

The Reactions of Some Pyranilydeneiminium Salts With Amines. Part I.

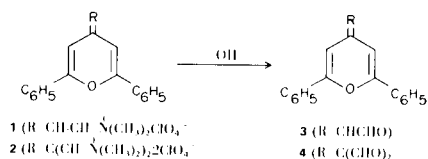
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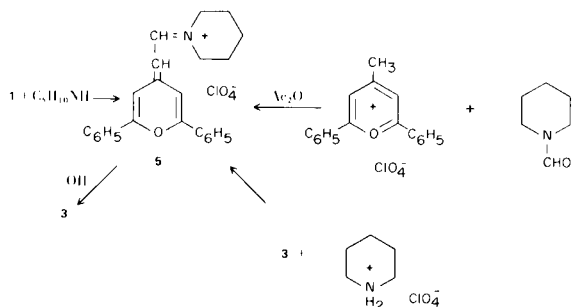
The iminium salt, *N,N*-dimethyl-*N*-[2-(2,6-diphenyl-4*H*-pyran-4-ylidene)ethylidene]iminium perchlorate (**1**), reacts with secondary amines, such as piperidine, by exchanging the dimethyl-amino function for a piperidine. Primary amines react with **1** to give 1-alkyl-2-phenyl-4-phenacylidene-1,4-dihydropyridines. The bisiminium salt, *N,N,N',N'*-tetramethyl-*N,N'*-[2-(2,6-diphenyl-4*H*-pyran-4-ylidene)-1,3-propanediylidene]bis(iminium perchlorate) (**2**), reacts with ammonia to give 3,6-diphenylcopyrine and with primary amines to give the corresponding *N,N'*-dialkyl quaternary copyrines. The salt **2** reacts with secondary amines with exchange of the dimethylamino groups of **2** by the secondary amine and addition of the amine at the 2-position of the pyran ring.

The preparation and hydrolysis of the iminium salts **1** and **2** have been described previously (1). These salts gave the aldehydes **3** and **4** on alkaline hydrolysis.

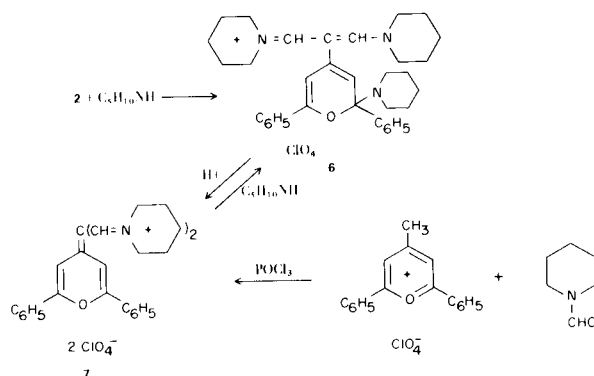


The present work describes the reactions of **1** and **2** with amines.

The salt **1** reacted with secondary amines, *e.g.*, piperidine, simply by exchange of the dimethylamino moiety by piperidine to give **5**. This reaction is characteristic of iminium salts (2). Compound **5** was also prepared from 4-methyl-2,6-diphenylpyrylium perchlorate and *N*-formylpiperidine, as well as by the reaction of the aldehyde **3** with piperidinium perchlorate in methanol. Alkaline hydrolysis of **5** gave the aldehyde **3**.

