

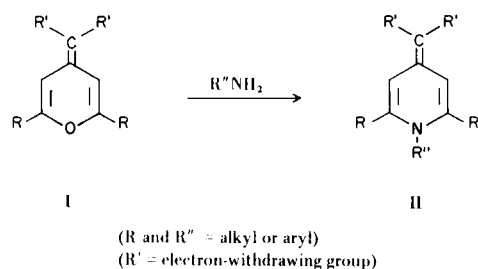
## Reactions of Some 4-Methylene-4*H*-pyran Derivatives with Primary and Secondary Amines

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4-Dicyanomethylene-4*H*-pyrans react with secondary amines to give 2-aminopyridine and 2-pyridone derivatives which, in turn, have been used to prepare copyrine derivatives. These pyrans and primary amines gave copyrine and iminopyridone derivatives in addition to the dicyanomethylene-1,4-dihydropyridines, which had been reported previously. Reaction of cyanocarbamoylmethylene-4*H*-pyrans with secondary amines gave 2-pyrones, and with primary amines, gave copyrines and 1,4-dihydropyridine derivatives.

The literature contains a number of reports (1) that pyrans of Type I react with primary amines to form the corresponding 1,4-dihydropyridine derivatives II.



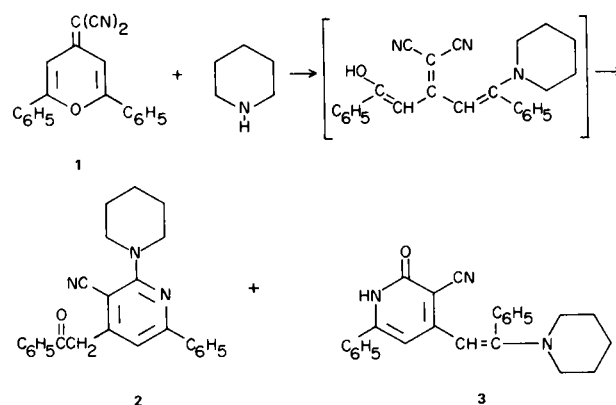
The present paper describes several examples of reactions of I with primary amines that do not proceed in this manner, and some reactions of I with secondary amines that yield pyridine and naphthyridine derivatives which are formed by an interesting series of rearrangements.

### REACTIONS WITH SECONDARY AMINES

When pyran **1** was refluxed with piperidine, two products were isolated which have been assigned structures **2** and **3** on the basis of physical data. These assignments were confirmed by alternate syntheses. Compound **2** was the major product. The overall reaction is shown in Scheme I, and the mechanism is considered later (see Schemes XII and XIII).

The enamine **3** was hydrolyzed with acid to give 3-cyano-4-phenacyl-6-phenyl-2(1*H*)-pyridone (**4**), which had been prepared previously by Hauser, *et al.* (2) by the reaction of 3-cyano-4-methyl-6-phenyl-2(1*H*)-pyridone (**5**) and methyl benzoate in the presence of excess potassium amide. We have repeated this preparation and the product

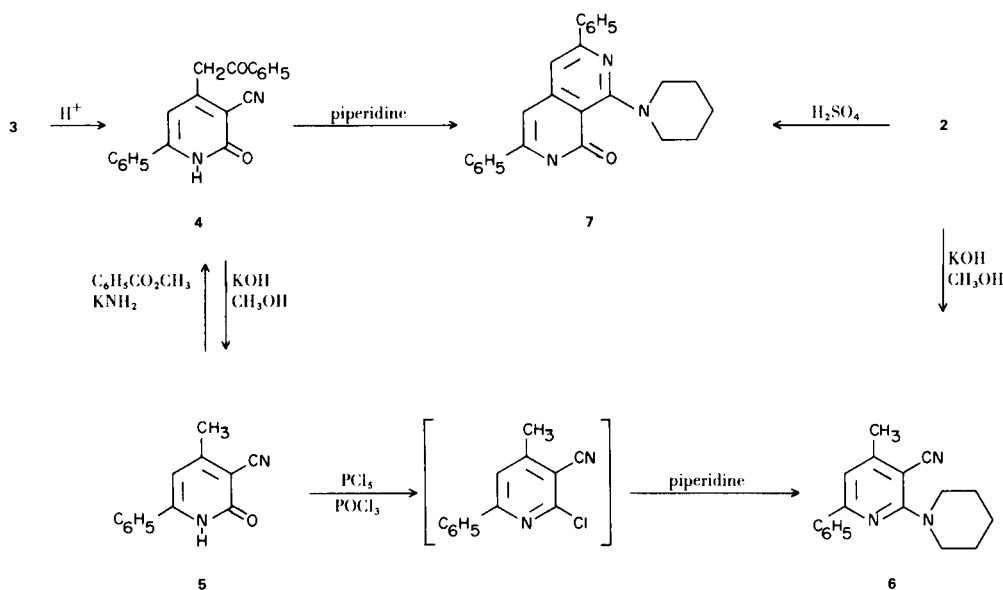
SCHEME I



has been shown to be identical with **4** obtained by the hydrolysis of **3**. The phenacyl group of **2** and that of **4** were hydrolyzed with methanolic potassium hydroxide to give 3-cyano-4-methyl-2-piperidino-6-phenylpyridine (**6**) and **5**, respectively. Compound **4** was reduced with sodium borohydride to give 3-cyano-4-(2-hydroxy-2-phenylethyl)-6-phenyl-2(1*H*)-pyridone, which may be subsequently dehydrated to the styryl derivative. The structure of **6** was established by causing **5** to react with a mixture of phosphorus oxychloride and phosphorus pentachloride and treating the resulting chloropyridine derivative with piperidine to give **6**. Compounds **2** and **4** were further interrelated by treating **4** with piperidine to give the naphthyridine derivative, **7**, which was also formed by treatment of **2** with sulfuric acid (other examples of reactions of these types are described later in the paper).

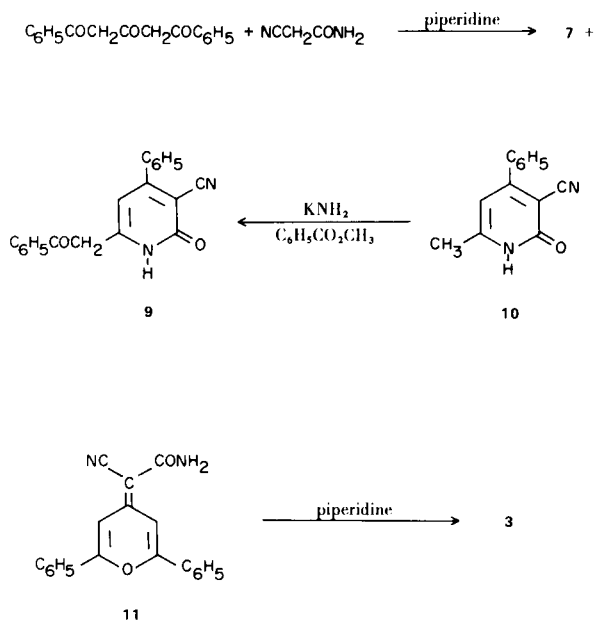
We found that **7** was formed when 1,5-diphenylpentane-1,3,5-trione (**8**) and cyanoacetamide were allowed to react in the presence of piperidine; 3-cyano-6-phenacyl-4-phenyl-2(1*H*)-pyridone (**9**) was also isolated from this reaction. The structure of **9** was confirmed by an inde-

SCHEME II



pendent synthesis from 3-cyano-4-phenyl-6-methyl-2(1*H*)-pyridone (**10**) and methyl benzoate in the presence of potassium amide. The reaction of 4-(cyanocarbonylmethylene)-2,6-diphenyl-4*H*-pyran (**11**) with piperidine gave **3**, in contrast to the results obtained with the triketone (see Scheme III).

