(9440); $^1$H NMR (350 MHz, $CDCl_3$) $\delta$ 1.24 (s, 6 H, $CH_3$), 1.65 (m, 2 H-6), 2.15 (m, 2 H-3 and 2 H-7), 2.32 (m, 2 H-5), 5.12 (td, $J$ = 4 and 2 Hz, 1 H-8); 5.38 (br, $w_{1/2}$ = 10 Hz, 1 H-4). Anal. ($C_{11}H_{16}O$) C, H.

***trans*-2,3-Dimethyl-3,5,6,7-tetrahydro-2*H*-1-benzopyran (3d)**: bp 68–70 °C (0.5 mmHg); UV (EtOH) $\lambda_{max}$ nm ($\epsilon$) 229 (9200), 250 (8200); $^1$H NMR (350 MHz, $CDCl_3$) $\delta$ 0.96 (d, $J$ = 7 Hz, $CH_3$ C-3), 1.28 (d, $J$ = 6.3 Hz, $CH_3$ C-2), 1.65 (m, 2 H-6), 2.17 (m, 1 H-3 and 2 H-7), 2.32 (m, 2 H-5), 3.44 (qd, $J$ = 6.3 and 9 Hz, 1 H-2), 5.13 (td, $J$ = 4 and 2 Hz, 1 H-8), 5.27 (br, $w_{1/2}$ = 5.6 Hz, 1 H-4). Anal. ($C_{11}H_{16}O$) C, H.

**[4-$^2$H]-2-Methyl-3,5,6,7-tetrahydro-2*H*-1-benzopyran (3b-[4-$^2$H])**. This compound was obtained as described above using $LiAlD_4$ in an overall yield from **1b** of 40%: $^1$H NMR ($CDCl_3$) $\delta$ 1.28 (d, $J$ = 6 Hz, $CH_3$) 1.50–1.75 (m, 2 H-6), 2.0–2.4 (m, 2 H-3, 2 H-5 and 2 H-7), 3.90 (m, 1 H-2), 5.12 (t, $J$ = 4 Hz, 1 H-8).

**Registry No.** **1a**, 29798-89-8; **1b**, 13738-56-2; **1c**, 29798-90-1; **1d**, 29767-23-5; **2a**, 92545-32-9; **2b**, 92545-33-0; **2c**, 92545-34-1; **2d**, 92545-35-2; **3a**, 62691-02-5; **3b**, 92545-36-3; **3b**-[4-$^2$H], 92545-39-6; **3c**, 92545-37-4; **3d**, 92545-38-5.

## 11,11,12,12-Tetracyanoanthraquinodimethane

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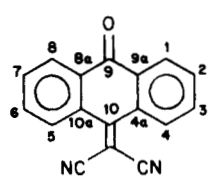
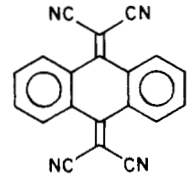
*Received May 10, 1984*

While the majority of sterically congested anthraquinones such as 1,4-, 1,5-, or 1,8-disubstituted anthraquinones display only minor structural deformations (e.g., longer bond lengths, wider bond angles, etc.) and remain relatively planar in structure,[1] 10-(dicyanomethylene)-anthrone **1** is a highly distorted molecule.[2] Structurally,



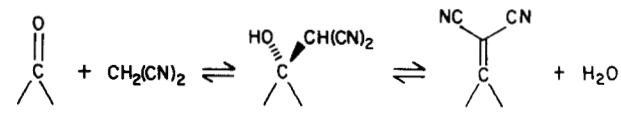

**1**




**2**

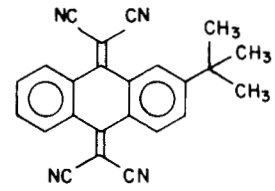
**1** exists in a butterfly-like conformation with the two benzo moieties buckling in one direction while the central quinonoid ring adopts a boat conformation with its extremities pointing in the other direction.[3] The carbonyl and dicyanomethylidene functions are respectively bent by 11° and 36.5° from the plane described by $C_{4a}$–$C_{9a}$–$C_{8a}$–$C_{10a}$. Even with these distortions, the distance between the cyano carbon and $C_4$ or $C_5$ is still 2.84 Å, which is shorter than the value of 3.0 Å for non-bonded interactions of this type.[3] In light of this, we expect 11,11,12,12-tetracyanoanthraquinodimethane (**2**) to be an excessively overcrowded and severely deformed molecule. We describe here a facile synthesis and some molecular properties of this structurally interesting compound.[4]