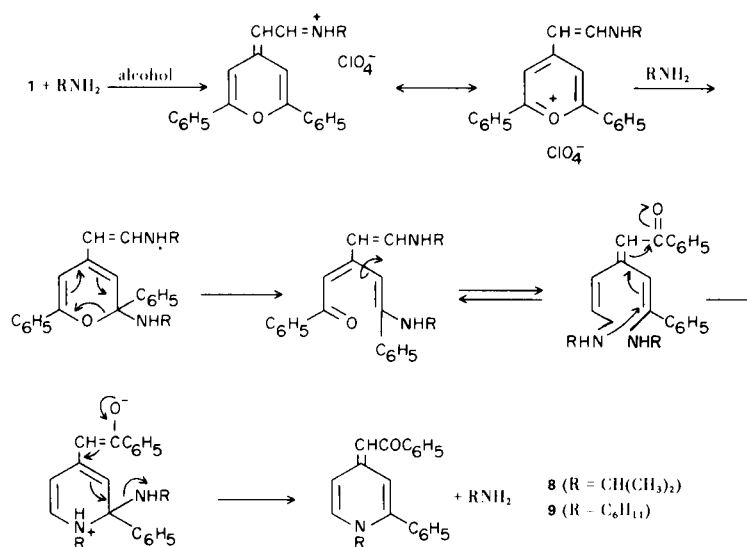


The bisiminium salt **2** reacted with piperidine to give **6** as the result of amine exchange plus the addition of a third mole of piperidine. This structure was assigned because addition of perchloric acid to **6** formed **7**, which was also synthesized from 4-methyl-2,6-diphenylpyrylium perchlorate and *N*-formylpiperidine in the presence of phosphoryl chloride. The addition of piperidine to **7** yielded **6**. These transformations do not exclude the possibility that the tris-adduct is a valence isomer of **6** in which the pyran ring has cleaved to form a ketodienamine.

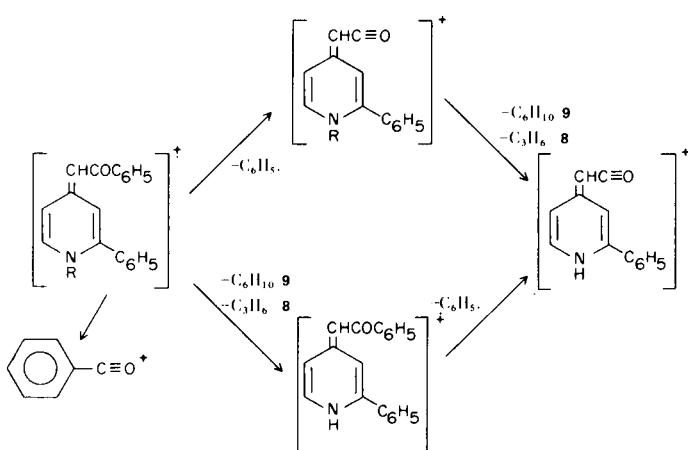


The iminium salt **1** reacted with the primary amines, isopropylamine and cyclohexylamine, to give products **8** and **9**, which are the result of a rearrangement of the pyran ring (3). The formation of **8** and **9** are represented in a stepwise fashion in Scheme I, and the reaction sequence is seen to be similar to those proposed for the reaction of primary amines with other methylenepyran bearing electron-withdrawing substituents on the methylene group (4).

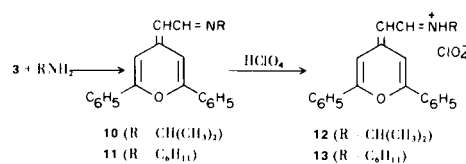
SCHEME I



SCHEME II

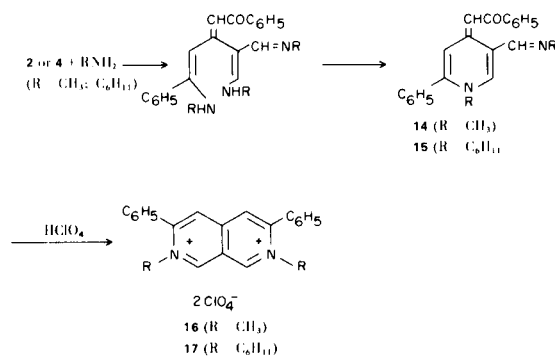


SCHEME III



The bisiminium salt **2** reacted with primary amines to give a very interesting new class of compounds, the diquaternarized copyrines. For example, methylamine and cyclohexylamine reacted with **2** to give the dihydro-pyridine derivatives **14** and **15**, which, on treatment with perchloric acid in alcohol, gave the Q salts **16** and **17**. Compounds **14** and **15** were obtained in quantitative yield when the bisaldehyde **4** was used in place of **2**. A reaction sequence for these reactions is shown in Scheme IV, but most of the details are omitted, since the reaction path is very similar to that shown in Scheme I.