SCHEME III



The adjacency of the cyano group and the phenacyl group in compounds such as **2** and **4** leads to some interesting transformations, since nucleophiles attack these

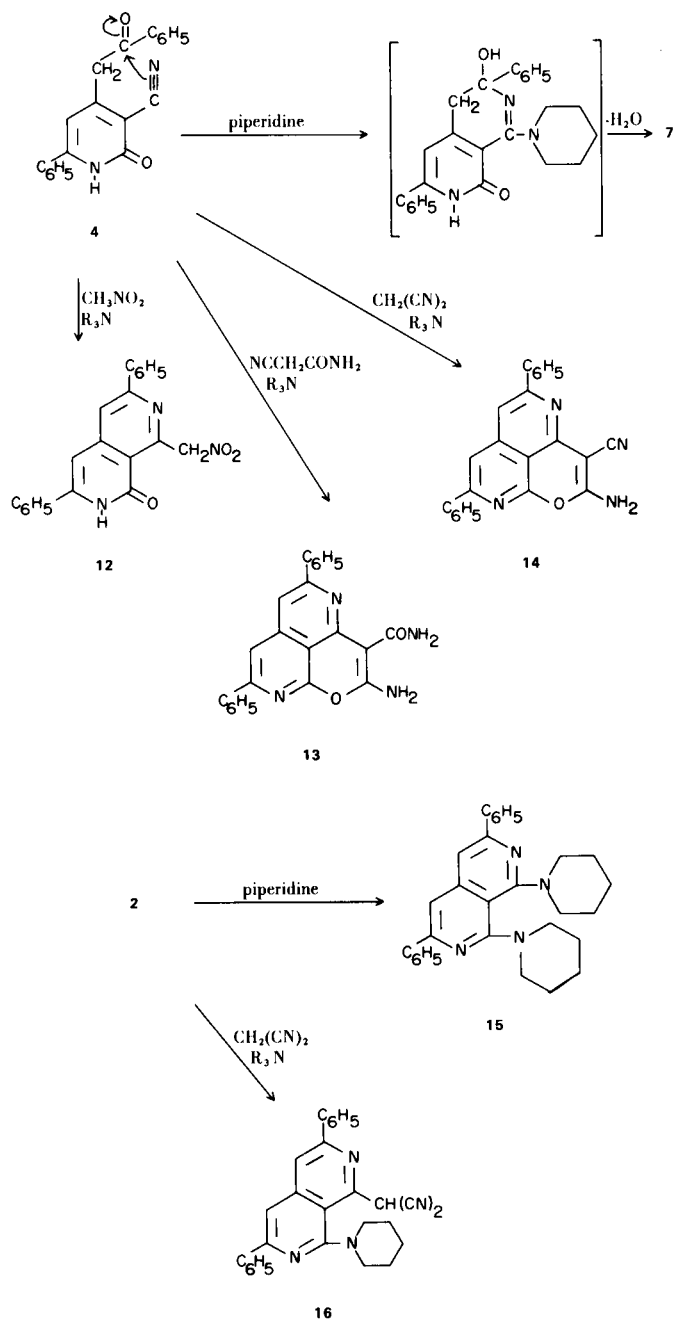
compounds (particularly **4**) with great ease to form naphthyridine derivatives. A few reactions of this type are given in Scheme IV, and the probable mechanism is indicated for the reaction of **4** with piperidine. The tricyclic structure, **13**, was assigned on the basis of the ir spectrum, which shows no absorption in the regions characteristic of the nitrile and pyridone groups but does show absorption for amino and amide groups. In addition, the mass spectrum shows a very strong parent peak with weak fragment peaks, indicative of a compound having considerable aromaticity. The ir and mass spectra also substantiate structure **14** and the nmr spectrum shows an amino group at  $\delta$  7.2 ppm (2H) and no aliphatic protons.

Treatment of the enamine **3** with acid under various conditions has given three products (Scheme V). It has been pointed out (see Scheme II) that acid hydrolysis gave the phenacyl compound **4**. The conditions used in this case consisted in adding dilute hydrochloric acid to a hot solution of **3** in acetic acid so that **4** immediately precipitated from the reaction mixture. If the reaction was carried out in such a manner that **4** did not precipitate, the product was **17**. The reaction of **3** with concentrated sulfuric acid gave **18**.

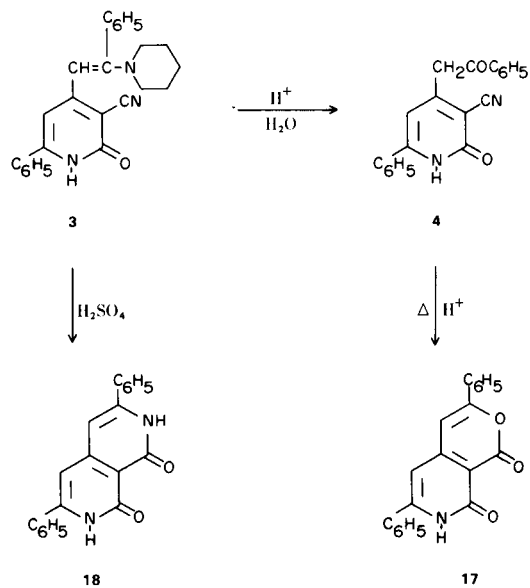
As expected, other secondary amines reacted with **1** in the same manner as piperidine. For example, morpholine and **1** gave the aminopyridine derivative **19** along with a smaller amount of the pyridone **20**.

The reactions of secondary amines with **1** were extended to the pyran derivative **21**. For example, **21** and morpholine gave the naphthyridine **22** (Scheme VII). The structure of **22** was demonstrated by an alternate synthesis.

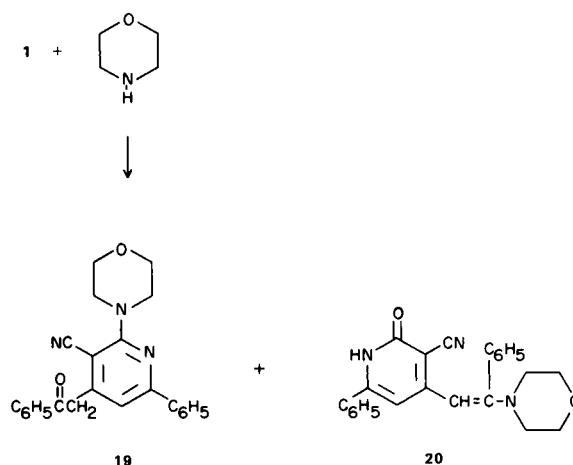
SCHEME IV



SCHEME V



SCHEME VI



*i.e.*, benzylation of 3-cyano-4-methyl-1,6-diphenyl-2(1*H*)-pyridone (**23**) to give **24**, followed by the reaction of **24** with morpholine.

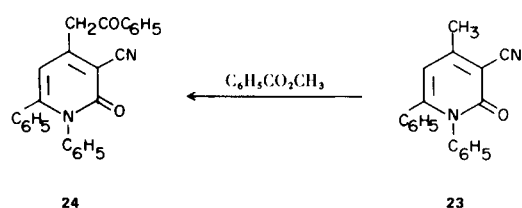
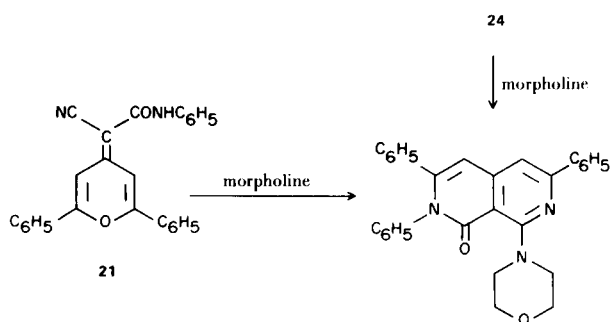
#### REACTIONS WITH PRIMARY AMINES

Methylamine, butylamine and benzylamine react with **1** at steam bath temperature to give a mixture of 1,4-

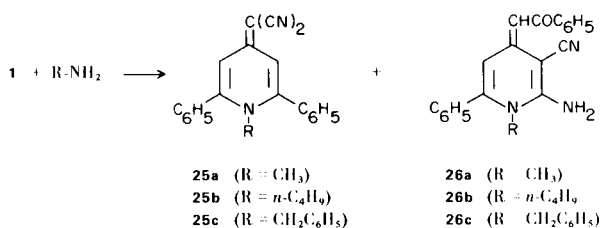
dihydropyridine derivatives **25a-25c** and aminopyridine derivatives **26a-26c** (Scheme VIII). The latter compounds were assigned the designated tautomeric structures on the basis of their nmr spectra (see Experimental).

The three amines react with **1** at higher temperatures (150-180°) to give the products shown in Scheme IX. Under these conditions, the results are different with each amine. It is assumed that **27** was formed from the hydrolysis of **26a** by aqueous methylamine at the elevated temperature. Compound **28** is probably formed from **26c** and benzylamine, since this reaction was shown to take place, but it is interesting that **28** is the sole product in view of the fact that **25c** does not react with refluxing

