The Reactions of Cyanoacetic Acid with 2,6-Diphenyl-4-pyrone

J. A. VanAllan, G. A. Reynolds, and D. P. Maier

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

Received May 27, 1968

Cyanoacetic acid reacts with 2,6-diphenyl-4-pyrone (**1**) under neutral conditions to give a salt (**2**), and under basic conditions to give 4-(cyanomethylene)-2,6-diphenyl-4H-pyran (**4**). In hot acetic anhydride the same reactants give 1,3-dicyano-1,3-bis(2,6-diphenyl-4H-pyranylidene-4)acetone (**7**). A proof of structure and a proposal for the formation of **7** is given.

The product obtained by the reaction of 2,6-diphenyl-4-pyrone (**1**) and cyanoacetic acid in ethyl acetate has been assigned structure **2a** on the basis of the electronic and nmr spectra. The electronic spectrum of **2a** is almost identical with that of 2,6-diphenyl-4-hydroxypyrylium perchlorate (**2b**) (see Table I), and the nmr spectrum of **2a** shows the methylene protons as a singlet at τ 6.49 (2 H), the protons at the 3,5 positions of the pyrylium ring as a singlet at 3.18 (2 H), the hydroxyl proton at -4.6 (1 H), and the aromatic protons as a multiplet at 2.2–2.8 (10 H).

Table I

Electronic Spectra[a]

Compound no.	λ_{max}, mμ ($\epsilon \times 10^{-3}$) λ_1	λ_2	λ_3	λ_4	λ_5
1	263 (20.6)			340 (12.4)	
2a	252 (21.5)		280 (25.3)		
2b	252 (20.2)		282 (24.5)		
3		270 (15.0)	280 (14.5)	327 (7.4)	~350 (6.0)
4	253 (18.5)	261 (18.6)	288 (21.3) 293 (20.9)	341 (23.6)	
5	232 (24.8)		274 (35.7)	392 (32.4)	537 (87.0)
6		262 (12.6)	366 (17.6)	406 (32.0)	422 (28.4)
7			333 (38.5)	465 (54.7)	480 (57.5)
8	257 (30.2)	~295 (8.7)		409 (21.4)	
9	263 (15.0)		376 (12.1)	460 (57.6)	
10a	259 (19.9)	308 (15.7)	388 (24.1)	~415 (14.7)	
10b	259 (20.5)	316 (20.2)	390 (34.4)	400 (35.5)	
11	256 (15.2)	318 (22.0)	386 (28.0)		~406 (17.0)
12	258 (15.8)	333 (20.9)	393 (35.4)		~420 (30.0)
13a	260 (12.4)		378 (32.3)		
13b	250 (18.0)		388 (46.3)		
14	258 (53.0)		280 (64.7)		
15	235 (37.8)		275 (42.0)	400 (52.5)	575 (77.0)
17	230 (21.0)		268 (26.4)	379 (27.2)	543 (120.8)

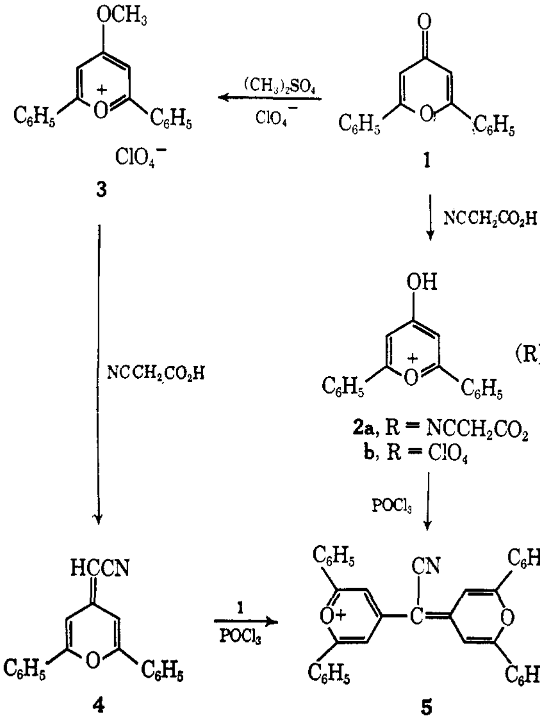
[a] All spectra were determined in acetonitrile using a Cary Model 15 spectrophotometer.