**Scheme I**

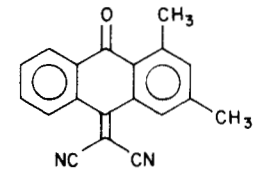



**3**

Although malononitrile generally condenses with aromatic carbonyl compounds with great ease,[5-7] its condensation with anthraquinone, however, cannot be executed under standard conditions. the excessive overcrowding in **2** obviously shifts the equilibrium of condensation in favor of the reactants and precludes the otherwise simple condensation (Scheme I). This difficulty, however, may be overcome if the tetrahedral intermediate **3** of the condensation could be forced to liberate water in an irreversible manner. We found that the Lewis acid $TiCl_4$ was an effective agent for promoting the condensation in the following manner: first, it activated the carbonyl functions of anthraquinone for condensation through complexation; second, it removed water from **3** irreversibly. Thus, when a mixture of anthraquinone and malononitrile was treated with excess $TiCl_4$ and pyridine as a base at room temperature for several hours, **2** was obtained in good yield. Similarly, 2-*tert*-butylanthraquinone condensed readily with malononitrile to afford 11,11,12,12-tetracyano-2-*tert*-butylanthraquinodimethane (**4**) under the same conditions. This method of condensation was in fact so effective that the monosubstituted species **1** could not be isolated under the reaction conditions. To obtain the monosubstituted species under these conditions, we found it necessary to introduce a blocking group into the antraquinone structure to prevent the second condensation. Accordingly, when 1,3-dimethylanthraquinone was subjected to the same reaction conditions, only 1,3-dimethyl-10-(dicyanomethylene)anthrone (**5**) was formed exclusively.




**4**




**5**

In structural analogy to **1**, **2** should have a butterfly-like conformation. The degree of deformation in **2**, however, should be far more severe than that in **1**. The electron affinity[8] of **2** was measured to be 2.21 eV, which is significantly lower than the value of ~2.45 eV expected for a planar structure of this molecule.[9] Apparently, the buckling of the benzo moieties and the severe out-of-plane distortion of the two dicyanomethylidene functions have deprived the latter, to a great extent, of the conjugation between them. In addition, despite its reasonably high electron affinity, **2** failed to form charge-transfer complexes even with strong electron donors such as tetrathiafulvalene (TTF). This anomalous behavior is to be expected if **2**

(1) For recent review, see: Berstein, J.; Cohen, M. D.; Leiserowitz, L. In "The Chemistry of the Quinonoid Compounds"; Patai, S., Ed.; Wiley: New York, 1974; Chapter 2.
(2) Takimoto, H.; Krbechek, L. *J. Org. Chem.* **1962**, *27*, 4688.
(3) Silverman, J.; Yannoni, N. F. *J. Chem. Soc.* **1967**, 194.
(4) During the course of our work, two separate, somewhat complicated multistep syntheses were reported: (a) Hhota, S.; Tosaka, T.; Sonoda, N.; Shimotsuma, W. European Pat. Appl. 61264. (b) Yamaguchi, S.; Tatemitsu, H.; Sakata, Y.; Misumi, S. *Chem. Lett.* **1983**, 1229. After submission of this manuscript, it came to our attention that a synthesis similar to ours had just been reported. See: Aumuller, A.; Hunig, S. *Liebigs Ann. Chem.* **1984**, 618.
(5) Mowry, D. T. *J. Am. Chem. Soc.* **1945**, *67*, 1050.
(6) Zabicky, J. *J. Chem. Soc.* **1961**, 683.
(7) Mukherjee, T. K. *J. Org. Chem.* **1965**, *30*, 644.
(8) Electron affinity (EA) was determined from half-wave reduction potential ($E_{1/2}$) according to the equation EA = $-E_{1/2}$ + 2.49 (eV); see: Chen, E. C. M.; Wentworth, W. E. *J. Chem. Phys.* **1975**, *63*, 3183. Cyclic voltammetry was carried out in $CH_2Cl_2$ with tetrabutylammonium perchlorate as supporting electrolyte and Ag/AgCl. KCl as reference electrode.
(9) If **2** were a planar molecule, the difference between its EA and that of anthraquinone should be approximately the same as that between 7,7,8,8-tetracyanoquinodimethane and *p*-benzoquinone (~0.83 eV).