SCHEME VII

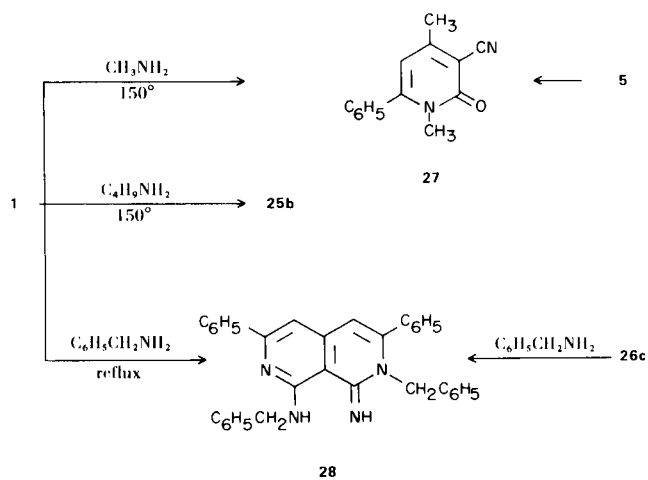


SCHEME VIII



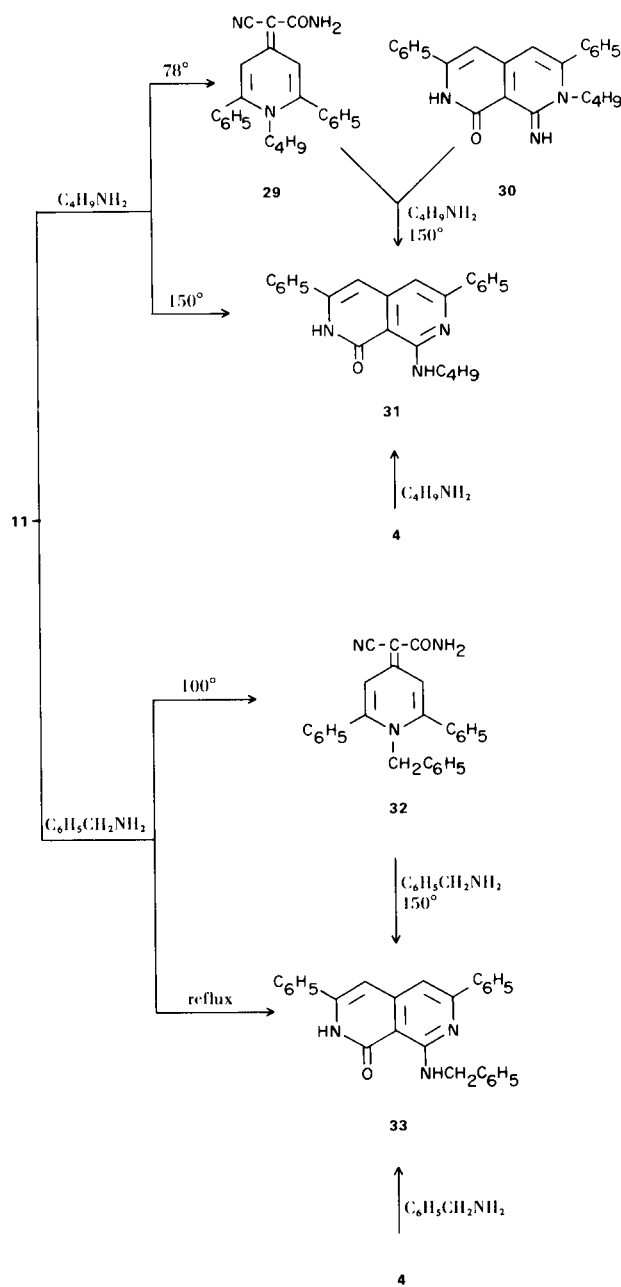
benzylamine. We expected to obtain a copyrine derivative corresponding to **28** from the reaction of **1** with butylamine, but none was isolated.

SCHEME IX



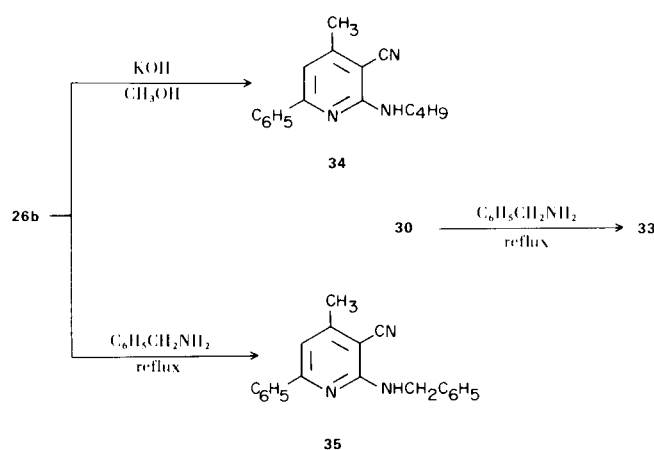
Butylamine and benzylamine react with the cyanoamide derivative **11** to give the products shown in Scheme X. The formation of the products **31** and **33** indicates that Dimroth rearrangements have taken place under the influence of amines at elevated temperatures. The transformation of **29** and **32** to **31** and **33**, respectively, suggests that the former compounds are intermediates, and the isolation of **30** and its transformation to **31** implies that this type of compound can be another intermediate along the reaction path to **31** and **33**.

SCHEME X



Other examples of Dimroth rearrangements which we have encountered are: treatment of **26b** with methanolic potassium hydroxide to give **34** (rearrangement and deacylation); treatment of **26b** with refluxing benzylamine to give **35** (rearrangement, deacylation and amine exchange); and refluxing **30** with benzylamine to give **33** (rearrangement and amine exchange).

SCHEME XI



### ABSORPTION AND MASS SPECTRA

The electronic spectra of the foregoing compounds serve as a convenient guide to the type of material which

is formed. For example, the dihydropyridine derivative **25a** obtained from **1** and methylamine (see Scheme VIII) was also prepared from 4-methoxy-1-methyl-2,6-diphenylpyridinium perchlorate and malononitrile. Its structure being thus confirmed, its electronic spectrum serves as a reference compound for similarly constituted compounds, as shown in Table I.

TABLE I

### Absorption Spectra of Dihydropyridines

Compound Number	$\lambda$ max $m\mu$ ( $\epsilon \times 10^{-3}$ ) in acetonitrile	
<b>25a</b>	263 (14.0)	382 (33.0)
<b>25b</b>	253 (11.0)	373 (36.4)
<b>25c</b>	265 (13.5)	380 (33.1)
<b>29</b>	260 (12.3)	378 (32.3)
<b>32</b>	261 (13.2)	377 (33.0)

The spectra of the phenacylidene derivatives **26a-26c** show a marked pH dependency, as shown in Table II, for **26b**. The other examples gave similar effects, but accurate curves were not run.

TABLE II

### Absorption Spectra of Phenacylidene Compounds

Compound Number	$\lambda$ max $m\mu$ ( $\epsilon \times 10^{-3}$ ) in Solvents Indicated		
	Alcohol	Alcohol + HCl	Alcohol + KOH
<b>26a</b>	246 (12.2)	424 (22.8)	
	304 (8.1)	~440 (21.3)	
	342 (4.9)		
<b>26b</b>	237 (12.8)	420 (22.8)	255 (14.8)
	302 (8.0)	440 (20.8)	305 (6.8)
	345 (5.2)	348 (10.0)	400 (16.2)
			425 (18.6)
<b>27c</b>	248 (12.0)	422 (23.0)	
	303 (7.9)	440 (21.0)	
	348 (5.0)		

The spectra of the copyrines **28**, **31** and **33** closely resemble those of **7**, which indicates that all of these compounds have the same generic structure and, further, that **28**, **31** and **33** do not exist in the imino form. The imino derivative **30** does not conform to this pattern, which is consonant with its different structure.

TABLE III

## Absorption Spectra of Copyrines

Compound Number	$\lambda$ max $m\mu$ ( $\epsilon \times 10^{-3}$ )	Solvent
<b>28</b>	245 (25.0)	acetonitrile
	284 (23.5)	
	375 (16.0)	
<b>31</b>	248 (23.5)	alcohol
	275 (32.0)	
	394 (16.8)	
<b>33</b>	245 (24.0)	chloroform
	277 (32.8)	
	395 (16.6)	
<b>7</b>	255 (27.5)	dichloromethane
	280 (26.0)	
	387 ( 9.8)	
<b>30</b>	255 (28.0)	acetonitrile
	380 (13.3)	

The mass spectra for generic species show a characteristic fragmentation pattern. The parent peaks determine the molecular size of the compound, and the fragment ions are diagnostically useful. For example, in all cases where an imino group is present, a large parent peak minus one mass unit is always present; and the parent peak is more abundant for the more aromatic systems. If the compounds contain butyl or piperidino groups, the fragmentation is dominated by these groups. The significant peaks for some representative pyridine and copyrine derivatives are given in Table IV.

## MECHANISMS OF REACTIONS

A general reaction scheme that accounts for the products that are formed from **1** and primary or secondary amines at lower temperatures is shown in Scheme XII. In order to explain the formation of the small amount of **3** from the reaction of **1** and piperidine, it is assumed that the reaction sequence shown in Scheme XIII competes with the cyclization of **B** to give **C**.

Compound **1** and dry piperidine still gave some **3**, and the addition of a little water caused slightly higher yields of **3**.

A reaction scheme for the reactions of **11** with primary and secondary amines at lower temperatures is given in Scheme XIV.

At higher temperatures (150° and refluxing benzylamine were used in the present work), several examples of the Dimroth rearrangement (**3**) were observed with a primary amine as the base. In some cases, exchange of the amino group occurred. The conversion of **30** to **33** will be used to illustrate a probable reaction sequence for a Dimroth rearrangement with amine exchange.

It should be pointed out that nucleophiles other than amines react with **1** to give pyridine derivatives. For example, **1** and methanolic potassium hydroxide gave **36**, which was hydrolyzed with acid to give **17** and with base to give 3-cyano-2-methoxy-4-methyl-6-phenylpyridine (**37**). The latter compound was also prepared by alkylation of the thallium salt of **5** with methyl iodide.

## EXPERIMENTAL (4)

4-(Dicyanomethylene)-2,6-diphenyl-4H-pyran (**1**).