Thermolytic decomposition of **2a** in the heated inlet of the mass spectrometer occurs to give **1**, acetonitrile, and carbon dioxide.

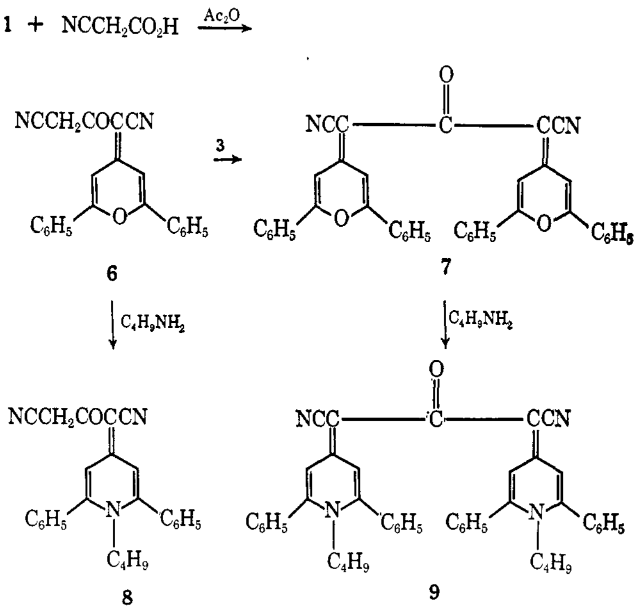
Treatment of **2a** with phosphorus oxychloride gave the dye **5**. Dimethyl sulfate converts **1** into the pyrylium salt **3**[1] which was isolated as the perchlorate, and reaction of **3** with cyanoacetic acid under basic conditions gave **4**. A mixture of **4**, **1**, and phosphorous oxychloride gave the dye **5**. These reactions are summarized in Scheme I.

The pyrone **1** and cyanoacetic acid react in acetic anhydride at reflux temperature to give **6**. A similar compound has been prepared from 2,6-dimethyl-4-pyrone and cyanoacetic acid.[2] To demonstrate the presence of a reactive methylene group in **6**, the latter compound was condensed with an equivalent of **3** under basic conditions to give **7**. The reaction of **6** and **7** with *n*-butylamine gave **8** and **9**, respectively, a reaction which is typical of 4-dehydro-4H-pyrans.[2,3] These reactions are illustrated in Scheme II.

Scheme I



Scheme II



---

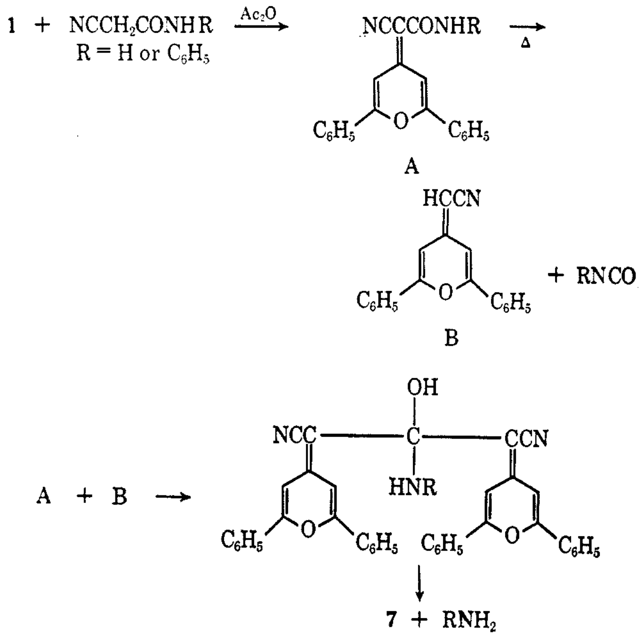
(1) G. Traverso, *Ann. Chim.* (Rome), **46**, 821 (1956).

(2) S. Yamamara, K. Kato, and H. Herato, *Tetrahedron Lett.*, 1637 (1967).

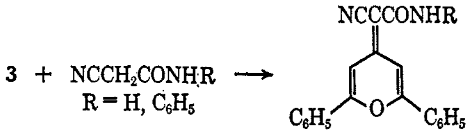
(3) F. Eiden, *Naturwissenschaften*, **47**, 61 (1960); *Arch. Pharm.* (Weinheim), **295**, 607 (1962).

