, methanol and ether and recrystallised from acetic acid as yellow prisms (2 g, 31%), mp 295-297°; ir (potassium bromide): 2900, 2840, 1620, 1590, 1500, 1450 m, 1270, 1080, 860 60, 680 cm^{-1} ; ^1H nmr (trifluoroacetic acid): 8.75 (s, 1 H), 8.5-7.75 (m, 11 H), 2.4 (broad s, 9 H), 2.0 (broad s, 6 H).

Anal. Calcd. for $\text{C}_{27}\text{H}_{27}\text{ClO}_5$: C, 69.4; H, 5.8. Found: C, 69.5; H, 5.9.

REFERENCES AND NOTES

- [1a] A. R. Katritzky, *Tetrahedron*, **36**, 679 (1980); [b] A. R. Katritzky and C. Marson, *Angew. Chem., Int. Ed. Engl.*, **23**, 420 (1984).
- [2] A. R. Katritzky, A. Chermprapai, R. C. Patel, and A. Tarraga-Tomas, *J. Org. Chem.*, **47**, 492 (1982).
- [3] A. R. Katritzky, N. Dabbas, R. C. Patel, and A. J. Cozens, in preparation.
- [4] A. R. Katritzky, A. Prout, B. J. Agha, and M. Alajarin-Ceron, *Synthesis*, 959 (1981).
- [5] A. T. Balaban, W. Schroth, and G. Fischer, *Adv. Heterocycl. Chem.*, **10**, 241 (1969).
- [6] A. R. Katritzky and R. Awartani, *Tetrahedron*, **38**, 2505 (1982).
- [7] A. R. Katritzky, Y. Yang, B. Gabrielsen, and J. Marquet, *J. Chem. Soc., Perkin Trans. II*, 857 (1984).
- [8] A. I. Vogel, "Textbook of Practical Organic Chemistry", 4th Ed, Longman, London, 1978, p 796.