The preparation of this compound has been described previously (**5**). In addition, the following methods have been used.

(a) A mixture of 2.5 g. of 2,6-diphenyl-4-pyrone, 1 g. of malononitrile, and 7 ml. of phosphorus oxychloride was heated for 2 hours on a steam bath, cooled, poured into 50 ml. of methyl alcohol, and the solid was collected and recrystallized from 1,2,3-trichloropropane to give 2.4 g. (81%) of **1**, m.p. 266-267°.

(b) A mixture of 5.3 g. of 1,5-diphenylpentane-1,3,5-trione, 2 g. of malononitrile, and 5 ml. of phosphorus oxychloride was allowed to react as described in (a) to give **1** in 74% yield. The absorption spectrum of **1** in acetonitrile shows the following:  $\lambda$  max ( $\epsilon \times 10^{-3}$ ): 256 (15.2); 318 (22.1); 376-386 (25.5-28.0);  $\sim 406 m\mu$  (17.0).

3-Cyano-4-phenacyl-6-phenyl-2-piperidinopyridine (**2**).

A mixture of 60 g. of **1** and 200 ml. of piperidine was refluxed for 24 hours and then evaporated to dryness under reduced pressure. The residue was recrystallized from 200 ml. of acetic acid to give 46 g. of **2**, m.p. 168-169°.

The filtrate from the recrystallization was diluted with water to give 5 g. of crude **3**.

The uv absorption of **2** shows the following:  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ): 243 (24.2); 270 (27.7); 360  $m\mu$  (4.3). The nmr spectrum in dimethylsulfoxide  $d_6$  (DMSO- $d_6$ ) shows absorption for the piperidino protons at  $\delta$  3.72 (M, 4H) and  $\delta$  4.2 (M, 6H),  $-\text{CH}_2\text{CO}$  at  $\delta$  4.63 (S, 2H), and aromatic protons at  $\delta$  7.4-8.2 ppm. (M, 11H).

*Anal.* Calcd. for  $\text{C}_{25}\text{H}_{23}\text{N}_3\text{O}$ : C, 78.7; H, 6.1; N, 11.0. Found: C, 78.9; H, 6.2; N, 11.0.

Compound **2** formed a dinitrophenylhydrazone, m.p. 210-211°.

*Anal.* Calcd. for  $\text{C}_{31}\text{H}_{27}\text{N}_7\text{O}_4$ : C, 66.3; H, 4.9; N, 17.5. Found: C, 66.1; H, 5.0; N, 17.8.

3-Cyano-6-phenyl-4-( $\alpha$ -piperidinostyryl)-2(1H)-pyridone (**3**).

A solution of 16.3 g. of 4-(cyanocarbamoylmethylene)-2,6-diphenyl-4H-pyran (**5**) (**11**) in 100 ml. of piperidine was heated to



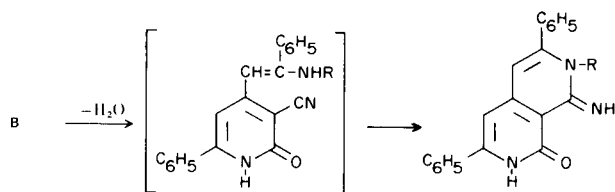
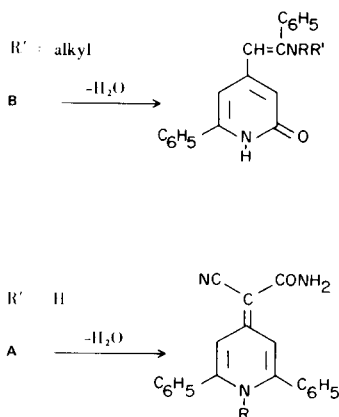
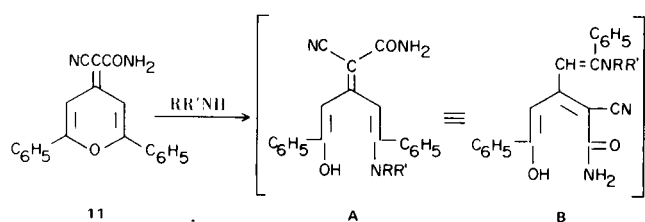
TABLE IV

## Mass Spectral Data

Phenacylidene Pyridine Derivatives	m/e (Relative Intensity)							
	M+	M-H	M-C <sub>6</sub> H <sub>5</sub>	M-C <sub>6</sub> H <sub>5</sub> CO	C <sub>6</sub> H <sub>5</sub> CO	M-CH <sub>3</sub>	M-C <sub>2</sub> H <sub>5</sub>	M-C <sub>3</sub> H <sub>7</sub>
<b>26a</b>	327 (36.2)	326 (67.2)	250 ( 3.1)	222 ( 3.1)	105 (100)	M-CH <sub>3</sub> 353 ( 8.9)	M-C <sub>2</sub> H <sub>5</sub> 340 ( 2.2)	M-C <sub>3</sub> H <sub>7</sub> 326 (20.9)
<b>26b</b>	369 ( 6.7)	368 (16.7)	292 ( 0.3)	264 ( 0.3)	105 (100)	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> 91 (84.8)		M-C <sub>4</sub> H <sub>8</sub> 313 ( 7.6)
<b>26c</b>	403 (29.1)	402 (48.5)	326 ( 1.6)	298 (10.0)	105 (100)			
Copyrine Derivatives	M+	M-H	M-C <sub>7</sub> H <sub>6</sub>	M-C <sub>7</sub> H <sub>7</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> NH	C <sub>6</sub> H <sub>5</sub> CNH	
<b>28</b>	492 (11.2)	491 (11.8)	402 (51.8)	401 (100)	91 (64.7)	106 ( 5.3)	104 ( 8.2)	
<b>30</b>	369 (18.8)	368 (25.0)	M-C <sub>2</sub> H <sub>5</sub> 340 (12.5)	M-C <sub>3</sub> H <sub>7</sub> 326 (32.5)	M-C <sub>4</sub> H <sub>8</sub> 313 (100)	M-C <sub>6</sub> H <sub>5</sub> 292 (18.8)	104 ( 4.5)	
<b>31</b>	369 (50.0)	368 ( 3.3)	340 (67.7)	M-C <sub>3</sub> H <sub>6</sub> 327 (100)	M-C <sub>3</sub> H <sub>7</sub> 326 (83.3)	M-C <sub>4</sub> H <sub>8</sub> 313 (87.7)	104 ( 6.7)	
<b>33</b>	403 (100)	402 (15.6)	M-C <sub>6</sub> H <sub>5</sub> 326 ( 3.9)	...	...	...		C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> NH 106 (13.8)
<b>7</b>	381 (82.6)	380 (10.9)	M-C <sub>5</sub> H <sub>8</sub> 313 (100)	M-C <sub>5</sub> H <sub>9</sub> N 299 (40.0)	298 (18.8)	297 (11.9)	104 ( 4.4)	



SCHEME XIV



separated in a few seconds. The mixture was cooled to room temperature and the solid was collected, washed with alcohol, and recrystallized from acetic acid yielding 4 g. of **4**, m.p. 261-262°.

*Anal.* Calcd. for  $C_{20}H_{14}N_2O_2$ : C, 76.4; H, 4.5; N, 8.9. Found: C, 76.3; H, 4.7; N, 8.6.

A sample of **4** was prepared by the procedure of Hauser (2), and the products by both procedures were shown to be identical by ir and m.p. of a mixture.

As noted previously (2), the absorption spectra of **4** are very sensitive to pH and solvents. For example, we found the following  $\lambda$  max ( $\epsilon \times 10^{-3}$ ): in alcohol 275 (20.0), 353 (17.6), 415  $\mu$  (11.2); alcohol plus a drop of hydrochloric acid 278 (21.6), 381  $\mu$  (24.0) broad; alcohol plus a drop of 10% methanolic potassium hydroxide 252 (18.5), 355 (12.8), 425  $\mu$  (16.7); acetonitrile 247 (22.4), 362  $\mu$  (14.4).

A 1 g. sample of **4** in 20 ml. of 95% ethanol was stirred and 0.5 g. of sodium borohydride was added in several portions. The solution was stirred for 15 minutes, chilled and acidified with dilute hydrochloric acid. Recrystallization of the resulting solid from acetonitrile afforded 0.5 g. of 3-cyano-4-(2-hydroxy-2-phenylethyl)-6-phenyl-2(1H)-pyridone, m.p. 202-203°.

*Anal.* Calcd. for  $C_{20}H_{16}N_2O_2$ : C, 75.9; H, 5.1; N, 8.9. Found: C, 76.1; H, 5.3; N, 8.6.

If care was not taken during the acidification step, the hydroxy

compound was dehydrated to give 3-cyano-6-phenyl-4-styryl-2(1H)-pyridone, m.p. 293-294° from alcohol.

*Anal.* Calcd. for  $C_{20}H_{14}N_2O$ : C, 80.5; H, 4.7; N, 9.4. Found: C, 80.3; H, 5.0; N, 9.1.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are 270 (47.5) and 355  $\mu$  (10.0).

