In the case of the benzoic anhydride–Ia reaction mixture, the extraction left 10.5 g of a mixture of IIa and IIIa (74.2% yield). Fractional recrystallization of this mixture with acetone afforded 8.7 g of IIa, mp 104–106°, and 1.1 g of IIIa, mp 101–103°. The ether extract was washed several times with a 5% NaOH solution, and the aqueous layer was acidified by the addition of Dry Ice. Extraction of the aqueous solution with fresh ether, drying with anhydrous $MgSO_4$ and evaporation of the ether yielded 0.5 g of benzoic acid, mp 121–122°. The benzoic anhydride–Ib reaction mixture was treated in a similar manner, resulting in the isolation of 8.8 g of the ether-insoluble IIb (59% yield), mp 136–138°, and 1.8 g of benzoic acid. Finally, the original water-washed ether layer was dried with anhydrous $MgSO_4$ and evaporated to dryness. Recrystallization of the crude semisolid from petroleum ether resulted in the recovery of 2.3 g of IV, mp 67–69°. Mixture melting points of isolated IIa, IIb, IIIa, IV, and benzoic acid with the corresponding authentic samples were not depressed.

Registry No.—Benzoic anhydride, 93-97-0; IIa, 16888-96-3; IIb, 16888-97-4; IIIa, 16888-98-5; IIIb, 16888-99-6.

The Condensation of Enamines with Substituted *p*-Benzoquinones

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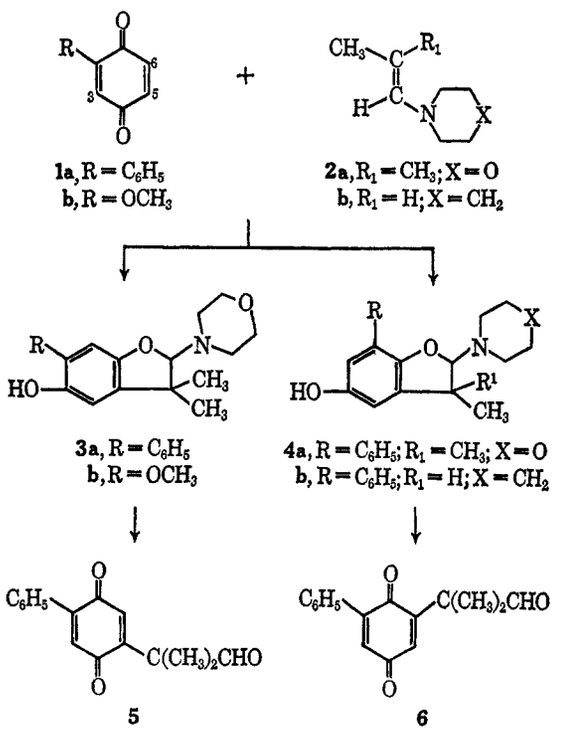
The introduction of a formylalkyl group into quinones by oxidation of 2-amino-2,3-dihydrobenzofurans **3**, which are available from the interaction of quinones **1** and enamines **2**,[1-3] was recently reported[1] (see Scheme I). The purported preparation of the 5-phenyl-2-formylalkylquinone **5**, mp 142–143°, by oxidation of the dihydrobenzofuran **3a** is illustrative of this procedure. Our experience[4] with the condensation of benzoquinones and enamines led us to believe that the quinone of mp 142–143° is, in fact, the 6-phenyl isomer **6**. Thus, inasmuch as the formation of the dihydrobenzofurans **3** and **4** probably proceeds by nucleophilic addition of the enamine to the benzoquinone and subsequent cyclization,[3] the position assumed by the quinone substituent in the product will reflect its electronic and steric character. Electron-withdrawing groups direct reaction toward C-3 in **1** or, alternatively, in the presence of strong steric effects, *e.g.*, phenyl, toward C-6, whereas electron-donating groups favor condensation at C-5.[5]

