Benzodioxole Chemistry. 3.[1a] Preparation and Selected Reactions of 3a,4,7,7a-Tetrahydro-4,7-methano-1,3-benzodioxole-2,8-diones.[1b] Novel Hydroxide Ion Induced Aromatization of Carbonyl-Bridged Cyclic Carbonates[1c]

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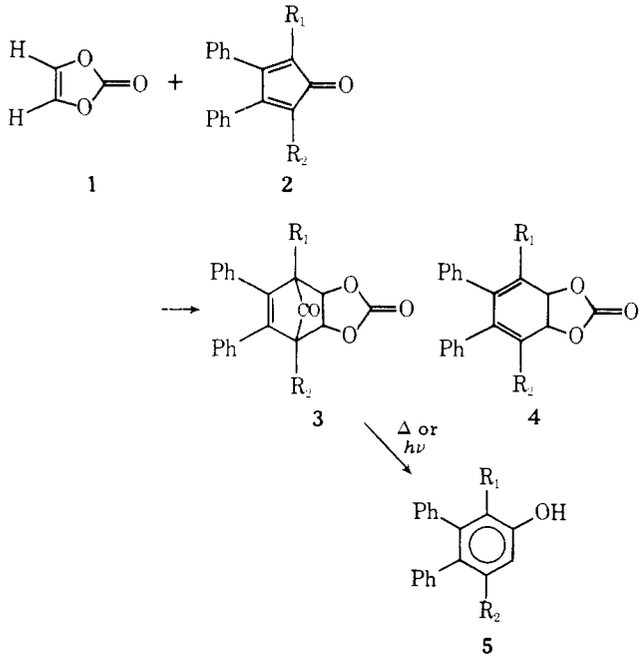
Received November 9, 1978

Synthesis of five 4,5,6,7-tetrasubstituted-3a,4,7,7a-tetrahydro-4,7-methano-1,3-benzodioxole-2,8-diones (**3b–f**) by the reaction of vinylene carbonate (**1**) with the appropriate cyclopentadienone (**2b–f**) in refluxing benzene or xylene is reported. Thermolysis (refluxing bromobenzene) of **3b** and **3d–f**, as well as the previously prepared **3a**, produces phenols **5a,b,d–f** in good to excellent yields; **3c**, however, is converted into dienecarbonate **4c** (in addition to **5c**) under these conditions. Dienecarbonate **4c** is also prepared (60%) from **1** and **2c** in refluxing xylene (24 h). The photochemistry of the system was probed using **3a**, **3b**, **3d**, and **3c** as models and, in the first three cases, conversion to phenols **5a**, **5b**, and **5d** occurs in fair to good yields, while in the last case a good yield of **4c** is obtained. On treatment with 1 molar equiv of potassium carbonate in aqueous dimethylformamide at room temperature **3a–f** undergo clean, high-yield conversion to the aromatic products **6a–f**. The sequence 1 + 2 → 3 → 6 represents a facile route to aromatic compounds, especially those containing heat- or acid-sensitive substituents. Thus, it provides what is believed to be the only example (aside from the original work) of the utilization of **1** in the manner for which it was originally conceived by Newman, i.e., as a molecule which would yield "an adduct easily convertible to an aromatic structure." Finally, plausible reaction schemes are presented to account for the observed transformations.

A number of years ago we became interested in substituted 3a,4,7,7a-tetrahydro-4,7-methano-1,3-benzodioxole-2,8-diones (**3**) as potential precursors to catechols. At that time there was little physical and chemical data available on this ring system except for that reported by Yates and Hyre[3] on tetraphenyl derivative **3a**. We therefore initiated a research effort aimed at delineating the spectral and chemical properties of this heterocyclic system and in this paper we report our findings to date.

Synthesis and Spectral Properties of 3. The substituted benzodioxolediones **3** were prepared by the (2 + 4) cycloaddition of vinylene carbonate (**1**) to the appropriately substituted cyclopentadienones **2** as described earlier;[3] pertinent information relating to the syntheses and properties of **3** is summarized in Table I. For most of the cases cited in Table I the major product from **1** and **2** was the corresponding **3**; however, the reaction with **2c** in refluxing xylene (2.5 h) yielded a second product, **4c** (25%), for which high-resolution mass spectral molecular weight and elemental analysis indicated a formula of $C_{23}H_{18}O_7$. This information, a singlet (2 H) at δ 6.02 in the NMR spectrum (in addition to the required number of aromatic and carbomethoxy protons), and the presence of infrared absorptions at 1710, 1740, and 1810 cm^{-1} suggested decarbonylation product **4c**[4] as a likely candidate. Reinforcement for this assignment was provided by the fact that **4c** was the only product obtained on extending the reflux time to 24 h, carbon monoxide being evolved in the process.