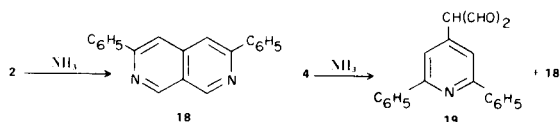
SCHEME IV



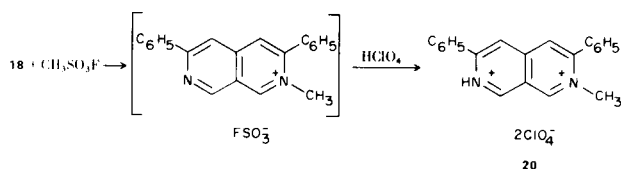
The assignment of structures **8** and **9** is based on the mass spectral cracking pattern, Scheme II, and the nmr spectra (for the values and relative intensities, see the experimental section).

The nmr data are given in the experimental section and are straightforward. The possibility that the structures of the products obtained from the reaction of **1** and the primary amines were **10** and **11** rather than **8** and **9** was eliminated by synthesizing **10** and **11** (see Scheme III) and showing that the two classes of compounds have very different physical properties. The structures of **10** and **11** were confirmed by protonating them to give the iminium salts **12** and **13**, which were shown to have electronic spectra similar to those of **1**.

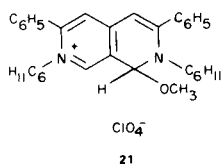
If aqueous ammonia was substituted for the primary amine in the reaction with **2**, the product was 3,6-diphenylcopyrine (**18**). However, the bisaldehyde **4** reacted with ammonia to give only a small amount of **18**, the main product being the pyridine derivative **19**.



Methylation of **18** with methyl fluorosulfonate gave the monoquaternized copyring, which was isolated as the protonated bisperchlorate **20**.



The reactions of **16** and **17** have not yet been examined, but it has been noted that, as expected, the compounds are extremely sensitive to nucleophilic attack. For example, recrystallization of **17** from methanol gave the adduct **21**. When **16** and **17** were dissolved in acetonitrile, a large change in the electronic absorption spectra



took place in comparison to the spectra in chloroform or acidic media, but no attempt was made to isolate products.

The structural assignments of salts **16**, **17**, and **20** were based mainly on the nmr spectra, which are recorded in Table I.

It was interesting that all of the protons on the heterocyclic rings exchanged with deuterium oxide. Exchange of a proton that is ortho to a quaternized heteroatom is common, but exchange of a hydrogen in the meta-position is unusual, although it has been reported in the case of pyrylium salts (**5**).

EXPERIMENTAL (6)

N-[2-(2,6-Diphenyl-4*H*-pyran-4-ylidene)ethylidene]piperidinium Perchlorate (**6**).

(a) A mixture of 3 g. of **1**, 3 ml. of piperidine, and 15 ml. of methyl alcohol was heated on a steam bath for 5 minutes, cooled, and the solid was collected and crystallized from nitromethane giving 2.7 g. of **5**, m.p. 295-296°. The λ_{max} ($\epsilon \times 10^{-3}$) are 250 (16.0), 275 (10.0), 335 (22.0), 422 (58.5), and 448 nm. (48.7).

Anal. Calcd. for $\text{C}_{24}\text{H}_{24}\text{ClNO}_5$: C, 65.3; H, 5.5; N, 3.2. Found: C, 65.1; H, 5.7; N, 3.3.

(b) A solution of 2.5 g. of 4-methyl-2,6-diphenylpyrylium perchlorate, 3 ml. of *N*-formylpiperidine, and 12 ml. of acetic anhydride was refluxed for 3 hours, chilled, and the solid was collected and recrystallized yielding 2.2 g. of **5** with a m.p. and ir that are identical with those of the material obtained by method (A).

(c) A mixture of equivalent amounts of **3** and piperidinium perchlorate in alcohol was refluxed for 12 minutes and worked up as described in Method (a) to give a quantitative yield of **5**.

N-[2-(2,6-Diphenyl-3-piperidine-2*H*-pyran-4-yl)-3-piperidinoallylidene]piperidinium Perchlorate (**6**).

A mixture of 3 g. of **2**, 10 ml. of piperidine, and 50 ml. of methyl alcohol was refluxed for 3 hours, chilled, and the solid was collected and crystallized from methyl alcohol; yield 2.9 g.; m.p. 149-150°. The λ_{max} ($\epsilon \times 10^{-3}$) are 260 (15.0), 320 (34.0), and 437 nm. (30.0).