Indeed, as predicted by these considerations, condensation of 2-phenyl-1,4-benzoquinone (**1a**) with isobutenylmorpholine (**2a**)[6] gave 70% 7-phenyldihydrobenzofuran **4a** (δ 6.45 and 6.75, J = 3.0 cps), accompanied by 7% 6 isomer **3a** (δ 6.67). The reaction of **1a** with 1-propenylpiperidine (**2b**)[7] to give

SCHEME I



62% dihydrobenzofuran **4b** (δ 6.46 and 6.78, J = 3.0 cps) as the sole product further illustrates the directive influence of the phenyl substituent. In the instance of 2-methoxy-1,4-benzoquinone (**1b**), reaction with **2a** affords the expected 6-methoxydihydrobenzofuran **3b** (87%) (δ 6.45 and 6.51, unsplit). The position of the aryl substituent in the dihydrobenzofurans **3** and **4** follow from the cited proton resonances and their splitting patterns.

Oxidation of the 6-phenyldihydrobenzofuran **3a** with ferric chloride[1] afforded the 5-phenylquinone **5**, mp 127–128° (δ 6.60 and 6.78, unsplit), whereas a similar oxidation of the 7-phenyl isomer **4a** gave the 6-phenylquinone **6**, mp 141–142° (δ 6.76 and 6.84, J = 2.4 cps). These data clearly indicate that the quinone of mp 142–143°, to which structure **5** was previously assigned,[1] must possess the isomeric structure **6**. Moreover, the reaction of quinones and enamines in this and related examples proceeds in a predictable manner, the verification of which is readily furnished by nmr spectroscopy.[8]

Experimental Section[9]

Reaction of 1,4-Benzoquinones with Enamines.—The following experiment illustrates the general procedure. A solution of 1.49 g (10 mmol) of isobutenylmorpholine (**2a**) in 3 ml of methanol was added dropwise over 30 min to an ice-cooled, stirred mixture of 1.84 g (10 mmol) of 2-phenyl-1,4-benzoquinone (**1a**) in 7 ml of methanol. The solid dissolved to give a red solution that was stirred at ambient temperature for 1 hr. The solvent was removed, and the residue was dissolved in ether. This solution was passed through a magnesia–silica gel column, using ether as the eluting solvent. The yellow eluate was

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(2) K. C. Brannock, R. D. Burpitt, H. E. Davis, H. S. Pridgen, and J. G. Thweatt, *J. Org. Chem.*, **29**, 2579 (1964).
(3) G. Domschke, *J. Prakt. Chem.*, **32**, 144 (1966).
(4) (a) G. R. Allen, Jr., C. Pidacks, and M. J. Weiss, *J. Amer. Chem. Soc.*, **88**, 2536 (1966); (b) G. R. Allen, Jr., and M. J. Weiss, *J. Org. Chem.*, **33**, 198 (1968); (c) R. Littell and G. R. Allen, Jr., *ibid.*, **33**, 2064 (1968).
(5) H. S. Wilgus, III, E. Frauenglass, E. T. Jones, R. F. Porter, and J. W. Gates, Jr., *ibid.*, **29**, 594 (1964).
(6) E. Benzing, *Angew. Chem.*, **71**, 521 (1959).
(7) C. Mannich and H. Davidsen, *Ber.*, **69**, 2106 (1936).
(8) These results indicate that the Bunte salt derived from 2-phenyl-1,4-benzoquinone is most likely sodium 2,5-dihydroxy-3-biphenylylthiosulfate rather than sodium 2,5-dihydroxy-4-biphenylylthiosulfate: W. Alcalay, *Helv. Chim. Acta*, **30**, 578 (1947). If true, the derived 2-methylmercapto-1,4-benzoquinone is the 6-phenyl isomer, rather than the previously assigned 5-phenyl isomer.
(9) Melting points are uncorrected. Evaporations were carried out under reduced pressure. Nmr spectra were determined in deuteriochloroform using tetramethylsilane as an internal standard on a Varian A-60 spectrometer.

evaporated to give 3.47 g of an oil that was purified by partition chromatography[10] on diatomaceous silica using a heptane–methanol (1:1) solvent system. The fraction with peak hold-back volume 4.0 (v_m/v_s = 2.7) was evaporated; recrystallization of the residue from acetone–hexane gave 238 mg (7%) of **2,3-dihydro-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-6-phenylbenzofuran** (**3a**) as white crystals, mp 215–217°.