a, $R_1 = R_2 =$ Ph; b, R_1 = Me; R_2 = Ph
c, $R_1 = R_2 =$ COOMe; d, $R_1 = R_2$ = Me
e, $R_1 = R_2 =$ Et; f, $R_1 = R_2 =$ *n*-Pr
g, R_1 = Ph; R_2 = Me

As expected, the infrared spectra of **3** displayed prominent bands at ca. 1810 and 1780 cm^{-1}, attributable to the C–O stretching vibration of the cyclic carbonate[5] and bridged ketone carbonyl,[6] respectively, while the NMR spectra were characterized by a singlet (2 H, methine protons) at δ 5.00–5.90. The mass spectra of **3a,b,d–f** displayed molecular ion peaks of varying intensities as well as definite peaks corresponding to the loss of 72 mass units (CO + CO_2) from the molecular ion. By comparison, **3c** showed, in addition to a strong parent peak, a base peak at *m/e* 346 (− CO − CO_2 − O) but no significant peak corresponding to loss of CO + CO_2.

Thermolyses of 3. Yates and Hyre prepared 2,3,4,5-tetraphenylphenol (**5a**) in high yield by heating **3a** above its decomposition point.[3] We have now demonstrated that thermolytic conversion to phenols is a general reaction of **3** and have prepared phenols **5a–f** in good to excellent yields (with one exception, vide infra) by thermolysis of **3a–f** in refluxing bromobenzene (Table II). The single phenol obtained from thermolysis of **3b** had previously been assigned[7] structure **5g** on the basis of the best match between observed ^{13}C NMR chemical shift and calculated shift values.[8] Recently, however, a ^{13}C NMR proton-coupled spectrum of the phenol was obtained and it failed to show the expected splitting (quartet of doublets) of the methyl carbon signal by the hydrogen in the ring position ortho to it. Based on this evidence we are forced to conclude that the product obtained from thermolysis of **3b** is phenol **5b**, rather than **5g**.

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Table I. 3a,4,7,7a-Tetrahydro-4,7-methano-1,3-benzoidioxole-2,8-diones (3a–f)

compd	registry no.	reflux time h[a]	% yield	mp, °C (solvent[b])	ν C=O (bridge), cm^{-1}	ν C=O (carbonate), cm^{-1}	δ methine	formula[c]
3a	34420-10-5				1785	1810	5.85	$C_{32}H_{22}O_4$[d]
3b	56406-95-2	2	50	215 dec (B)	1780	1810	5.53 (J = 7.6) 6.17 (J = 7.6)	$C_{27}H_{20}O_4$
3c	69517-18-6	21[e]	87	198 dec (B-P)	1790	1815	5.80	$C_{24}H_{18}O_8$
3d	56406-94-1	3	76	178.5 dec (B)	1770	1815	5.05	$C_{22}H_{18}O_4$
3e	56406-97-4	2.5	42	145–146 (I)	1790	1820	5.21	$C_{24}H_{22}O_4$
3f	69517-19-7	2.5	54	151–152.5 (B-P)	1780 (sh)	1795	5.21	$C_{26}H_{26}O_4$

[a] Xylene solvent unless otherwise indicated. [b] B = benzene, I = 2-propanol, P = petroleum ether (bp 30–60 °C). [c] Satisfactory analytical data (±0.3% for C, H) were reported for **3b–3f**. [d] Reference 3. [e] Benzene solvent.

Table II. Phenols 5a,b,d–f[a] from Thermolyses

substrate	product	registry no.	% yield	mp, °C (solvent[b])	formula[c]
3a	**5a**	56406-88-3	94	188–190 (B-P)	$C_{30}H_{22}O$[d]
3b	**5b**	69517-20-0	83	157–159 (A)	$C_{25}H_{20}O$
3d	**5d**	56406-89-4	100	135–136 (L)	$C_{20}H_{18}O$[e]
3e	**5e**	56406-92-9	100	123–125 (L)	$C_{22}H_{22}O$
3f	**5f**	69517-21-1	100	82–84	$C_{24}H_{26}O$

[a] Reactions were run in refluxing bromobenzene for 24 h. All compounds gave satisfactory NMR spectra and were homogeneous by TLC. [b] A = acetic acid, B = benzene, L = petroleum ether (bp 60–80 °C), P = petroleum ether (bp 30–60 °C). [c] Satisfactory analytical data (±0.3% for C, H) were given for **5e**; accurate mass measurements (±2 ppm) were reported for **3b** and **3f**. [d] Reference 3. [e] Analyzed as the acetate derivative; mp 135–136 °C after recrystallization from petroleum ether (bp 60–110 °C). Anal Calcd. for $C_{22}H_{20}O_2$: C, 83.52; H, 6.37. Found: C, 83.45; H, 6.23.