Cyanoacetamide and cyanoacetanilide both react with **1** in boiling acetic anhydride to give **7**. One possible route to **7** from these components is shown in Scheme III.

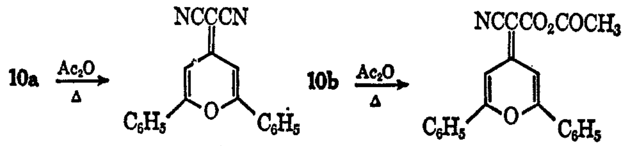
SCHEME III



As a test of the reaction sequence shown in Scheme III, the compounds **10a** and **10b** were prepared by the reaction of **3** with cyanoacetamide and cyanoacetanilide, respectively. However, it was found that heating **10a** in acetic anhydride gave **11** rather than **7**, and **10b** under the same conditions gave **12**. Compound **11** is known and is probably formed by the dehydration of the amide group of **10a**.



10a, R = H
b, R = C_6H_5

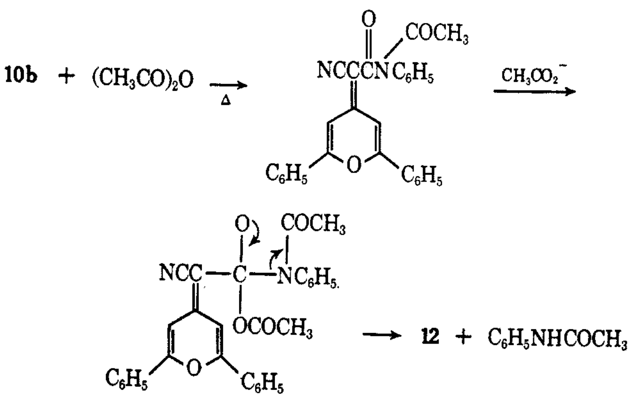


11 **12**

The structure of **12** was established by the electronic spectrum which is similar to that of **10a**: the infrared (ir) spectrum shows strong absorption at 5.65 and 5.78 μ which is assignable to the anhydride function; and mass spectrometric data show a parent peak at *m/e* 357 and a fragmentation typical of an anhydride group. The probable reaction path leading to **12** is shown in Scheme IV.

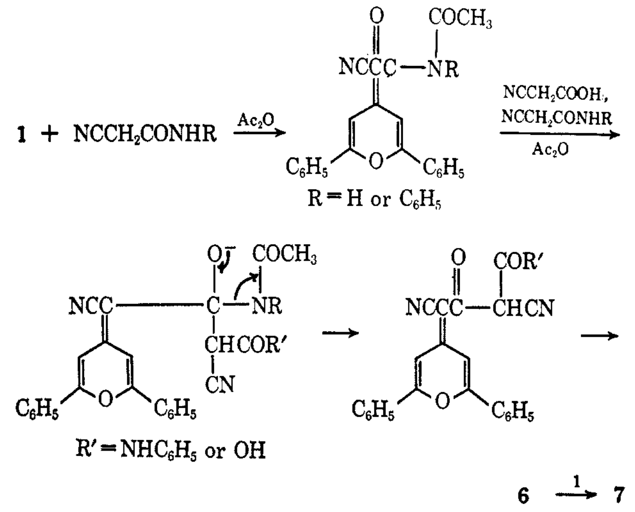
If an equivalent of cyanoacetic acid or cyanoacetanilide is heated with **10b** in acetic anhydride, the product is **6** rather than **12**. This result is due to either the stronger nucleophilic character of cyanoacetic acid and cyanoacetanilide compared with that of acetate or to a favorable equilibrium.

SCHEME IV

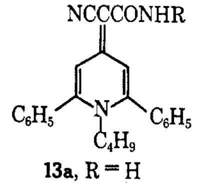


On the basis of the data presented above, the reaction path outlined in Scheme III has been shown to be wrong, and that presented in Scheme V is consistent with the experimental data.[4]

SCHEME V



Compounds **10a** and **10b** were converted into the pyridinium salts **13a** and **13b** by means of *n*-butylamine.