3-Cyano-4-methyl-6-phenyl-piperidinopyridine (**6**).

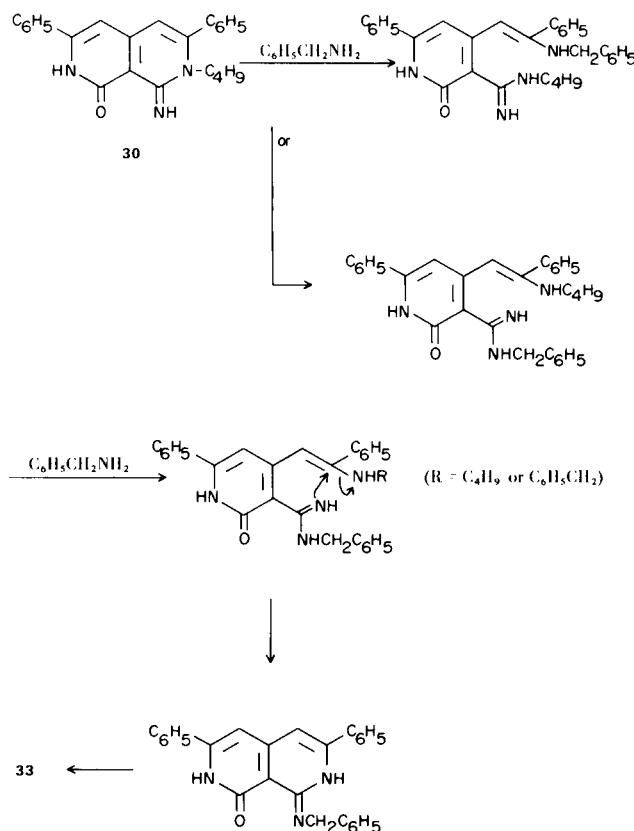
(a) A mixture of 4 g. of **2** and 50 ml. of 10% methanolic potassium hydroxide was refluxed for 3 hours; the solid was removed and recrystallized from butyl alcohol, yielding 2.9 g. of **6**, m.p. 104-105°.

(b) A mixture of 1 g. of 3-cyano-4-methyl-6-phenyl-2(1H)-pyridone (**5**), 2 g. of phosphorus pentachloride and 10 ml. of phosphorus oxychloride was refluxed for 6 hours, evaporated to dryness at reduced pressure, and the viscous residue was poured into a mixture of chloroform and ice water. The chloroform layer was dried (magnesium sulfate) and mixed with 2 ml. of piperidine. The mixture was heated on the steam bath and the chloroform thereby evaporated. The residue was dissolved in hot acetic acid, the solution diluted with water, and the solid was collected and recrystallized from ligroin (b.p. 100-115°) to give 0.6 g. of **6**, m.p. 104-105°.

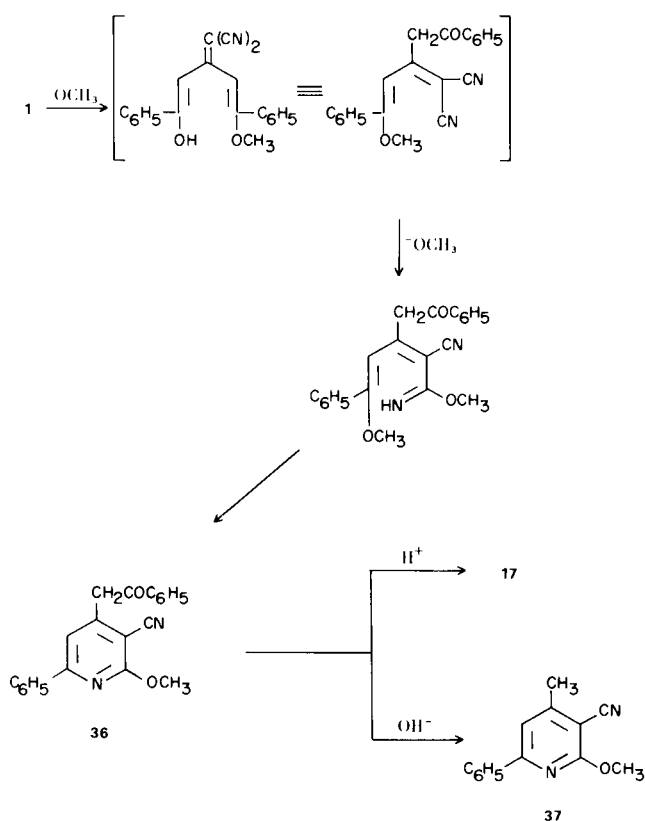
The  $\lambda$  max ( $\epsilon \times 10^{-3}$ ) in acetonitrile are 255 (7.3), 332 (7.8), and 360 (6.5).

*Anal.* Calcd. for  $C_{18}H_{19}N_3$ : C, 78.0; H, 6.9; N, 15.2. Found: C, 78.0; H, 6.8; N, 15.1.

SCHEME XV



SCHEME XVI



### 3,6-Diphenyl-8-piperidino-2H-copyrin-1-one (7).

(a) A mixture of 2 g. of **4** and 10 ml. of piperidine was heated on a steam bath for 1 hour, diluted with water until cloudy, and chilled. The solid was collected and crystallized from ethoxyethanol to give 1.3 g. of **7**, m.p. 237-238°.

(b) A solution of 4 g. of **2** in 10 ml. of concentrated sulfuric acid was heated on the steam bath for 20 hours, poured into water, and the solid was collected and recrystallized; yield 2.8 g., m.p. 237-238°.

The nmr in  $\text{DMSO-d}_6$  shows piperidine protons at  $\delta$  1.62 (M, 4H) and  $\delta$  3.35 (M, 6H), proton in 5-position at  $\delta$  6.75 (S, 1H), and aromatic protons including proton in 4-position at  $\delta$  7.4-8.2 ppm. (M, 11H).

*Anal.* Calcd. for  $\text{C}_{25}\text{H}_{23}\text{N}_3\text{O}$ : C, 78.7; H, 6.1; N, 11.0. Found: C, 78.5; H, 6.3; N, 11.1.

### 3-Cyano-6-phenacyl-4-phenyl-2(1H)-pyridone (9).

(a) A solution of 15.9 g. of 1,5-diphenylpentane-1,3,5-trione and 6 g. of cyanoacetamide in 30 ml. of piperidine was heated at reflux for 2 hours and poured into 75 ml. of methyl alcohol. Recrystallization of the solid from ethanol gave 7.7 g. of **9**, m.p. 237-238°. The mother liquors were poured into 100 ml. of water to give an oil which gradually solidified. The solid was washed with hot alcohol and recrystallized from *o*-dichlorobenzene, yielding 4.1 g. of **9**, m.p. 224-225°.

*Anal.* Calcd. for  $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_2$ : C, 76.4; H, 4.5; N, 8.9. Found: C, 76.4; H, 4.6; N, 8.9.

(b) A mixture of potassium amide (from 2 g. of potassium and 250 ml. of ammonia) and 3 g. of 3-cyano-6-methyl-4-phenyl-2(1H)-pyridone (**6**) (**10**) was stirred for 1 hour, 3 ml. of methyl benzoate

in 10 ml. of ether was added, and the stirring was continued for another hour. The ammonia was allowed to evaporate, water and ether were added to the residue, and the water phase was acidified with hydrochloric acid. The solid was collected and recrystallized twice from ethyl alcohol, yielding 0.5 g. of **9**, m.p. 224-225°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are 238 (32.2), 270 (11.7), 343 (8.9), and 455  $m\mu$  (10.7). The  $\lambda$  max in ethyl alcohol are 242 (27.2), 278 (10.2), 345 (9.8), and 447  $m\mu$  (3.9); addition of several drops of acetic acid to the alcohol solution gave  $\lambda$  max at 278 (10.1) and 345  $m\mu$  (10.3).

The nmr spectrum in  $\text{DMSO-d}_6$  shows the  $-\text{COCH}_2-$  protons at  $\delta$  4.5 (S, 2H), proton at 5-position at  $\delta$  6.42 (S, 1H), and aromatic protons at  $\delta$  7.5-8.1 ppm. (M, 10H).

### 8-Nitromethyl-3,6-diphenyl-2H-copyrin-1-one (12).

(a) A mixture of 1 g. of **4**, 2 ml. of *N,N*-di-isopropylethylamine and 25 ml. of nitromethane was refluxed for 3 hours, the solution was chilled, and the resulting solid was crystallized from nitromethane, yielding 0.8 g. of **12**, m.p. 288-289°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are 278 (34.0), 327 (16.0), 348 (15.0), 410 (3.2), and 433  $m\mu$  (4.2).

*Anal.* Calcd. for  $\text{C}_{21}\text{H}_{15}\text{N}_3\text{O}_3$ : C, 70.6; H, 4.2; N, 11.8. Found: C, 70.3; H, 4.2; N, 11.5.