Table III. Results of Exploratory Photolyses[a]

substrate	product	% yield
3a	**5a**	60[b]
3b	**5b**	45[c]
3c	**4c**	45[b]
3d	**5d**	57[c]

[a] Photolyses were run for 4 h. [b] Isolated yield. [c] Estimated yield based on NMR analysis of acetylated photolysate (see Experimental Section).

A possible mechanistic rationalization for the formation of **5** from **3** has been postulated[7] and it implicates diene **4** as a precursor to **5**. Some evidence in favor of the intervention of **4** was found in the results obtained on thermolysis of dicarbomethoxy derivative **3c**. In this case, the only solid material isolated was diene carbonate **4c** (34%), while NMR analysis of the residual oil indicated a mixture of **4c** (~40%) and phenol **5c** (~60%). Furthermore, thermolysis of **4c** itself in refluxing bromobenzene (70 h) led to 50% conversion to phenol **5c**. Unfortunately, attempts to obtain evidence for the formation of the corresponding dienes **4** (e.g., **4d**) by TLC monitoring of the thermolyses were unsuccessful; gradual disappearance of starting **3** was accompanied by concomitant formation of phenol **5**. Perhaps the fact that **4c** could be isolated from the thermolyzate attests to its greater stability compared to the other dienes due to the added resonance stabilization afforded by the ester groups. Such an argument has been advanced by White[9] to explain the fact that cyclone **2c** exists predominantly as a monomer at 25 °C, rather than as the dimer.

Exploratory Photolyses of 3. Inasmuch as Braun[10] has shown that the LiCl-catalyzed pyrolysis of 1,2-divinylethylene carbonate produces *trans*-1,2-divinylethylene oxide (in addition to 4,5-dihydrooxepin), it seemed reasonable to explore the photolysis of **3** as a possible route to the biologically interesting[11] arene oxides. Conceivably, such molecules might serve as intermediates on the reaction profile between dienes **4** and phenols **5** and might also prove to be stable under photolytic conditions. Accordingly, tetrahydrofuran solutions (~5×10^{-3} M) of four representative benzodioxolediones (**3a–d**) were irradiated with light of 254 nm wavelength for 4 h and the progress of the reaction was monitored by TLC. The results were substantially the same as those obtained in the thermolyses, although the reactions were less clean. Thus, **3a, 3b,** and **3d** yielded phenols **5a, 5b,** and **5d** in fair to good yields, while **3c** was converted mainly to diene carbonate **4c** (45+%) (Table III). In none of the cases did we find any evidence of arene oxide formation as judged by NMR analysis of the crude reaction mixtures. In corroboration of these findings, termination of the photolysis of **3a** after 1 h yielded a mixture of starting material and **5a** as the only components.

Aromatization Reaction. As was mentioned earlier, our initial interest in **3** focused on their use in the preparation of substituted catechols. It was thought that hydrolysis of the carbonate function to the corresponding diol followed by decarbonylation–aromatization (one step or two) would be a reasonable route to the desired catechols. In our early work[1c] we explored the feasibility of the sequence using **3a** as a model and were disappointed to find that it was unperturbed by various acidic hydrolysis conditions [e.g., boiling 0.3 M hydrochloric acid (24 h); boiling concentrated hydrochloric acid (up to 5 days)]; quantitative recovery of starting material was realized in all cases. Yet, refluxing a slurry of **3a** in 10% aqueous potassium hydroxide or simply stirring a solution of **3a** in 4% aqueous dimethylformamide containing 1 molar equiv of potassium carbonate (2 h at room temperature) did lead to reaction and the formation of a pale pink solid (~100%) identified as 1,2,3,4-tetraphenylbenzene (**6a**). Since that time we have extended this "aromatization" reaction using potassium carbonate in aqueous dimethylformamide to include benzodioxolediones **3b–f** and have established this as a general reaction for this heterocyclic system by the high-yield conversion to aromatic hydrocarbons **6b–f**. Under these same reaction conditions diene carbonate **4c** was converted to phenol **5c** as expected.