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.80; H, 6.97; N, 4.29.

The fraction with peak hold-back volume 6.0 was evaporated; the residue was recrystallized from acetone–hexane to furnish 2.033 g (70%) of **2,3-dihydro-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-7-phenylbenzofuran** (**4a**) as white crystals, mp 164–165°.

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.53; H, 7.10; N, 4.26.

Reaction of 4.70 g (37.5 mmol) of 1-piperidyl-1-propene (**2b**) and 4.60 g (25 mmol) of 2-phenyl-1,4-benzoquinone (**1a**) in benzene gave 3.65 g of **2,3-dihydro-5-hydroxy-3-methyl-7-phenyl-2-(1-piperidyl)benzofuran** (**4b**) as crystals, mp 130–133°, by direct crystallization. Partition chromatography of the material in the filtrate using a heptane–methanol (1:1) system afforded an additional 1.13 g (62%) of crystals, mp 135–137°, in that fraction with peak hold-back volume 3.4 (V_m/V_s = 2.5). A sample was recrystallized from ether–hexane to give white crystals, mp 135–137°.

Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.91; H, 7.51; N, 4.52.

Treatment of 1.38 g (10 mmol) of 2-methoxy-1,4-benzoquinone (**1b**) with 1.49 g (10 mmol) of isobutenylmorpholine (**2a**) in methylene chloride, solvent removal, and trituration of the residue with ether gave 2.44 g (87%) of **2,3-dihydro-5-hydroxy-6-methoxy-3,3-dimethyl-2-(4-morpholinyl)benzofuran** (**3b**) as crystals, mp 157–161°. A sample recrystallized from methanol had mp 168–169°.

Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.49; H, 7.58; N, 5.01. Found: C, 64.23; H, 7.29; N, 4.71.

Oxidation of the 2-Amino-2,3-dihydrobenzofurans.—The following experiment illustrates the general procedure. A solution of 1.080 g (2.0 mmol) of ferric chloride hexahydrate in 7.5 ml of water was added dropwise with stirring to a suspension of 650 mg (1.0 mmol) of 2,3-dihydro-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-7-phenylbenzofuran (**4a**) in 75% methanol. The mixture was stirred for 3 hr after completion of the addition, at which time it was bright yellow. The solid was collected by filtration and dissolved in methylene chloride. This solution was passed through a magnesia–silica gel column using methylene chloride as the eluting solvent. The yellow eluate was evaporated to give a residue that was recrystallized twice from ether to give 340 mg (67%) of **α-(6-phenyl-2-*p*-quinoyl)isobutyraldehyde** (**6**) as orange crystals: mp 141–142°; λ_{max} 291 mμ (ε 4840), 314 (5340).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.30; H, 5.63; N, 0.0.

In the manner described above, treatment of 120 mg (0.36 mmol) of 2,3-dihydo-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-6-phenylbenzofuran (**3a**) with 270 mg (1.0 mmol) of ferric chloride hexahydrate furnished 43 mg (43%) of **α-(5-phenyl-2-*p*-quinoyl)isobutyraldehyde** (**5**) as needles, mp 127–128°, after recrystallization from ether–hexane: λ_{max} 300 mμ (ε 5970), 312 (6480).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.65; H, 5.42; N, 0.0.