### 2-Amino-3-carbamoyl-5,8-diphenylpyrano[2,3,4-ij]copyrine (13).

(a) A mixture of 1 g. of **4**, 0.5 g. of cyanoacetamide, 0.5 ml. of *N,N*-di-isopropylethylamine, and 35 ml. of pyridine was refluxed for 1 hour, diluted with water, chilled, and the solid was collected and recrystallized from dimethylformamide (DMF) yielding 0.8 g. of **13**, m.p. 300-301°.

*Anal.* Calcd. for  $\text{C}_{23}\text{H}_{16}\text{N}_4\text{O}_2$ : C, 72.6; H, 4.2; N, 14.7. Found: C, 72.3; H, 4.5; N, 14.7.

(b) A solution of 2.7 g. of the triketone **8**, 3 g. of cyanoacetamide, 2 ml. of *N,N*-di-isopropylethylamine, and 5 ml. of pyridine was heated on a steam bath for 5 hours and cooled. Dilution with ethyl alcohol and crystallization of the solid provided 2.7 g. of **13**.

The  $\lambda$  max (DMF) ( $\epsilon \times 10^{-3}$ ) of **13** are 265 (44.5), 355-365  $m\mu$  (11.9).

The nmr spectrum in  $\text{DMSO-d}_6$  shows absorption at  $\delta$  7.4-8.2 for the aromatic protons and  $\text{NH}_2$  (M about 14H) and  $\delta$  10.4 ppm. for the other  $\text{NH}_2$  (broad S about 2H).

### 2-Amino-3-cyano-5,8-diphenylpyrano[2,3,4-ij]copyrine (14).

(a) A mixture of 1 g. of **4** and 0.5 g. of malononitrile was allowed to react as described in procedure (a) for the preparation of **13** giving 0.9 g. of **14**, m.p. 345-346°.

(b) Malononitrile and the triketone **8** were allowed to react as described in procedure (b) for the preparation of **13**, yielding 0.8 g. of **14**, which melted at 345-346° after recrystallization from DMF.

The  $\lambda$  max (DMF) ( $\epsilon \times 10^{-3}$ ) of **14** are 275 (38.8),  $\sim$  312 (11.5), and 400  $m\mu$  (11.8).

The nmr spectrum in  $\text{DMSO-d}_6$  shows absorption at  $\delta$  5.7-6.5 for the aromatic protons (M, 12H) and  $\delta$  7.2 ppm for the amino protons (broad S, 2H).

*Anal.* Calcd. for  $\text{C}_{23}\text{H}_{14}\text{N}_4\text{O}$ : C, 76.2; H, 3.9; N, 15.5. Found: C, 75.9; H, 4.2; N, 15.2.

### 3,6-Diphenyl-1,8-dipiperidinocopyrine (15).

A solution of 4 g. of **2** in 25 ml. of piperidine was heated under reflux for 20 hours, diluted with 100 ml. of methyl alcohol, and the solid was collected and crystallized from ethoxyethanol, yielding 3.1 g. of **15**, m.p. 195-196°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) of **15** are 263 (39.1), 337 (11.5), and 358  $m\mu$  (9.4).

The nmr spectrum in deuteriochloroform shows the piperidino protons at  $\delta$  1.64 (M, 12H) and  $\delta$  3.54 (M, 8H), the protons in the 4- and 5-positions at  $\delta$  7.35 (S, 2H), and the aromatic protons at  $\delta$  7.3-8.25 ppm. (M, 10H).

*Anal.* Calcd. for  $C_{30}H_{32}N_4$ : C, 80.3; H, 7.2; N, 12.5. Found: C, 80.0; H, 7.1; N, 12.4.

#### 1-Dicyanomethyl-3,6-diphenyl-8-piperidinocopyrine (**16**).

A mixture of 1 g. of **2**, 0.5 g. of malononitrile, 0.5 ml. of *N,N*-di-isopropylethylamine, and 25 ml. of pyridine was refluxed for 18 hours, chilled, and the solid that separated (0.2 g.) was shown to be unreacted **2**. The mother liquor was diluted with water and the solid collected and recrystallized twice from alcohol to give 0.5 g. of **16**, m.p. 171-172°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are 278 (56.0), 370 (14.7), and 458  $m\mu$  (18.0).

*Anal.* Calcd. for  $C_{28}H_{23}N_5$ : C, 78.3; H, 5.4; N, 16.3. Found: C, 78.1; H, 5.5; N, 16.0.

#### 3,6-Diphenyl-2*H*,7*H*-pyrano[3,4-*c*]pyridine-1,8-dione (**17**).

A solution of 5 g. of **3** in 150 ml. of acetic acid and 5 ml. of concentrated hydrochloric acid was refluxed for 15 minutes and cooled. Crystallization of the solid from aqueous acetic acid yielded 3.6 g. of **17**, m.p. 301-302°.

The  $\lambda$  max (DMF) ( $\epsilon \times 10^{-3}$ ) is 359  $m\mu$  (26.0).

The nmr spectrum in trifluoroacetic acid shows the proton in either the 4- or 5-position at  $\delta$  7.43 (S, 1H), the other of these protons at  $\delta$  7.6 (S, 1H), and the aromatic protons at  $\delta$  7.6-8.1 (M, 10H).

*Anal.* Calcd. for  $C_{20}H_{13}NO_3$ : C, 76.2; H, 4.2; N, 4.4. Found: C, 76.5; H, 4.0; N, 4.5.

#### 3,6-Diphenyl-2*H*,7*H*-copyrine-1,8-dione (**18**).

A solution of 5 g. of **3** in 50 ml. of concentrated sulfuric acid was heated on a steam bath overnight and poured onto ice. The solid was collected, boiled with pyridine, washed with alcohol, and recrystallized from DMF, yielding 4.1 g. of **18**, m.p. 307-308°.

The  $\lambda$  max are the same as the reported values (2).

*Anal.* Calcd. for  $C_{20}H_{14}N_2O_2$ : C, 76.4; H, 4.5; N, 8.9. Found: C, 76.4; H, 4.4; N, 9.0.

#### 3-Cyano-2-morpholino-4-phenacyl-6-phenylpyridine (**19**).

A mixture of 9 g. of **1** and 65 ml. of morpholine was refluxed for 5 hours, cooled, diluted with 100 ml. of methyl alcohol, and the precipitate was collected and crystallized from butyl alcohol, giving 5 g. of **19**, m.p. 194-195°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are 269 (30.8), and 352  $m\mu$  (8.4).

The nmr in  $DMSO-d_6$  shows absorption for the morpholine protons at  $\delta$  3.75 (S, 8H), for  $-CH_2CO$  at  $\delta$  4.72 (S, 2H), and aromatic protons at  $\delta$  7.4-8.2 ppm. (M, 11H).

*Anal.* Calcd. for  $C_{24}H_{21}N_3O_2$ : C, 75.2; H, 5.5; N, 11.0. Found: C, 75.5; H, 5.2; N, 10.9.

The mother liquors were evaporated to dryness, the residue was boiled with methanol, and the insoluble material was crystallized from ethoxyethanol, giving 1.8 g. of 3-cyano-4-( $\alpha$ -morpholinostyryl)-6-phenyl-2(1*H*)-pyridone (**20**), m.p. 304-305°.

The nmr spectrum in  $DMSO-d_6$  shows absorption for the morpholine protons at  $\delta$  3.2 (M, 4H) and  $\delta$  4.7 (M, 4H), for the vinyl proton at  $\delta$  5.23 (S, 1H), for the proton in the 5-position at  $\delta$  5.73 (S, 1H), and for the aromatic protons at  $\delta$  6.8-7.7 ppm. (M, 10H).

*Anal.* Calcd. for  $C_{24}H_{21}N_3O_2$ : C, 75.2; H, 5.5; N, 11.0. Found: C, 75.1; H, 5.7; N, 11.1.

#### 1-Morpholino-3,6,7-triphenyl(7*H*)-copyrin-8-one (**22**).

A mixture of 4 g. of 4-cyano-*N*-phenylcarbamoylmethylene-2,6-diphenyl-4*H*-pyran (**21**) (5) and 20 ml. of morpholine was heated under reflux for 20 hours, cooled, diluted with 50 ml. of methyl alcohol, and the solid that formed was recrystallized from pyridine yielding 3.3 g. of **22**, m.p. 284-285°.

The  $\lambda$  max (chloroform) ( $\epsilon \times 10^{-3}$ ) are 278 (32.8) and 387  $m\mu$  (9.8).

The exact mass determined by high resolution mass spectrometry was 459.1941 (calcd., 459.1947).

The nmr spectrum in trifluoroacetic acid shows absorption for the morpholine protons at  $\delta$  4.15 (broad singlet 4H) and  $\delta$  4.38 (broad singlet 4H), and aromatic protons at  $\delta$  8.2-7.1 ppm. (M, 17H).

*Anal.* Calcd. for  $C_{30}H_{25}N_3O_2$ : C, 78.4; H, 5.5; N, 9.2. Found: C, 78.2; H, 5.6; N, 9.2.

Compound **22** was also prepared by refluxing a mixture of 1 g. of **24** (see below) and 5 ml. of morpholine for 15 minutes, chilling, and collecting the solid (1.1 g.), m.p. 283-284°. The ir spectra of the samples prepared by both procedures were identical.