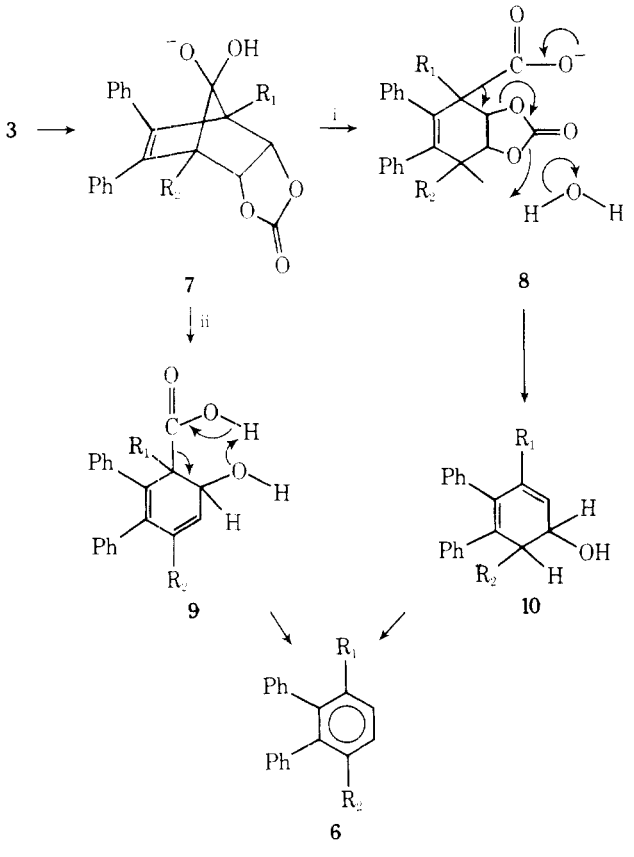
In Table IV are given isolated yields and physical properties

Table IV. Products 6a–f[a] from "Aromatization" Reaction

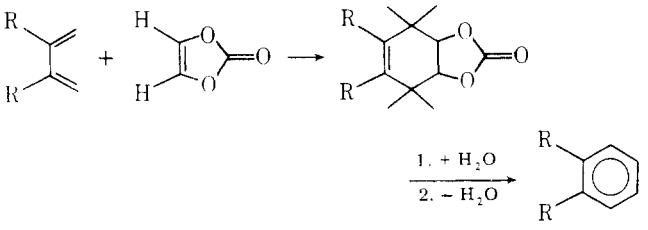
substrate	product	registry no.	% yield[b]	mp, °C (solvent[c])	formula[d]
3a	**6a**	1487-12-3	96	190–192[e]	$C_{30}H_{22}$
3b	**6b**	69517-26-6	92	95–97 (E)	$C_{25}H_{20}$
3c	**6c**	19799-32-7	88	116–117.5[f]	$C_{22}H_{18}O_4$
3d	**6d**	13102-23-3	80	110–112[e]	$C_{20}H_{18}$
3e	**6e**	69517-27-7	80	78–79 (M)	$C_{22}H_{22}$
3f	**6f**	7541-91-5	84	41–43 (E-W)	$C_{24}H_{26}$

[a] Reactions were run for 24 h at room temperature. All compounds gave satisfactory NMR and mass spectra and the analytical samples were homogeneous by TLC. [b] Isolated yields of nearly pure compound. [c] E = ethanol, M = methanol, W = water. [d] Satisfactory analytical data (±0.3% for C, H) were reported for **6b** and **6e**; and an accurate mass measurement (±0.3 ppm) was reported for compound **6f** in this table. [e] These products have been described before: see ref 4 and 13. [f] Lit. mp 118–119 °C: O. Dann, K.-J. Bamberg, and H. Sucker, *Pharmazie*, **23**, 135 (1968).

Scheme I



Scheme II



of the products obtained from the "aromatization" reaction. The reactions were normally allowed to continue for 24 h to maximize yields; however, in the case of **3a**, workup of the reaction only 15 min after the addition of the potassium carbonate gave results identical with those employing longer reaction times. The progress of the reaction could readily be followed by TLC and the products **6a–f** were easily isolated by pouring the reaction mixture over ice followed by filtration of the resultant solid.