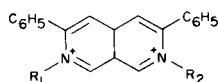
Anal. Calcd. for $\text{C}_{35}\text{H}_{44}\text{ClN}_3\text{O}_5$: C, 67.6; H, 7.1; N, 6.7. Found: C, 67.9; H, 7.3; N, 6.5.

N,N'-[2-(2,6-Diphenyl-4*H*-pyran-4-ylidene)-1,3-propanediylidene]bis(piperidinium Perchlorate) (**7**).

(a) To 20 ml. of cold *N*-formylpiperidine was added 5 ml. of phosphoryl chloride followed by 5 g. of 4-methyl-2,6-diphenylpyrylium perchlorate. The solution was heated on a steam bath

TABLE I

Nmr Chemical Shifts δ ppm in Trifluoroacetic Acid



$\text{R}_1 = \text{R}_2 = \text{CH}_3$

CH_3 , 4.47 (S, 6H)

Aromatic, 7.58 (S, 10H)

H_4 and H_5 , 8.39 (S, 2H)

H_1 and H_8 , 10.2 (S, 2H)

$\text{R}_1 = \text{R}_2 = \text{C}_6\text{H}_{11}$

C_6H_{11} , 1.5-2.0 (M, 22H)

Aromatic, 7.65 (S, 10H)

H_4 and H_5 , 8.42 (S, 2H)

H_1 and H_8 , 10.3 (S, 2H)

$\text{R}_1 = \text{H}; \text{R}_2 = \text{CH}_3$

CH_3 , 4.60 (S, 3H)

Aromatic, 7.77-8.27 (M, 10H)

H_4 , 8.66 (S, 1H)

H_5 , 8.93 (S, 1H)

H_1 , 10.5 (S, 1H)

H_8 , 10.6 (S, 1H)

for ½ hour, poured into 100 ml. of methyl alcohol, and 5 ml. of 70% perchloric acid was added. The mixture was chilled and the solid was collected and crystallized from formic acid; m.p. 248-249°; yield 4.6 g. The λ max ($\epsilon \times 10^{-3}$) are 268 (16.3), 358 (31.9), and 438 nm. (48.4).

Anal. Calcd. for $C_{30}H_{34}Cl_2N_2O_9$: C, 56.6; H, 5.3; N, 4.4; Cl, 11.0. Found: C, 56.7; H, 5.1; N, 4.5; Cl, 10.8.

(b) A solution of 1 g. of **6** in 25 ml. of alcohol was treated with 1 ml. of 70% perchloric acid giving 1 g. of **7**, m.p. 248-249°.

1,4-Dihydro-4-phenacylidene-2-phenyl-1-isopropylpyridine (**8**).

A mixture of 2 g. of **1**, 3 ml. of isopropylamine, and 75 ml. of methylene chloride was stirred for 1 hour. The solution was shaken with water and the organic phase was evaporated under vacuum. The residue was extracted with 75 ml. of boiling toluene, the toluene solution was cooled to room temperature, and the solution was decanted from some gum that separated. The solution was diluted with a little petroleum ether, and after standing for an hour, it was again decanted from some gum. The process was repeated until the addition of petroleum ether caused a solid to separate. The mixture was then chilled in a deep freeze and the solid was collected and crystallized from ethyl acetate yielding 1.1 g. of **8**, m.p. 202-203°. The nmr spectrum in deuteriochloroform shows the following absorptions: CH_3 , δ 1.3 (D, 6H); Me_2CH , 4.25 (quintet, 1H); $CHCO$, δ 6.07 (S, 1H); and aromatic, δ 7.2-8.05 ppm (M, 12H). The mass spectrum shows the following peaks: 315 (100) M^+ ; 272 (50) $M-CH(CH_3)_2$; 238 (36) $M-C_6H_5$; 196 (97) 238 $-CH_3CH=CH_2$; 105 (11) C_6H_5CO . The λ max ($\epsilon \times 10^{-3}$) are 249 (13.0) and 423 nm. (43.5).

Anal. Calcd. for $C_{22}H_{21}NO$: C, 83.8; H, 6.7; N, 4.4. Found: C, 83.6; H, 6.8; N, 4.1.

1-Cyclohexyl-1,4-dihydro-4-phenacylidene-2-phenylpyridine (**9**).