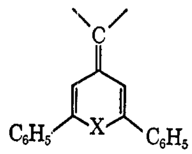
13a, R = H
b, R = C_6H_5

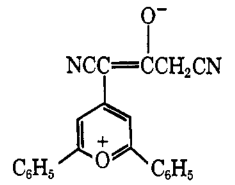
Table I contains the absorption spectra of the compounds described in this paper. All of the compounds with the exception of **1**, **2**, and **5** contain the conjugated system A. The basic absorption pattern of the compounds of type A is similar but modified by substituents in the following manner. The long-wavelength band of **4** (341 mμ) is shifted to about 388 mμ, and shoulders appear at about 415 mμ in **10a** and **10b**. The corresponding nitrogen analogs **13a** and **13b** absorb again at about 388 mμ, but no shoulders were observed. The

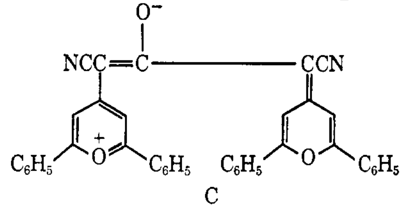
---

[4] A referee has suggested another process for the formation of **6** through the formation of 1,3-dicyanoacetone from cyanoacetic acid or cyanoacetanilide and acetic anhydride. Dicyanoacetone and **1** would give **6**. We were unable to isolate dicyanoacetone from the reaction of cyanoacetic acid with acetic anhydride, but this does not prove that dicyanoacetone is not an unstable intermediate.

ketones **6** and **7** show absorption at 422 and 480 mμ, which may arise from the charged species B and C, respectively. The nitrogen homologs of **6** and **7** show absorption at 409 and 460 mμ, respectively, again suggesting some contribution from a dipolar form. The spectrum of **12** is similar to **11**, indicating that the same basic structure is present in both compounds.

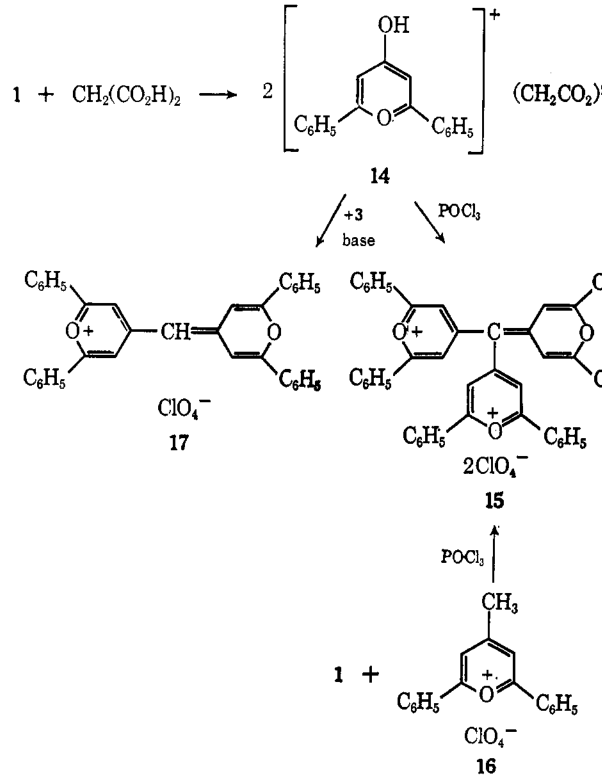

A


B


C

The reaction of 2,6-diphenyl-4-pyrone (**1**) has been extended to malonic acid. In a similar fashion to cyanoacetic acid, malonic acid reacts with **1** in ethyl acetate to give di(4-hydroxy-2,6-diphenylpyrylium) malonate (**14**). With phosphorous oxychloride, **14** yields the dye **15** which may also be obtained from **16** and **1** in the presence of phosphorous oxychloride.

Scheme VI



The magenta dye **17** is formed by the reaction of **14** with **3** under basic conditions. These reactions are summarized in Scheme VI above.

Experimental Section[5]

4-Hydroxy-2,6-diphenylpyrylium Cyanoacetate (2a).—A solution of 5 g (0.02 mol) of **1** and 1.7 g (0.02 mol) cyanoacetic acid in 75 ml of ethyl acetate was refluxed for 15 min. The mixture was cooled, and the solid was collected and recrystallized from ethyl acetate to give an 80% yield of product: mp 141°; mass spectrum thermally decomposes in the heated inlet (235°) to **1**, CO_2, and CH_3CN.

Anal. Calcd for $C_{20}H_{15}NO_4$: C, 72.2; H, 4.5; N, 4.2. Found: C, 72.2; H, 4.3; N, 4.2.