In light of our previous observation that the reaction of **3a** with sodium methoxide–methanol yields a single product[12] derived from attack of methoxide ion at the carbonyl bridge, it is quite likely that the overall "aromatization" process is triggered by initial attack by hydroxide ion at the same site to produce ion **7**. Conversion of **7** into **6** could then conceivably proceed by either one of two possible pathways (Scheme I). Route i depicts the conversion as involving carboxylate anion **8**, while route ii implicates hydroxycarboxylic acid **9** as an intermediate. In either case, a driving force for the overall transformation is provided by formation of carbon dioxide and water, as well as the final aromatic system of **6**. The generation of **8** by hydroxide ion attack at the bridge carbonyl of **3** followed by ring opening to a carbanion and proton transfer is supported by several precedents[13,14] in the literature. By the same token, if the endo configuration of **3** is assumed, loss of carbon dioxide to yield **9** could proceed by the familiar Grob fragmentation reaction.[15] At present, the available information does not provide sufficient evidence to favor one route over the other; however, we are attempting to accumulate further information on the details of this mechanism and this will be reported in due course.

The synthetic significance of the overall sequence **1** + **2** → **6** becomes apparent when one considers some of the reasoning which prompted the conception and original preparation of the vinylene carbonate (**1**) molecule. Thus, in his definitive paper on **1**, Newman[16] indicated that he viewed it as a replacement for maleic anhydride "which would not only approximate maleic anhydride from the steric aspect but *would also yield an adduct readily convertible to an aromatic structure.*" He devised a general sequence for accomplishing the synthesis and then applied it in a four-step synthesis of *o*-xylene from 2,3-dimethylbutadiene and **1** (31% overall yield) as shown in Scheme II. However, to the author's knowledge, the utilization of **1** in the preparation of aromatic compounds has not been extensively explored. It is therefore felt that, given the availability of a large number of cyclopentadienones[17] (or their immediate precursors[18]), the sequence **1** + **2** → **3** → **6** provides a reasonable alternative to Newman's proposed sequence and, in addition, represents a facile route to aromatic compounds, especially those containing heat- or acid-sensitive substituents.

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind., and by the Section on Microanalytical Services and Instrumentation, Laboratory of Chemistry, NIAMDD, NIH. IR spectra were obtained as paraffin oil mulls and $CHCl_3$ solutions on Perkin-Elmer 257 and 599 and Beckmann IR 8 spectrophotometers. ^1H NMR spectra were measured on Varian A-60 and EM-360 spectrometers with Me_4Si as internal standard. ^{13}C NMR spectra were measured on a Varian CFT-20 spectrometer. The low-resolution mass spectra were obtained on Hitachi RMU-6E and AEI MS-902 instruments, while the high-resolution spectra were obtained on the latter instrument. Silica gel GF plates for analytical TLC were purchased from Analtech, Inc., Ne-

wark, Del. Photolyses were carried out in a Rayonet Photochemical Reactor (Model RPR-100) equipped with 16 R.P.R. 2537-Å lamps.

General Procedure for the Preparation of Substituted 3a,4,7,7a-Tetrahydro-4,7-methano-1,3-benzodioxole-2,8-diones (3a–f). A mixture of vinylene carbonate[19] (1; 12 mmol), the appropriate cyclopentadiene[17] **2a–f** (5.0 mmol), and solvent (20 mL) was heated at reflux for the indicated length of time (Table I) with stirring. The hot solution was filtered to remove any insoluble material and the solvent was evaporated in vacuo to yield either solid or an oil which crystallized on trituration with petroleum ether (bp 30–60 °C) or benzene–petroleum ether (bp 30–60 °C).

Preparation of 4,7-Bis(carbomethoxy)-5,6-diphenyl-3a,7a-dihydrobenzodioxol-2-one (4c). A solution of 1.0 g (12.0 mmol) of 1 and 1.70 g (5.00 mmol) of **2c**[9] in 20 mL of xylene was stirred and heated at reflux for 24 h in a flask fitted with tubing which ran into a bubbler containing saturated $PdCl_2$ solution. During the reaction, carbon monoxide was evolved as evidenced by the formation of a palladium mirror on the walls of the bubbler. At the end of the reflux period, the solution was cooled to room temperature and then placed in a freezer overnight during which time solid material deposited. Filtration yielded 1.35 g (67%) of nearly pure **4c**, which showed, after recrystallization from 2-propanol: mp 155–157 °C; IR (paraffin oil) 1810, 1740, 1710 cm^{-1}; NMR ($CDCl_3$) δ 7.28–6.70 (m, 10 H, aromatic), 6.02 (s, 2 H, methine H), 3.49 (s, 6 H, $COOCH_3$).

Anal. Calcd for $C_{23}H_{18}O_7$: C, 67.98; H, 4.46. Found: C, 67.74; H, 4.73. Calcd for $C_{23}H_{18}O_7$: *m/e* 406.1051. Found: *m/e* 406.1064.