A solution of 3 g. of **1** and 12 ml. of cyclohexylamine was heated on a steam bath for 1 hour and the excess amine was removed *in vacuo*. The residue was dissolved in pyridine and the solution was diluted with water giving a solid which was recrystallized from toluene; m.p. 169-170°; yield 2.4 g. The mass spectrum shows: 355 (100) M^+ ; 354 (14) $M-1$; 278 (10) $M-C_6H_5$; 273 (55) $M-C_6H_{10}$; 196 (100) 273 $-C_6H_5$; 105 (10) C_6H_5CO . The λ max ($\epsilon \times 10^{-3}$) are 250 (13.5) and 425 nm. (43.8).

Anal. Calcd. for $C_{25}H_{25}NO$: C, 84.5; H, 7.1; N, 3.9. Found: C, 84.4; H, 7.1; N, 3.9.

4-(2-Isopropylimino-1-ethylidene)-2,6-diphenyl-4H-pyran (**10**).

A mixture of 0.5 g. of **3**, 5 ml. of alcohol, and 3 ml. of isopropylamine was refluxed for 5 minutes, diluted with 8 ml. of water, chilled, and the solid crystallized from ligroin (b.p. 100-115°) yielding 0.3 g. of **10**, m.p. 114-115°. The mass spectrum shows: 315 (60) M^+ ; 314 (17) $M-1$; 300 (100) $M-CH_3$; 298 (28) $M-OH$; 259 (53) $M-(CH_3)_2C=N$; 210 (9.3) $M-C_6H_5CO$; 105 (40) C_6H_5CO . The λ max ($\epsilon \times 10^{-3}$) are 252 (15.8), 276 (20.0), and 348 nm. (29.0).

Anal. Calcd. for $C_{22}H_{21}NO$: C, 83.8; H, 6.7; N, 4.4. Found: C, 83.7; H, 6.6; N, 4.5.

4-(2-Cyclohexylimino-1-ethylidene)-2,6-diphenyl-4H-pyran (**11**).

A mixture of 2 g. of **3**, 2 ml. of cyclohexylamine, and 10 ml. of alcohol was refluxed for 30 minutes, chilled, and the solid was crystallized from alcohol yielding 2.2 g. of **11**, m.p. 174-175°. The nmr spectrum (deuteriochloroform) shows: cyclohexyl, δ 1.68 (M, 10H); $=CH-CN$, δ 5.67 (D, 1H, 19Hz); H_5 , δ 4.53 (S, 1H);

H_3 , δ 6.85 (S, 1H); and $-CH=N$, δ 8.34 ppm (S, 1H, 19Hz). The mass spectrum shows: 355 (75) M^+ ; 354 (27) $M-1$; 338 (30) $M-OH$; 259 (100) $M-N=C_6H_{10}$; 250 (15) $M-C_6H_5CO$; 246 (18) $M-CHN=C_6H_{10}$; 233 (20) $M-CH=CHN=C_6H_{10}$; 105 (80) C_6H_5CO . The λ max ($\epsilon \times 10^{-3}$) are 255 (14.5), 278 (18.5), and 350 nm. (48.0).

Anal. Calcd. for $C_{25}H_{25}NO$: C, 84.5; H, 7.1; N, 3.9. Found: C, 84.5; H, 7.3; N, 3.6.

N-[2-(2,6-Diphenyl-4H-pyran-4-ylidene)ethylidene]isopropylammonium Perchlorate (**12**).

A solution of 0.1 g. of **10**, 5 drops of 70% perchloric acid, and 2 ml. of alcohol was allowed to stand overnight and the solid was collected, m.p. 175-176°. The λ max ($\epsilon \times 10^{-3}$) are 250 (12.5), 267 (12.7); 335 (16.7), 422 (40.5), and 441 nm. (38.0).

N-[2-(2,6-Diphenyl-4H-pyran-4-ylidene)ethylidene]cyclohexylammonium Perchlorate (**13**).

This compound was prepared from **11** by the procedure described for **12**; m.p. 214-215°. The λ max ($\epsilon \times 10^{-3}$) are 250 (12.9), 268 (12.9), 335 (16.7), 420 (40.8), and 440 nm. (38.1).