4-Hydroxy-2,6-diphenylpyrylium Perchlorate (2b).—A solution of 5 g of **1** in 50 ml of acetonitrile was mixed with 3 ml of 70% perchloric acid, and the precipitate was collected and recrystallized from acetonitrile, giving a 94% yield of **2b**: mp 237–238°.

Anal. Calcd for $C_{17}H_{13}ClO_6$: C, 58.6; H, 3.7; Cl, 10.6. Found: C, 58.7; H, 3.7; Cl, 10.4.

4-Methoxy-2,6-diphenylpyrylium Perchlorate (3).—A mixture of 15 g of **1** and 35 ml of dimethyl sulfate was heated on the steam bath for 3 hr and cooled, and ether (100 ml) was added. The precipitate was collected, washed with ether, and dissolved in methanol. The addition of 7 ml of 70% perchloric acid caused **3** to separate, and the solid was collected and recrystallized from acetonitrile; yield 83%; mp 257–258°.

Anal. Calcd for $C_{18}H_{15}ClO_5$: C, 59.7; H, 4.1; Cl, 9.7. Found: C, 59.3; H, 4.5; Cl, 9.9.

4-(Cyanomethylene)-2,6-diphenyl-4H-pyran (4).—A solution of 3.6 g (0.01 mol) of **3**, 2 g of cyanoacetic acid, and 4 ml of N,N-diisopropylethylamine in 30 ml of acetonitrile was heated under reflux for 2 hr, poured into water, and the precipitate collected and crystallized from alcohol and then acetic acid: yield 45%; mp 145–150°; *m/e* 271, 242, 215, 105, 102, 77.

Anal. Calcd for $C_{19}H_{13}NO$: C, 84.1; H, 4.8; N, 5.2. Found: C, 84.7; H, 4.7; N, 5.4.

4-[Cyano-(2,6-diphenyl-4H-pyran-4-yl)methylidene]-2,6-diphenylpyrylium Perchlorate (5). A.—A solution of 2.0 g of **2** in 4 ml of phosphorous oxychloride was heated for 3 hr at 95–100°. The reaction mixture was poured into methanol, and 2 ml of 70% perchloric acid was added. The precipitated dye was collected and extracted with methanol in a Soxhlet extractor. The dye **5** crystallized from the extract: yield 33%; mp 321–322°.

Anal. Calcd for $C_{36}H_{24}ClNO_6$: C, 71.8; H, 4.0; N, 2.3. Found: C, 71.4; H, 4.1; N, 2.2.

B.—Alternatively, a mixture of 1.4 g of **4** and 1.4 g of **1** in 5 ml of phosphorous oxychloride was treated in the same manner to give **5** in 77% yield.

4-(Cyanoacetylcyanomethylene)-2,6-diphenyl-4H-pyran (6).—A solution of 5.0 g (0.02 mol) of **1** and 3.0 g (0.035 mol) of cyanoacetic acid in 15 ml of acetic anhydride was heated at 90–95° for 3 hr and then cooled to give **6**: mp 261–262° from 1,2,3-trichloropropane; yield 75%; *m/e* 338, 298, 105, 102, 77.

Anal. Calcd for $C_{22}H_{14}N_2O_2$: C, 78.0; H, 4.3; N, 8.3. Found: C, 77.9; H, 4.5; N, 8.1.

The mother liquors were concentrated, and the solid which was obtained was recrystallized from N,N-dimethylformamide, giving 1 g of **7**.

1,3-Dicyano-1,3-bis(2,6-diphenyl-4H-pyranylidene-4)acetone (7). A.—A solution of 1.7 g of **6** and 1.8 g of **3** in 30 ml of acetonitrile was heated to reflux, and 2.0 ml of N,N-diisopropylethylamine was added. After 2 hr at 90–95°, the mixture was cooled and **7** was collected and recrystallized from N,N-dimethylformamide: mp 344–345°; yield 86%; *m/e* 568, 298, 270, 105, 77.

Anal. Calcd for $C_{39}H_{24}N_2O_3$: C, 82.4; H, 4.2; N, 4.9. Found: C, 82.1; H, 4.5; N, 5.1.