A mixture of 1 and **2c** (same quantities as above) were refluxed in benzene for 2.5 h and the solvent was evaporated. Trituration of the resulting oil with benzene–petroleum ether (bp 30–60 °C) yielded 1.4 g (67%) of **3c**, while 0.5 g (25%) of **4c** was obtained on concentration of the mother liquor.

General Procedure for the Thermolytic Preparation of Substituted Phenols 5a,b,d–f. The Diels–Alder adduct **3** (500 mg) in bromobenzene (7 mL) was stirred and heated at reflux for 24 h. The hot solution was filtered to remove any insoluble material and the solvent was evaporated in vacuo to yield either solid or an oil which crystallized on trituration with petroleum ether (bp 30–60 °C) or benzene–petroleum ether (bp 30–60 °C). See Table II.

Thermolysis of 3c in Refluxing Bromobenzene. A solution of **3c** (360 mg, 0.83 mmol) in bromobenzene (5 mL) was heated at reflux with stirring for 24 h. Evaporation of solvent yielded a viscous oil which crystallized on trituration with 2-propanol. Filtration afforded 115 mg (34%) of **4c**, and evaporation of solvent from the filtrate yielded an oil (200 mg) consisting of a mixture of **5c** (~60%) and **4c** (~40%). The product distribution was determined by comparison of the NMR integrations for characteristic peaks at δ 6.02 (**4c**) and 7.37 (**5c**) in the spectrum of the mixture.

Thermolysis of 4c in Refluxing Bromobenzene (70 h). A solution of **4c** (401 mg, 0.988 mmol) in bromobenzene (6 mL) was heated at reflux with stirring until TLC analysis (Et_2O–hexane, 1:1) indicated no further change (70 h). The solution was concentrated in vacuo to yield an oil which was chromatographed on a silica gel (Woelm, for dry-column chromatography) column. The fraction eluted with Et_2O–hexane (1:1, 200 mL) provided, after solvent evaporation, 179 mg (50%) of nearly pure **5c**, which showed, after recrystallization from EtOH–H_2O: mp 150–151.5 °C; IR ($CHCl_3$) 3300,[20] 1730, 1670[21] cm^{-1}; NMR ($CDCl_3$) δ 10.20 (s, 1 H, D_2O exchangeable, OH), 7.37 (s, 1 H, aromatic H ortho to OH and COOMe), 7.25–6.75 (m, 10 H, aromatic), 3.5 (s, 3 H, $COOCH_3$), 3.37 (s, 3 H, $COOCH_3$). The analytical sample was homogeneous on TLC ($CHCl_3$ and Et_2O–hexane, 1:2).

Calcd for $C_{22}H_{18}O_5$: *m/e* 362.1153. Found: *m/e* 362.1150.

General Procedure for the Photolysis of 3a–d. A solution of the appropriate **3** (1.00 mmol) in dry tetrahydrofuran (200 mL) was photolyzed for the indicated amount of time (Table III) and the solvent was evaporated in vacuo to yield an oil. In the case of **3a** and **3c** the oils crystallized to provide nearly pure **5a** (60%) and **4c** (45%). The oils obtained from **3b** and **3d** could not be induced to crystallized so they were acetylated directly by treatment with acetic anhydride–pyridine solution (1.5 mL of pyridine in 15 mL of acetic anhydride heated at reflux 15 min and cooled[22]). Deuteriochloroform solutions of the total crude acetylation mixtures were spiked with a known weight of anisole and the weight of the acetates (and therefore the phenols) was estimated by comparison of the NMR integrations of the anisole methoxyl peak (δ 3.70) with the acetoxy peaks (δ 2.25 for **5b** acetate and 2.28 for **5d** acetate).

Periodic monitoring of the reactions by TLC (Et_2O–hexane, 1:1) failed to show the build-up of any intermediate substance. In agreement with these results, photolysis of **3a** (mmol in 200 mL of THF) for 1 h led to the recovery of unreacted **3a** (33%) and to the production of an oil consisting mainly of **5a** (NMR and IR analysis).

General Procedure for the "Aromatization Reaction" (Preparation of 6a–f). The Diels–Alder adduct **3** (200 mg) was dissolved in dimethylformamide (24 mL)–water (1.0 mL) and to the vigorously stirred solution was added anhydrous potassium carbonate (1 molar equiv). After 24 h the reaction mixture was poured over ice (~25 g), stirred for 30 min, and filtered to yield **6** of >90% purity by TLC (Table IV).

TLC analysis (Et_2O–hexane, 1:4) of the reaction mixture after 15 min under the above conditions showed that **3a** had been completely consumed and only a single spot (same R_f value as pure **6a**) was in evidence.