Anal. Calcd. for $C_{25}H_{26}ClNO_5$: C, 65.9; H, 5.7; N, 3.1. Found: C, 65.6; H, 5.8; N, 2.9.

4-Phenacylidene-1,4-dihydro-1-methyl-5-methyliminoethyl-2-phenylpyridine (**14**).

(a) A mixture of 0.01 mole of **2**, 5 ml. of 40% aqueous methylamine, and 20 ml. of alcohol was refluxed for 1 hour, chilled, and the solid was collected and crystallized from alcohol to give a 69% yield of **14**, m.p. 187-188°.

(b) A solution of 2 g. of **4**, 10 ml. of 40% aqueous methylamine, and 20 ml. of alcohol was refluxed for 1 hour, chilled, and the solid was collected and crystallized from alcohol yielding 14 in quantitative yield. The λ max ($\epsilon \times 10^{-3}$) are 255 (16.1) and 420 nm. (28.5).

Anal. Calcd. for $C_{22}H_{20}N_2O$: C, 80.5; H, 6.1; N, 8.5. Found: C, 80.2; H, 6.3; N, 8.8.

4-Phenacylidene-1-Cyclohexyl-1,4-dihydro-5-cyclohexyliminoethyl-2-phenylpyridine (**15**).

(a) Procedure (a) used for the preparation of **14** was employed with cyclohexylamine and ethyl acetate as the solvent. The yield of **15** was 70%, m.p. 175-176° (from pyridine).

(b) Procedure (b) described for **14** was repeated with cyclohexylamine giving **15** in 97% yield. The λ max ($\epsilon \times 10^{-3}$) are 225 (23.2), 255 (18.7), and 425 nm. (36.6). The mass spectrum shows: 464 (0.8) M^+ ; 381 (3.3) $M-C_6H_{11}$; 359 (100) $M-C_6H_5CO$; 299 (8.3) 381 $-C_6H_{10}$; 277 (32) 259 $-C_6H_{10}$; and 105 (25) C_6H_5CO .

Anal. Calcd. for $C_{32}H_{36}N_2O$: C, 82.7; H, 7.8; N, 6.0. Found: C, 82.6; H, 7.6; N, 5.8.

2,7-Dimethyl-3,6-diphenylcopyrinium Diperchlorate (**16**).

A solution of 3 g. of **14**, 20 ml. of methyl alcohol, and 2 ml. of 70% perchloric acid was chilled, and the solid was collected and crystallized from dilute aqueous perchloric acid giving 3.1 g. of **16**, m.p. 240-242° dec. The λ max ($\epsilon \times 10^{-3}$) (run in acetonitrile plus a few drops of perchloric acid) are 280 (15.0), 300 (15.0), and 340 nm. (14.0).

Anal. Calcd. for $C_{22}H_{20}Cl_2N_2O_8$: C, 51.7; H, 3.9; N, 5.5; Cl, 13.9. Found: C, 51.3; H, 4.1; N, 5.5; Cl, 13.6.

2,7-Bis(cyclohexyl)-3,6-diphenylcopyrinium Diperchlorate (**17**).

This compound was obtained in 61% yield by the procedure

described for the preparation of **16** by using cyclohexylamine; m.p. 236-237° dec. (from acetic acid). The λ max ($\epsilon \times 10^{-3}$) (acetonitrile plus perchloric acid) are 238 (45.0), and 270-340 nm. (about 14).

Anal. Calcd. for $C_{32}H_{36}Cl_2N_2O_8$: C, 59.4; H, 5.6; N, 4.3. Found: C, 59.2; H, 5.5; N, 4.2.

3,6-Diphenylcopyrine (**18**).

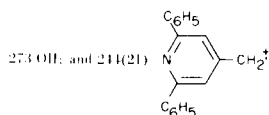
A mixture of 0.01 mole of **2** in 60 ml. of methyl alcohol and 12 ml. of ammonium hydroxide was heated on the steam bath for 3 hours, and after filtering, the filtrate was chilled and the solid was collected and crystallized from alcohol yielding 60% of **18** m.p. 162-163°.