B and C.—A solution of 5.0 g of **1** and 3.5 g of cyanoacetanilide (or 2.5 g of cyanoacetamide) in 30 ml of acetic anhydride was heated at reflux for 4 hr. The mixture was cooled, and the solid was collected and recrystallized to yield 78% from cyanoacetanilide and 69% from cyanoacetamide.

1-*n*-Butyl-4-(cyanoacetylcyanomethylene)-2,6-diphenyl-1,4-dihydropyridine (8).—A solution of 2.0 g of **6** and 4 ml of *n*-

---

[5] The mass spectra were obtained by using either a 60° sector-type mass spectrometer, or a Consolidated Electrodynamics Model 21-110B mass spectrometer. The heated inlet was of the type described by V. J. Caldecourt [*Anal. Chem.*, **27**, 1670 (1955)] but constructed entirely of glass. The compounds which were not volatile in the heated inlet system were analyzed *via* the direct probe of the CEC 21-110B.

butylamine in 10 ml of ethoxyethanol was heated to 90–95° for 3 hr. The solvent was evaporated, methanol was added to the residue, and the product **8** was collected and recrystallized from butyl alcohol: yield 72%; mp 295–296°; *m/e* 393, 392, 364, 350, 337, 77.

Anal. Calcd for $C_{26}H_{23}N_3O$: C, 79.3; H, 5.8; N, 10.7. Found: C, 79.5; H, 5.9; N, 10.9.

1,3-Dicyano-1,3-bis(2,6-diphenyl-1-*n*-butyl-1,4-dihydropyridylidene-4)acetone (**9**).—A mixture of 1.0 g of **7** and 6 ml of *n*-butylamine was heated under reflux for 2 hr. The excess butylamine was removed by vacuum distillation, the residue was dissolved in methanol, and the product was precipitated by the addition of 3 ml of acetic acid in 10 ml of water. The solid was collected and recrystallized from acetonitrile giving a 50% yield of **9**, mp 310°.

Anal. Calcd for $C_{47}H_{42}N_4O$: C, 81.9; H, 6.1; N, 8.1. Found: C, 82.0; H, 6.3; N, 8.3.

4-(Cyanocarbamoylmethylene)-2,6-diphenylpyran (**10a**).—A solution of 14.5 g of **3** and 7.2 g of cyanoacetamide in 100 ml of acetonitrile was heated to reflux and 12 ml of N,N-diisopropylethylamine was added. The product which separated immediately was collected and recrystallized from 1,2,3-trichloropropane: yield 95%; mp 290°; *m/e* 314, 298, 105, 77. This compound slowly decomposed in the heated inlet system to **4** and **11**.

Anal. Calcd for $C_{20}H_{14}N_2O_2$: C, 76.4; H, 4.5; N, 8.9. Found: C, 76.1; H, 4.3; N, 8.9.

4-(Cyanophenylcarbamoylmethylene)-2,6-diphenylpyran (**10b**).—The compound was prepared by the method described for **10a** and was recrystallized from chlorobenzene: yield 93%; mp 240°; *m/e* 390, 298, 105, 77.

Anal. Calcd for $C_{26}H_{18}N_2O_2$: C, 80.0; H, 4.6; N, 7.2. Found: C, 80.0; H, 4.6; N, 7.1.

4-(Cyanocarbamoylmethylene-1-*n*-butyl-2,6-diphenyl-1,4-dihydropyridine (**13a**) **and 4-Cyanophenylcarbamoylmethylene-2,6-diphenyl-1,4-dihydropyridine** (**13b**).—These compounds were prepared from **10a** and **10b**, respectively, by the method described for the preparation of **9**. Compound **13a** was recrystallized from methanol and melted at 194–195°: yield 71%. This compound thermally decomposed in the heated inlet system to 1-butyl-4-cyanomethylidene-2,6-diphenyl-1,4-dihydropyridine and cyanic acid.

Anal. Calcd for $C_{24}H_{23}N_3O$: C, 78.2; H, 6.2; N, 11.4. Found: C, 77.9; H, 6.5; N, 11.5.

Compound **13b** was recrystallized from ethanol and melted at 185–186°: yield 84%. This compound thermally decomposed to the same dihydropyridine derivative as **13a** plus phenyl isocyanate.

Anal. Calcd for $C_{30}H_{27}N_3O$: C, 80.6; H, 6.0; N, 9.4. Found: C, 80.8; H, 6.0; N, 9.3.