Conversion of 4c into 5c. A solution of **4c** (400 mg, 1.00 mmol) dissolved in dimethylformamide (48 mL)–water (2.0 mL) was treated with anhydrous potassium carbonate (1 molar equiv) and the whole was vigorously stirred for 20 h. At the end of this time the solvent was evaporated in vacuo and the resulting solid was stirred with 1 M HCl (20 mL) for 2.5 h, filtered, washed with water (2 × 50 mL), and dried (drying pistol) to give a near quantitative yield of **5c**.

Acknowledgment. The author would like to thank Dr. Everette L. May (NIH) for the hospitality extended to him during a sabbatical year stay at NIH and Messrs. William S. Grove and Jeffrey W. R. Morton for their technical assistance. He also thanks Drs. Kenner C. Rice (NIH) and Arthur E. Jacobson (NIH) for numerous helpful discussions during the course of this work. Thanks are also due to the Central Fund for Research, The Pennsylvania State University, for partial financial support of the research.

Registry No.—**1**, 872-36-6; **2a**, 479-33-4; **2b**, 33535-80-7; **2c**, 16691-79-5; **2d**, 26307-17-5; **2e**, 51932-77-5; **2f**, 61202-93-5; **4c**, 69517-24-4; **5b** acetate, 69517-28-8; **5c**, 35044-33-8; **5d** acetate, 69517-29-9; **7a**, 69517-22-2; **7b**, 69517-23-3; **7d**, 69517-25-5; methyl 6-hydroxy-1,2,3,4-tetraphenyl-2,4-cyclohexadiene-1-carboxylate, 52316-15-1.

References and Notes

(1) (a) We wish to consider our two earlier communications, ref 1c and 7, as Parts 1 and 2 of this series. (b) Dr. K. L. Loening, Director of Nomenclature, Chemical Abstracts Service, has advised us that these compounds can be correctly designated either as 3a,4,7,7a-tetrahydro-4,7-methano-1,3-benzodioxole-2,8-diones or as 5,6-dihydroxy-2-norbornen-7-one cyclic carbonates. We wish to thank Dr. Loening for his helpful interest. (c) Part of this material has been presented in a preliminary communication: E. A. Harrison, Jr., *Chem. Commun.*, 1090 (1971).
(2) Inquiries should be directed to the author at the York Campus address.
(3) P. Yates and J. E. Hyre, *J. Org. Chem.*, **27**, 4101 (1962).
(4) The formation of dienes derived from decarbonylation of carbonyl-bridge compounds similar to **3** is a well-known reaction: e.g., see (a) C. F. H. Allen and J. A. Van Allan, *J. Am. Chem. Soc.*, **64**, 1260 (1942); (b) K. MacKenzie, *J. Chem. Soc.*, 473 (1960); (c) B. Fuchs, *J. Chem. Soc. C*, 68 (1968); (d) G. Kretschmer, I. W. McCay, M. N. Paddon-Row, and R. N. Warrener, *Tetrahedron Lett.*, 1339 (1975).
(5) L. Hough, J. E. Riddle, R. S. Theobald, G. R. Barker, T. Douglas, and J. W. Spoors, *Chem. Ind. (London)*, 148 (1960).
(6) The C=O absorption of carbonyl-bridged six-membered rings occurs at 1780–1800 cm^{-1}: e.g., see (a) C. F. H. Allen, T. Davis, D. W. Stewart, and J. A. Van Allan, *J. Org. Chem.*, **20**, 306 (1955); (b) J. Meinwald and E. G. Miller, *Tetrahedron Lett.*, 253 (1960); (c) S. C. Clark and B. L. Johnson, *ibid.*, 617 (1967).
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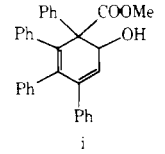

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Reaction of 2-Aminobenzazoles with Dimethyl 2-Aminofumarate. Synthesis and Nuclear Magnetic Resonance Spectroscopy of 4-Oxopyrimido[2,1-*b*]benzazoles