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were significantly deformed and nonplanar. Nevertheless, in the presence of water, the formation of colorful molecular complexes of **2** with certain electron donors such as TTF, anthracene, and thianthrene was observed. These complexes have a nonfixed stoichiometry containing $H_2O$ and exhibit high resisitivities. Furthermore, they are not stable and readily dissociate into individual components either on heating or by dissolution in solvent.

## Experimental Section

All melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. IR spectra were recorded on a Beckmann IR-4250 spectrophotometer with polystyrene as the calibration standard and UV–vis spectra on a Hewlett Packard UV/vis spectrophotometer. $^1H$ NMR spectra were recorded in $CDCl_3$ on a Bruker WP-80 spectrometer with tetramethylsilane as an internal standard. Low-resolution mass spectra were obtained on a Finnigan 4000 quadrupole instrument. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

**General Procedure for the Condensation of Anthraquinones with Malononitrile.** The following is an illustrative procedure for the condensation reaction.

To a well-stirred mixture of 20 mmol of anthraquinone and 3.5 g (55 mmol) of malononitrile in 125 mL of methylene chloride at an ice-bath temperature were added dropwise 11.5 mL of $TiC_4$ over a period of 20 min and 35 mL of pyridine over a period of 30 min. After the addition, the ice bath was removed to allow the reaction to continue at room temperature for another 5 h. The reaction mixture was evaporated and the residue was treated with 100 mL of 10% aqueous HCl solution with vigorous stirring. The solid product was filtered and washed several times with water and dried. Purification of the product was accomplished either by recrystallization from an appropriate solvent or by column chromatography.

**(a) 11,11,12,12,-Tetracyanoanthraquinodimethane (2):** recrystallized from acetic acid in 87% yield: mp >350 °C dec; $^1H$ NMR ($CDCl_3$) 7.8–8.6 (AA'BB'); IR (KBr pellet) 2235 $cm^{-1}$ (CN); UV–vis ($CH_2Cl_2$) $\lambda_{max}$ ($\epsilon$) 285 (30 500), 305 (16 300), 350 nm (26 000): MS, *m/e* (relative intensity): 304 (100), 277 (30), 250 (20), 223 (8), 212 (5), 198 (6), 152 (7), 138 (9), 125 (19), 111 (14). Anal. Calcd for $C_{20}H_8N_4$: C, 78.94; H, 2.65; N, 18.41. Found: C, 78.94; H, 2.83; N, 18.29.

**(b) 11,11,12,12-Tetracyano-2-*tert*-butylanthraquinodimethane (4):** purified by column chromatography on silica gel (ethyl acetate: hexane, 1:4) in 59% yield: mp 313–14 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 1.4 (s, 9 H), 7.6-8.4 (m, 7 H); IR (KBr pellet) 2235 (CN) $cm^{-1}$. Anal. Calcd for $C_{24}H_{16}N_4$: C, 79.98; H, 4.47; N, 15.54. Found: C, 80.09; H, 4.40; N, 15.51.

**(c) 1,3-Dimethyl-10-(dicyanomethylene)anthrone (5):** recrystallized from acetic acid in 72% yield: mp 215–16 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 2.45 (s, 3 H), 2.75 (s, 3 H), 7.3–8.3 (m, 6 H); IR (KBr pellet) 2230 (CN), 1680 (C=O) $cm^{-1}$. Anal. Calcd for $C_{19}H_{12}N_2O$: C, 80.26; H, 4.25; N, 9.85; O, 5.63. Found: C, 80.35; H, 4.23; N, 9.81; O, 5.67.

**Molecular Complexes of 11,11,12,12-Tetracyanoanthraquinodimethane (2).** The following preparation of the complex of **2** with anthracene is illustrative of the procedure. A mixture of 0.304 g (1 mmol) of **2** and 0.178 g (1 mmol) of anthracene was dissolved in 80 mL of acetonitrile by heating. The solution was poured into 240 mL of water with stirring, resulting in the formation of a purplish solid. The product was filtered and dried in vacuo at 50 °C for 24 h; the yield was 0.44 g. The product, when finely dispersed as particulates on a transparent substrate, displayed a charge-transfer band at 505 nm. When heated to ~300 °C, it turned into a purplish melt, but changed to a pale yellow solid on cooling. It also lost its color when dissolved in solvents (e.g., methylene chloride), indicating its dissociation into individual components.