#### 3-Cyano-4-methyl-1,6-diphenyl-2(1*H*)-pyridone (**23**).

A mixture of 20 g. of 1-phenylbutane-1,3-dione, 20 g. of cyanoacetanilide, 20 ml. of piperidine and 140 ml. of ethyl alcohol was refluxed for 24 hours and cooled. Removal of the precipitate and crystallization from formic acid afforded 15.7 g. of **23**, m.p. 269-270°. The mother liquors were diluted with water, and the solid was collected and crystallized from butyl alcohol to give 8 g. of 3-cyano-6-methyl-1,4-diphenyl-2(1*H*)-pyridone, m.p. 219-220°. The mass spectra were useful in assigning structures to these isomers: the higher melting isomer showed a fragmentation peak at  $m/e$  180 which we assign to the fragment  $(C_6H_5C=NC_6H_5)^+$ , and the other isomer showed a peak at  $m/e$  140 for the fragment  $(CH_3C=NC_6H_5)^+$ .

#### 3-Cyano-4-phenacyl-1,6-diphenyl-2(1*H*)-pyridone (**24**).

A solution of 2.8 g. of **23**, 2 ml. of methyl benzoate, and 75 ml. of dry pyridine was heated on a steam bath under nitrogen and 2 g. of 52% sodium hydride in mineral oil was added. The mixture was heated and stirred under nitrogen for 2 hours, cooled, and after the addition of 10 ml. of methyl alcohol, it was poured into 200 ml. of water. The sticky solid was collected and recrystallized twice from ethyl alcohol, giving 1 g. of **24**, m.p. 194-195°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are 240 (24.8), 275 (12.9), and 353  $m\mu$  (13.5); addition of a drop of methanolic potassium hydroxide shifted the maxima to  $\sim$  240 (21.8), 270 (13.7), 348 (10.6), and 428  $m\mu$  (7.5).

*Anal.* Calcd. for  $C_{26}H_{18}N_2O_2$ : C, 80.0; H, 4.6; N, 7.2. Found: C, 79.7; H, 4.9; N, 7.5.

#### 4-Dicyanomethylene-1-methyl-2,6-diphenyl-1,4-dihydropyridine (**25a**).

(a) To a refluxing solution of 2 g. of **1** in 35 ml. of pyridine was added three 1-ml. portions of 40% aqueous methylamine over a 1-hour period. The solution was diluted with water and the solid was collected and stirred with 50 ml. of 5% methanolic potassium hydroxide for 0.5 hour. The mixture was heated briefly to boiling, and the insoluble material was collected and crystallized from nitromethane yielding 1.8 g. of **25a**, m.p. 371-372°. The workup of the alkali-soluble fraction to give **26a** is described below.

(b) A mixture of 1 g. of 4-methoxy-1-methyl-2,6-diphenylpyridinium perchlorate, 0.5 g. of malononitrile, 0.8 ml. of *N,N*-diisopropylethylamine and 10 ml. of acetonitrile was refluxed for 0.5 hour, cooled, and the solid was collected and crystallized from nitromethane yielding 0.7 g. of **25a**, m.p. 376-377°.

*Anal.* Calcd. for  $C_{21}H_{15}N_3$ : C, 81.5; H, 4.9; N, 13.6. Found: C, 81.2; H, 4.9; N, 13.8.

1-*n*-Butyl-4-dicyanomethylene-2,6-diphenyl-1,4-dihydropyridine (**25b**).

A solution of 6 g. of **1**, 15 ml. of butylamine and 75 ml. of acetonitrile was heated overnight on a steam bath, chilled, and the solid was collected and extracted with methanolic potassium hydroxide as described in procedure (a) for **25a**. The yield of **25b** was 2.9 g., m.p. 194-195° (from butyl alcohol).

*Anal.* Calcd. for  $C_{24}H_{21}N_3$ : C, 82.0; H, 6.0; N, 12.0. Found: C, 81.9; H, 6.0; N, 12.2.

1-Benzyl-4-dicyanomethylene-2,6-diphenyl-1,4-dihydropyridine (**25c**).

A mixture of 5 g. of **1** and 25 ml. of benzylamine was heated at 70-80° for 2 hours, cooled, and added to dilute acetic acid. The solid which resulted was extracted with methanolic potassium hydroxide as described above yielding 1.5 g. of **25c**, m.p. 246-247° (from acetic acid).

*Anal.* Calcd. for  $C_{27}H_{19}N_3$ : C, 84.1; H, 5.0; N, 10.9. Found: C, 84.1; H, 4.8; N, 10.9.

2-Amino-3-cyano-1-methyl-4-phenacylidene-6-phenyl-1,4-dihydropyridine (**26a**).

The methanolic potassium hydroxide-soluble fraction from the preparation of **25a** (procedure a) was mixed with a large excess of solid carbon dioxide and the solid that separated was crystallized from nitromethane giving 0.5 g. of **26a**, m.p. 243-245°.

The nmr spectrum in  $DMSO-d_6$  shows absorption for  $N-CH_3$  at  $\delta$  3.25 (S, 3H), for  $=CHCO$  at  $\delta$  6.12 (S, 1H), for the aromatic protons at  $\delta$  7.38-7.9 (M, 10H), and for the proton in the 5-position at  $\delta$  8.22 ppm. (S, 1H). The vinyl proton slowly exchanged with deuterium oxide.

*Anal.* Calcd. for  $C_{21}H_{17}N_3O$ : C, 77.0; H, 5.2; N, 12.8. Found: C, 76.7; H, 5.4; N, 13.0.

2-Amino-1-*n*-butyl-3-cyano-4-phenacylidene-6-phenyl-1,4-dihydropyridine (**26b**).

The product was isolated from the base-soluble fraction of **25b** by the method described for **26a**. The yield of **26b** was 3.1 g. after crystallization from nitromethane, m.p. 246-247°.

The nmr spectrum in  $DMSO-d_6$  shows absorption at  $\delta$  0.45-1.55 (M, 7H) for  $NCCH_2CH_2CH_3$ , at  $\delta$  3.77 (broad T, 2H) for  $N-CH_2$ ,  $\delta$  6.18 (S, 1H) for  $=CHCO$ ,  $\delta$  7.39-7.9 (M, 10H), and  $\delta$  8.23 ppm. (S, 1H) for the proton in the 5-position. The vinyl proton slowly exchanged with deuterium oxide.

*Anal.* Calcd. for  $C_{24}H_{23}N_3O$ : C, 78.0; H, 6.3; N, 11.4. Found: C, 77.6; H, 6.1; N, 11.4.

2-Amino-1-benzyl-3-cyano-4-phenacylidene-6-phenyl-1,4-dihydropyridine (**26c**).

The product was isolated from the alkali-soluble fraction of **25c** as described above for **26a**. The yield of **26c** was 1.6 g., m.p. 181-182° (from alcohol).

*Anal.* Calcd. for  $C_{27}H_{21}N_3O$ : C, 80.4; H, 5.2; N, 10.4. Found: C, 80.7; H, 5.0; N, 10.3.

3-Cyano-1,4-dimethyl-6-phenyl-2(1H)-pyridone (**27**).

(a) A mixture of 5 g. of **1**, 30 ml. of 40% aqueous methyl-

amine and 20 ml. of methyl alcohol was heated in a bomb at 150° for 8 hours. The contents of the bomb was cooled and the solid that had separated was collected and crystallized from butyl alcohol yielding 3.1 g. of **27**, m.p. 270-271°.

(b) A solution of 2.1 g. of **5** in 30 ml. of hot DMF was added to 3 g. of thallium ethoxide (7). The solution was cooled, 5 ml. of methyl iodide was added, and the mixture was refluxed for 1 hour. The mixture was filtered to remove thallium salts and the filtrate was poured into dilute alkali. The white solid was collected and boiled with 100 ml. of ligroin (b.p. 100-115°) and filtered hot. The insoluble material was crystallized from alcohol yielding 1.2 g. of **27**, m.p. 271-272°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are  $\sim$  240 (9.0) and 345  $m\mu$  (17.5).

*Anal.* Calcd. for  $C_{14}H_{12}N_2O$ : C, 75.1; H, 5.4; N, 12.5. Found: C, 74.8; H, 5.6; N, 12.8.

The hot ligroin solution was chilled and 0.5 g. of 3-cyano-2-methoxy-4-methyl-6-phenylpyridine (**37**), m.p. 98-99°, was collected.

2-Benzyl-8-benzylamino-1-imino-3,6-diphenyl-1,2-dihydrocopyrine (**28**).

(a) A mixture of 6 g. of **1** and 25 ml. of benzylamine was refluxed for 3 hours, cooled, diluted with 50 ml. of methyl alcohol, and the solid was collected and crystallized from nitromethane yielding 4 g. of **28**, m.p. 184-185°.

The  $\lambda$  max (acetonitrile) ( $\epsilon \times 10^{-3}$ ) are 245 (25.0), 284 (23.5), and 365  $m\mu$  (16.0).