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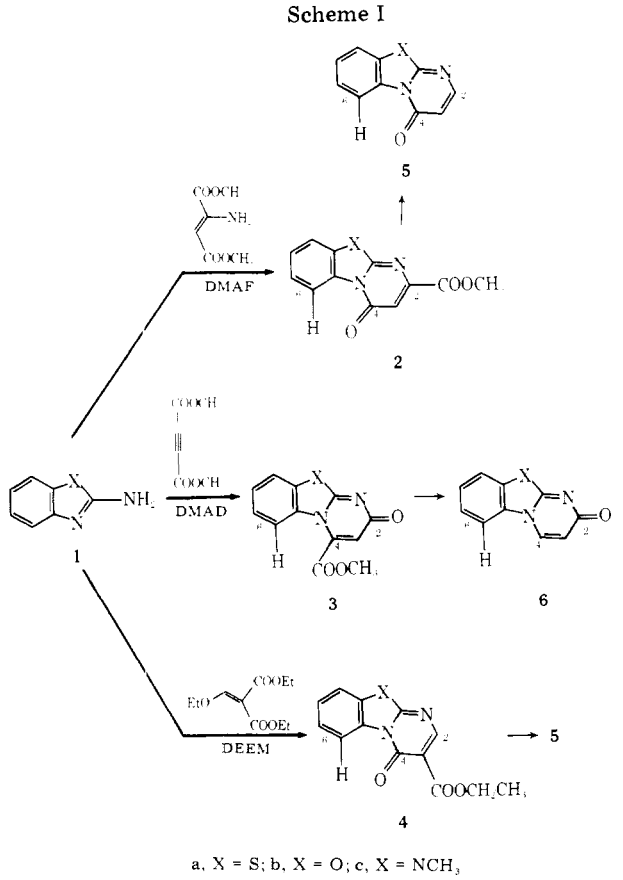
Received December 19, 1978

A convenient and apparently general procedure has been developed to prepare 4-oxopyrimido[2,1-*b*]benzazole-2-carboxylates by reaction of dimethyl 2-aminofumarate (DMAF) with 2-aminobenzothiazole, 2-aminobenzoxazole, or 2-amino-1-methylbenzimidazole. This new method complements the reaction of dimethyl acetylenedicarboxylate (DMAD) with these 2-aminobenzazoles since their reaction with DMAD gives the isomeric 2-oxopyrimido[2,1-*b*]benzazole-4-carboxylates. The esters derived from DMAF were hydrolyzed and decarboxylated to compounds which were identical with those obtained by hydrolysis and decarboxylation of the esters produced by reaction of each of the 2-aminobenzazoles with diethyl ethoxymethylenemalonate (DEEM). These decarboxylated derivatives are distinctly different from those obtained by hydrolysis and decarboxylation of the DMAD-derived esters. The assignments of compounds as 2-oxo or 4-oxo products were made on the basis of the ^1H NMR spectra, specifically by reference to the chemical shift of the absorbance assigned to the C-6 benzo ring proton.

During the course of a medicinal chemical project in our laboratories, we became interested in preparing compounds of structure **2** (Scheme I), where X = S, O, or NCH_3. Theoretically, such compounds might be available by Michael reaction of a 2-aminobenzazole **1** with dimethyl acetylenedicarboxylate (DMAD) at the 2-amino group, followed by cyclization onto the ring nitrogen. However, since the ring nitrogen is also a potential nucleophilic site for the initial Michael reaction, the possibility exists that the reaction will give the 2-oxo structure **3** rather than the 4-oxo structure **2**, which we desired.

Scheme I



a, X = S; b, X = O; c, X = NCH_3

A literature survey indicated that the reaction of DMAD with 2-aminobenzothiazole has been more thoroughly investigated than its reaction with the other 2-aminobenzazoles, and it seemed likely that, at least for this case, the usual product is in fact the 2-oxo isomer **3a**. This structure has been assigned on the basis of ^1H NMR data, including comparison with ^1H NMR data of compounds which have the 4-oxo structure but which do not have the ester functionality as in **2**.[1,2] Reimlinger et al., in a brief report, have described the reaction of **1a** with DMAD under various reaction conditions, one of which gave a chromatographically separable mixture of **2a** and **3a** which was isolated in yields of 2 and 6%, respectively.[3] The authors did not discuss the basis for their structural assignments. Finally, in a report which appeared after the commencement of our work, the structure of **3a** was established unequivocally by X-ray crystallography.[4]

The reaction of 2-aminobenzoxazole (**1b**) with DMAD has been reported to give **3b** rather than **2b**, and again the structure assignment is based on ^1H NMR evidence.[2] Reaction of 2-amino-1-methylbenzimidazole (**1c**) with DMAD has not been reported, although the reaction of 2-aminobenzimidazole (**1**, X = NH) apparently also gives a tricyclic compound of the 2-oxo (**3**) rather than 4-oxo (**2**) structure.[2] No X-ray analyses have been reported in these cases; ^1H NMR data for the products, and for related but not isomeric compounds, were the basis for structural assignments.

At the time our work began we felt that the published

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