Registry No.—**3a**, 16793-13-8; **3b**, 16793-14-9; **4a**, 16793-15-0; **4b**, 16793-16-1; **5**, 14348-69-7; **6**, 16793-18-3.

Acknowledgment.—The author is indebted to Mr. C. Pidacks and his staff for the partition chromatography, to Mr. W. Fulmor and his associates for the spectral data, and to Mr. L. Brancone and his group for the microanalyses.

(10) For a complete description of this technique, as developed by Mr. C. Pidacks of these laboratories, see M. J. Weiss, R. E. Schaub, G. R. Allen, Jr., J. F. Poletto, C. Pidacks, R. B. Conrow, and C. J. Coscia, *Tetrahedron*, **20**, 357 (1964).

Preparation of A-Ring Conjugated Enones and the Corresponding α,β-Epoxy Ketones of 17β-Acetoxy-5α-androstane

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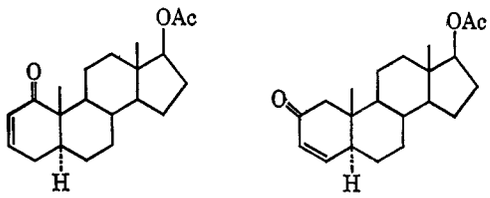
In connection with other studies, the title compounds were needed. While the A-ring conjugated enones (**1–4**) are already known, there were some different observations between those reported by earlier authors[1] and ours during the course of preparing the enones (**1**, **2**, and **4**). The epoxy ketones (*e.g.* **5**, **14**, **24**, and **26**) are believed to be interesting compounds for CD[2a] and biological[2b] studies. These compounds, except for **5**, have not been reported to date.



1

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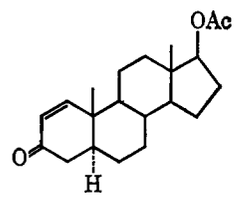

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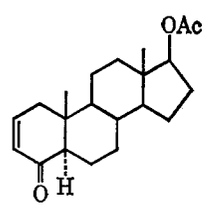
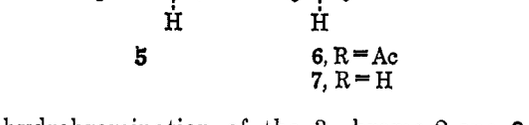


4

Reductive elimination of the 1α,2α-epoxy-3-one **5**[3] with 60% $NH_2NH_2 \cdot H_2O$ gave the enol **6** in 57% yield, which upon oxidation afforded the 2-en-1-one **1**. In our hands, the reaction of the epoxy ketone **5** with 100% $NH_2NH_2 \cdot H_2O$ according to Djerassi, *et al.*,[1a] who obtained only the enol **6** (40%), yielded a mixture of the enol **6** (12%) and the 2-ene-1α,17β-diol **7** (37%). Furthermore, the use of 95% $NH_2NH_2 \cdot H_2O$[1b] could not prevent cleavage of the C_{17} acetoxyl group.



5 **6**, R = Ac; **7**, R = H

Dehydrobromination of the 3α-bromo-2-one **9**, derived from the bromohydrin **8**,[4] with Li_2CO_3 alone af-

(1) (a) C. Djerassi, D. H. Williams, and B. Berkoz, *J. Org. Chem.*, **27**, 2205 (1962); (b) P. D. Klimstra and R. E. Counsell, *J. Med. Chem.*, **8**, 48 (1965); (c) P. D. Klimstra, U. S. Patent 3,166,578 (1965); *Chem. Abstr.*, **62**, 9207a (1965).

(2) (a) K. Kuriyama, H. Tada, Y. K. Sawa, S. Itô, and I. Itoh, *Tetrahedron Lett.*, 2539 (1968); (b) Dr. Miyake of our laboratory, unpublished results.

(3) W. M. Hoehn, *J. Org. Chem.*, **23**, 929 (1958).

(4) Kindly supplied by Dr. Komeno of our laboratory.