The nmr spectrum in  $DMSO-d_6$  at 100° shows absorption for the benzyl protons at  $\delta$  4.82 (M, 4H); proton in 4-position at  $\delta$  6.05 (S, 1H); proton in 5-position at  $\delta$  7.97 (S, 1H); aromatic protons at  $\delta$  7-8.15 (M, 10H); and  $-NH-$  at  $\delta$  11.8 ppm (T, 1H). Addition of deuterium oxide at 100° exchanges the  $-NH-$  and the spectrum shows two clean singlets for the benzyl protons at  $\delta$  4.77 and  $\delta$  4.85 ppm.

(b) A mixture of 0.5 g. of **26c** and 10 ml. of benzylamine was refluxed for 1.5 hours, cooled, and poured into dilute acetic acid. The solid was collected, boiled with alcohol, and filtered. The insoluble material was crystallized from nitromethane giving 0.3 g. of **28**, m.p. 184-185°. From the alcohol-soluble fraction, 0.1 g. of **26c** was recovered.

1-*n*-Butyl-4-cyanocarbamoylmethylene-2,6-diphenyl-1,4-dihydropyridine (**29**).

A mixture of 30 g. of **11** and 130 ml. of butylamine was refluxed overnight, cooled, and the solid was collected (this is crude **30**). The mother liquors were evaporated to dryness; the residue was washed with alcohol and crystallized from methyl alcohol yielding 15 g. of **29**, m.p. 194-195°.

2-*n*-Butyl-1-imino-3,6-diphenyl-2,7-dihydro-8(1H)-copyrinone (**30**).

The crude **30** obtained from the reaction described above was crystallized from DMF yielding 12 g. of **30**, m.p. 264-265°.

The nmr spectrum in dimethylsulfoxide shows  $-CCH_2CH_2CH_3$  at  $\delta$  0.45-1.63 (M, 7H),  $NCH_2C$  at  $\delta$  3.83 (T, 2H), proton in 4-position at  $\delta$  6.56 (S, 1H); proton in 5-position at  $\delta$  6.9 (S, 1H); aromatic protons at  $\delta$  7.38-9.83 (M, 10H), and  $\delta$  14 ppm. for the hydrogen-bonded OH (very broad peak).

*Anal.* Calcd. for  $C_{24}H_{23}N_3O$ : C, 78.0; H, 6.3; N, 11.4. Found: C, 77.9; H, 6.5; N, 11.6.

8-*n*-Butylamino-3,6-diphenyl-1(2H)-copyrinone (**31**).

(a) A mixture of 5 g. of **11** and 50 ml. of butylamine was heated in a bomb at 150° for 6 hours, evaporated to dryness, and

the residue was crystallized from ethoxyethanol yielding 3.3 g. of **31**, m.p. 199-200°.

*Anal.* Calcd. for C<sub>24</sub>H<sub>23</sub>N<sub>3</sub>O: C, 78.0; H, 6.3; N, 11.4. Found: C, 78.1; H, 6.1; N, 11.2.

(b) A mixture of 0.5 g. of **29** and 10 ml. of butylamine was heated in a bomb at 150° for 4 hours, evaporated to dryness, and the residue was crystallized from ethoxyethanol yielding 0.32 g. of **31**, m.p. 199-200°.

(c) The procedure described in (b) was repeated using **30** in place of **29** and 0.4 g. of **31** was obtained.

(d) A solution of 1 g. of **4** in 10 ml. of butylamine was refluxed for 2 hours and worked up as described in (a) to give 0.7 g. of **31**.

1-Benzyl-4-cyanocarbamoylmethylene-2,6-diphenyl-1,4-dihydropyridine (**32**).

A mixture of 3 g. of **11**, 5 ml. of benzylamine and 50 ml. of pyridine was heated on a steam bath for 2 hours and diluted with water. The solid was collected and crystallized from alcohol giving 3 g. of **32**, m.p. 255-256°.

*Anal.* Calcd. for C<sub>27</sub>H<sub>21</sub>N<sub>3</sub>O: C, 80.4; H, 5.2; N, 10.4. Found: C, 80.1; H, 5.6; N, 10.5.

8-Benzylamino-3,6-diphenyl-1(2H)-copyrnone (**33**).

(a) A solution of 4 g. of **11** in 25 ml. of benzylamine was refluxed overnight, diluted with methyl alcohol, and the solid was collected and crystallized from ethoxyethanol yielding 3.4 g. of **33**, m.p. 240-241°.

(b) A mixture of 2 g. of **4** and 15 ml. of benzylamine was heated on a steam bath for 1 hour and cooled. The solid which separated was crystallized from ethoxyethanol giving 1.7 g. of **33**, m.p. 240-241°.

(c) A mixture of 1 g. of **30** and 10 ml. of benzylamine was refluxed for 2 hours, diluted with aqueous acetic acid, and the solid was collected and crystallized from ethoxyethanol giving 0.5 g. of **33**.

The nmr spectrum in DMSO-d<sub>6</sub> shows N-CH<sub>2</sub>- at 4.93 (D, 2H), proton at 4-position at δ 6.8 (S, 1H), proton at 5-position at δ 7.28 (S, 1H), aromatic protons at δ 7.35-8.2 (M, 15H), NH at δ 10.0 (T, 1H) and another NH at δ 11.9 ppm. (S, 1H). The addition of deuterium oxide exchanges the NH protons and changes the NCH<sub>2</sub> to a singlet at δ 4.86 ppm.

*Anal.* Calcd. for C<sub>27</sub>H<sub>21</sub>N<sub>3</sub>O: C, 80.4; H, 5.2; N, 10.4. Found: C, 80.3; H, 5.1; N, 10.4.

2-n-Butylamino-3-cyano-4-methyl-6-phenylpyridine (**34**).

A mixture of 1.5 g. of **26b** and 25 ml. of 10% methanolic potassium hydroxide was refluxed overnight, cooled, and the solid was collected. After washing with water, the solid was crystallized from ligroin (b.p. 35-60°) yielding 0.8 g. of **34**, m.p. 86-87°.

The nmr spectrum in DMSO-d<sub>6</sub> shows CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>- at δ 0.82-1.75 (M, 7H), CH<sub>3</sub>- at δ 2.41 (S, 3H), N-CH<sub>2</sub>- at δ 3.37-3.67 (M, 2H), NH at δ 6.91 (T, 1H), proton 5-position at δ 7.2 (S, 1H), and aromatic protons at δ 7.44-8.18 ppm. (M, 5H). On addition of deuterium oxide a slow exchange of the NH took place and after heating to 140° to shift an interfering water peak, the N-CH<sub>2</sub> absorption was observed to be a triplet.

*Anal.* Calcd. for C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>: C, 76.9; H, 7.2; N, 15.8. Found: C, 76.5; H, 7.4; N, 15.5.

2-Benzylamino-3-cyano-4-methyl-6-phenylpyridine (**35**).

A mixture of 0.5 g. of **26b** and 5 ml. of benzylamine was refluxed for 2 hours, diluted with alcohol, chilled, and the solid

was collected and crystallized from ligroin (b.p. 35-60°) giving 0.26 g. of **35**, m.p. 89-90°.

*Anal.* Calcd. for C<sub>20</sub>H<sub>17</sub>N<sub>3</sub>: C, 80.3; H, 5.7; N, 14.0. Found: C, 80.2; H, 5.6; N, 13.9.

3-Cyano-2-methoxy-4-phenacyl-6-phenylpyridine (**36**).

A mixture of 5 g. of **1**, 2 g. of potassium hydroxide, 50 ml. of methyl alcohol, and 20 ml. of pyridine was refluxed 1 hour, evaporated to about 50 ml., and acidified with dilute hydrochloric acid. The solid was collected and recrystallized from alcohol to give 2 g. of **36**, m.p. 152-153°.

The λ max (acetonitrile) (ε × 10<sup>-3</sup>) are 247 (19.4) and 318 mμ (20.6).

*Anal.* Calcd. for C<sub>21</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>: C, 76.8; H, 4.9; N, 8.5. Found: C, 76.6; H, 5.0; N, 8.3.

A mixture of 0.5 g. of **36**, 15 ml. of acetic acid, and 15 ml. of concentrated hydrochloric acid was refluxed for 15 minutes, cooled, and the solid was collected and crystallized from aqueous acetic acid, giving 0.4 g. of **17**.

3-Cyano-2-methoxy-4-methyl-6-phenylpyridine (**37**).

(a) A mixture of 0.5 g. of **36**, 1 g. of potassium hydroxide, and 25 ml. of methyl alcohol was refluxed for 7 hours, diluted with water, and the solid was collected and crystallized from ligroin (b.p. 100-115°), yielding 0.3 g. of **37**, m.p. 96-98°.

The λ max (acetonitrile) (ε × 10<sup>-3</sup>) are 258 (13.6) and 312 mμ (23.5).

*Anal.* Calcd. for C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O: C, 75.1; H, 5.4; N, 12.5. Found: C, 75.5; H, 5.4; N, 12.8.

(b) Obtained as a by-product from the preparation of **27** by procedure (b).

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