4-(Dicyanomethylene)-2,6-diphenyl-4H-pyran (**11**). **A.**—A solution of 4.0 g of **10a** in 24 ml of acetic anhydride was heated for 18 hr, the mixture was cooled, and the solid was collected and recrystallized from nitromethane, giving a 74% yield of **11**: mp 267°; *m/e* 296, 267, 240, 105, 102, 77.

Anal. Calcd for $C_{20}H_{12}N_2O$: C, 81.0; H, 4.0; N, 9.5. Found: C, 81.4; H, 4.0; N, 9.5.

B.—A solution of 7.0 g of **3** and 2 g of malononitrile in 50 ml of acetonitrile was heated to reflux, and 5.0 ml of N,N-diisopropylethylamine was added. The mixture was chilled, and the solid was collected and recrystallized giving a 70% yield of **11**.

4-(Cyanoacetoxycarbonylmethylene)-2,6-diphenyl-4H-pyran (**12**).—A solution of 4.0 g of **10b** and 25 ml of acetic anhydride was heated to reflux for 16 hr and cooled, and the solid was collected and recrystallized from acetonitrile: yield 59%; mp 229–230°; *m/e* 357, 315, 298, 271, 105, 102, 77, 43.

Anal. Calcd for $C_{22}H_{15}NO_4$: C, 74.0; H, 4.2; N, 3.9. Found: C, 74.2; H, 4.0; N, 4.1.

Di(4-hydroxy-2,6-diphenylpyrylium) Malonate (**14**).—A mixture of 10 g of **1**, 4.2 g of malonic acid, and 200 ml of ethyl acetate was heated for 5 min on a steam bath and cooled, and the solid was collected and recrystallized from ethyl acetate: yield 98%; mp 125°. This compound thermally decomposed to **1** and acetic acid.

Anal. Calcd for $C_{37}H_{28}O_8$: C, 73.1; H, 4.7. Found: C, 73.4; H, 4.9.

***meso*-(2,6-Diphenylpyrylium-4)bis(2,6-diphenylpyrylium-4)monomethinecyanine Diperchlorate** (**15**). **A.**—A solution of 3 g (0.005 mol) of **14** and 3 ml of phosphorous oxychloride was heated on a steam bath for 2 hr, and 15 ml of ethyl alcohol was added to the reaction mixture. The mixture was chilled, 3 ml of 70% perchloric acid was added, and the solid was collected and recrystallized from acetonitrile: yield 47%; mp 315°; explodes.

Anal. Calcd for $C_{52}H_{36}Cl_2O_{11}$: C, 68.6; H, 3.9; Cl, 7.9. Found: C, 68.2; H, 4.1; Cl, 7.9.

B.—A mixture of 2.5 g (0.01 mol) of **1**, 1.73 g (0.005 mol) of 4-methyl-2,6-diphenylpyrylium perchlorate (**16**), and 9 ml of phosphorous oxychloride was heated for 2 hr on a steam bath, diluted with 100 ml of methanol, and chilled, and the solid was collected and recrystallized to give a 56% yield of product.

Bis(2,6-diphenylpyrylium)monomethinecyanine Perchlorate (**17**).—A mixture of 3 g (0.005 mol) of **14**, 3.5 g (0.01 mol) of **3**, 2 ml of N,N-diisopropylethylamine, and 25 ml of acetonitrile was refluxed for 3 hr and cooled, and the solid was collected and recrystallized from acetonitrile: yield 51%; mp 310–311°.

Anal. Calcd for $C_{35}H_{25}ClO_6$: C, 72.8; H, 4.3; Cl, 6.2. Found: C, 72.8; H, 4.6; Cl, 6.1.

Registry No.—**1**, 1029-94-3; **2a**, 17605-20-8; **2b**, 17539-76-3; **3**, 17539-77-4; **4**, 17539-78-5; **5**, 17558-09-7; **6**, 17533-57-2; **7**, 17533-58-3; **8**, 17533-59-4; **9**, 17533-60-7; **10a**, 17558-05-3; **10b**, 17533-61-8; **11**, 17533-62-9; **12**, 17558-06-4; **13a**, 17533-63-0; **13b**, 17605-21-9; **14**, 17558-07-5; **15**, 17558-08-6; **17**, 17558-10-0; cyanoacetic acid, 372-09-8.