The λ max ($\epsilon \times 10^{-3}$) are 220 (15.0) and 280 nm. (30.0). The addition of perchloric acid to the solution changed the absorption to 310 (37.0) and 355 nm. (24.7). The mass spectrum shows: 282 (100) M^+ ; 281 (35) $M-1$; and 103 (2.2) C_6H_5CN . The nmr (deuteriochloroform) shows: *m* and *p* hydrogens on the phenyls, δ 7.23-7.5 (M, 6H); H_4 and H_5 , δ 7.92 (D, 2H, $J = 2$ Hz); *o*-hydrogens on the phenyls, δ 8.01-8.18 (M, 4H); H_1 and H_8 δ 9.34 ppm (D, 2H, $J = 2$ Hz).

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.1; H, 5.0; N, 9.9. Found: C, 85.0; H, 5.2; N, 9.8.

4-Diformylmethyl-2,6-diphenylpyridine (**19**).

A mixture of 3 g. of **4**, 10 ml. of ammonium hydroxide, and 15 ml. of alcohol was refluxed for 1 hour, chilled, and 0.4 g. of **18** was collected. The filtrate was neutralized with acetic acid and the solid that separated was collected. The solid was dissolved in aqueous sodium carbonate and 0.1 g. of **18** was removed by filtration. The filtrate was acidified with acetic acid and the solid was collected and crystallized from acetic acid giving 2.1 g. of **19** m.p. 231-233°. The mass spectrum shows: 301 (100) M^+ ; 273 (52) $M-CO$; 256 (62).



Anal. Calcd. for $C_{20}H_{15}NO_2$: C, 79.7; H, 5.0; N, 4.7. Found: C, 79.9; H, 5.2; N, 4.7.

2-Methyl-3,6-diphenylcopyrinium diperchlorate (**20**).

A solution of 1 g. of **18**, 2 ml. of methyl fluorosulfonate, and 50 ml. of methylene chloride was heated on a steam bath for ½ hour, cooled, and the solid was collected. The solid was dissolved in hot acetic acid, 1 ml. of 70% perchloric acid was added, and after cooling, the solid was collected; yield, 1.2 g., m.p. 308-309°. The λ max ($\epsilon \times 10^{-3}$) in acetonitrile plus perchloric acid are 280 (18.0), 300 (21.8), and 345 nm. (21.2).

Anal. Calcd. for $C_{21}H_{18}Cl_2N_2O_8$: C, 50.7; H, 3.6; Cl, 14.3. Found: C, 50.6; H, 3.8; Cl, 14.2.

2,7-Bis(cyclohexyl)-1,2-dihydro-1-methoxy-3,6-diphenylcopyrinium Perchlorate (**21**).

A solution of 2 g. of **17** in 2.5 ml. of hot pyridine was diluted with water until a solid separated. The solid was collected and crystallized from methanol giving 1.4 g. of **21**, m.p. 173-174°.

Compound **21** was also obtained by boiling **17** with methanol, but the yield was much better by the first method. The λ max ($\epsilon \times 10^{-3}$) are 273 (11.6) and 415 nm. (42.0). The nmr spectrum in deuteriochloroform shows: Cyclohexyl, δ 0.67 (M, 22H); CH_3O , δ 3.40 (S, 3H); H_1 , δ 5.80 (S, 1H); H_4 , δ 6.4 (S, 1H); H_5 , δ 7.07 (S, 1H); aromatic, δ 7.41 (broad S, 10H), and H_8 , δ 9.02 ppm (S, 1H).

Anal. Calcd. for $C_{33}H_{39}ClN_2O_5$: C, 68.4; H, 6.8; N, 4.8. Found: C, 68.2; H, 6.8; N, 4.7.

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- (2) D. Beke, C. Szantay, and M. Barczai-Beke, *Ann. Chem.*, **636**, 150 (1960).
- (3) Other primary amines, e.g., methylamine and butylamine, gave noncrystalline products, which have not been characterized.
- (4) J. A. Van Allan, G. A. Reynolds, C. C. Petropoulos, and D. Maier, *J. Heterocyclic Chem.*, **7**, 495 (1970); J. A. Van Allan and G. A. Reynolds, *ibid.*, **8**, 367 (1971).
- (5) A. R. Katritski and C. D. Johnson, *Angew. Chem.*, **79**, 629 (1967).
- (6) The electronic spectra were determined in acetonitrile. The numbers in parenthesis under the mass spectral data refer to relative intensities.