The complex of **2** with tetrathiafulvalene is dark green in color while that with thianthrene is brownish in color. Attempts to record their charge-transfer absorptions were not successful because of the difficulty in dispersing them. Conductivity measurements on these complexes in the form of pressed pellets showed that they had very high resistivities.

**Acknowledgment.** We extend our gratitude to our colleague Dr. R. O. Loutfy for electrochemical characterization.

**Registry No.** **2**, 70359-39-6; **2**–anthracene complex, 92720-72-4; **2**–tetrathiafulvalene complex, 92720-73-5; **2**–thianthrene complex, 92720-74-6; **4**, 92720-70-2; **5**, 92720-71-3; $NCCH_2CN$, 109-77-3; $TiCl_4$, 7550-45-0; anthraquinone, 84-65-1; 2-*tert*-butylanthraquinone, 84-47-9; 1,3-dimethylanthraquinone, 3285-97-0; anthracene, 120-12-7; tetrathiafulvene, 31366-25-3; thianthrene, 92-85-3.

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# Oxygenated Analogues of 4-[(1*H*-Imidazol-4-yl)methyl]-2,5-dimethyloxazole

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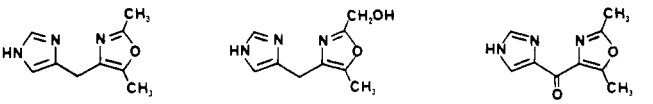
*Received May 29, 1984*

In a program to discover histidine decarboxylase inhibitors, histidine derivative **1**[1] was found to have analgesic properties in a number of our animal models. Subsequently, we synthesized the oxygenated analogues **2** and **3**. The syntheses of these compounds, reported here, led



1 2 3

to some approaches that may offer wider applicability for imidazolyloxazoles and related compounds with these substitution patterns.

The synthesis of **2** (Scheme I) was based on the classic Dakin–West reaction,[2,3] yielding keto amine **4** followed by specific acylation to keto amide **5**. 2-(Phenylmethoxy)-acetyl chloride (**7**), a key intermediate, was reported[4] in 35% yield by a three-step synthesis beginning with the alkoxide obtained from benzyl alcohol and sodium metal. We found a much improved yield (85–90%) of **7** if alkoxide was generated with sodium hydride. Subsequent acylation of the imidazole derivative **4** with **7** required initial acylimidazole formation through addition of 1 equiv of imidazole to acid chloride **7** prior to addition of **4**. This obviated the problem of simultaneous acylation of the imidazole ring of **4**. Cyclodehydration to the oxazole **6** was accomplished in refluxing phosphorus oxychloride in 83% yield after column chromatography. Several catalytic hydrogenolysis and chemical methods to remove the benzyl protecting group were employed unsuccessfully. However, lithium in a mixture of THF–liquid ammonia at −78 °C cleanly removed the protecting group to give the desired alcohol **2**.

The synthesis of **3** (Scheme II) began with the protected imidazole **8** reported by Breslow.[5] Unlike that group, we were not able to efficiently form the requisite anion of **8** using lithium disopropylamide under a number of reaction conditions and turned to *n*-butyllithium for the conversion. Subsequent reaction with aldehyde **9**[6] gave alcohol **10** in

(1) Wrede, F.; Keil, W. *Z. Phys. Chem.* **1931**, *203*, 279. This compound was synthesized in the laboratories of the late Dr. Edward Smissman, University of Kansas, and tested at McNeil in a collaborative research program.
(2) Dakin, H. D.; West, R. *J. Biol. Chem.* **1928**, *78*, 91, 745, 757.
(3) Iwakura, Y.; Toda, F.; Suzuki, H. *J. Org. Chem.* **1967**, *32*, 440.
(4) Bennington, F.; Morin, R. D. *J. Org. Chem.* **1961**, *26*, 194. Wenner, W.; Plati, J. T. *Ibid.* **1946**, *11*, 751.
(5) Tang, C. C.; Davalian, D.; Huang, P.; Breslow, R. *J. Am. Chem. Soc.* **1978**, *100*, 3918.

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