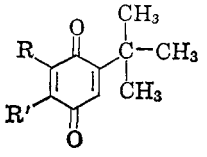
tion of such an enormous rate enhancement for the hydrolysis of a five-membered cyclic ester which contains a heteroatom other than phosphorus. The origin of the extraordinary lability of catechol cyclic sulfate is now under study.

E. T. Kaiser, I. R. Katz, T. F. Wulfers
Department of Chemistry, University of Chicago
Chicago, Illinois 60637
Received June 24, 1965

Photorearrangement of Di-*t*-butyl-*p*-benzoquinones

Sir:

The current general interest in the photochemistry of carbonyl compounds has recently been extended to studies involving several *p*-benzoquinone systems. Some early work demonstrated the photoreduction of *p*-benzoquinone to hydroquinone in alcoholic solvents.[1] More recently, photodimerization[2] of some substituted *p*-benzoquinones and photocycloaddition with olefins[3] has been observed. We wish to report here the photorearrangement of the di-*t*-butyl-*p*-benzoquinones Ia and Ib in alcohol solution.

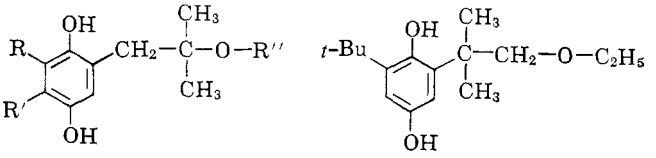


Ia, R = *t*-Bu; R′ = H
b, R = H; R′ = *t*-Bu

Photolysis[4] of a 0.2 *M* solution of Ia in ethanol for 24 hr. at 25–30° resulted in the isolation of an orange-red oil after solvent evaporation. Trituration of this oil with hexane provided a crystalline, white solid, 2.0 g. (38%), m.p. 128–130° (from hexane–benzene).

Elemental analysis (*Anal.* Calcd. for $C_{16}H_{26}O_3$: C, 72.10; H, 9.77. Found: C, 71.50; H, 9.92) and mass spectral determination of the molecular weight (mol. wt. 266) showed that this product (II) was a 1:1 adduct of the quinone and ethanol. An analogous product (III), m.p. 119.6–121.6°, was obtained in 50% yield when methanol was substituted for ethanol.

The infrared spectrum [λ_{max}, μ: 2.97 (s), 3.17 (s) (OH); 6.24 (m) (aromatic C=C); 9.02 (s), 9.46 (s) (–C–O–C–)] and the ultraviolet spectrum [λ_{max}^{THF}, mμ: 238 (ϵ 16,000); 297 (ϵ 47,500)] were indicative of a hindered phenolic system.[5] The n.m.r. spectrum provided confirmation for this structure: a broad peak at τ 5.0 (1 H) and a sharp singlet at τ 1.25 (1 H) found in the spectrum of IIa which disappeared on the addition of D_2O to the $CDCl_3$ solution pointed to the presence of one unhindered and one severely hindered hydroxyl group. Evidence for two mutually coupled aromatic protons was supplied by a pair of doublets (AB pattern) at τ 3.15 and 3.48. A quartet at τ 6.47 (J = 8.5 c.p.s., 2 H) and a triplet at 8.77 (J = 8.5 c.p.s., 3 H) constituted a clear indication for an ethoxy group. Taking into account the presence of two phenolic hydroxy groups, two aromatic protons, and two side chains, it became apparent that the ethoxy group could not be attached directly to the aromatic ring. Support for this conclusion was provided by the observation that two singlets at τ 8.40 (9 H) and 8.77 (6 H) account for only five of the six methyl groups that were present in Ia. A singlet was found at τ 7.20 (2 H) which signified that one of the original methyl groups had been converted into a methylene group. Hence, the adduct must be a hydroquinone which has one *t*-butyl side chain and one other side chain that contains an ethoxy group. Two reasonable structures (IIa and IIb) can be written for the adduct at this stage.



IIa, R = *t*-Bu; R′ = H; R″ = C_2H_5 IIb
III, R = *t*-Bu, R′ = H; R″ = CH_3
IV, R = H; R′ = *t*-Bu; R″ = C_2H_5
V, R = H; R′ = $CH_2C(CH_3)_2OC_2H_5$; R″ = C_2H_5

Further structural information was sought by the acetylation and oxidation of II. Treatment with acetic anhydride–pyridine converted II into a monoacetate[6] (VI), m.p. 63.5–65.5°. The n.m.r. spectrum of VI showed a sharp peak at τ 1.58 which disappeared very slowly on the treatment of a $CDCl_3$ solution of VI with D_2O. This behavior is in keeping with the hindered position of one of the hydroxyl groups in II.

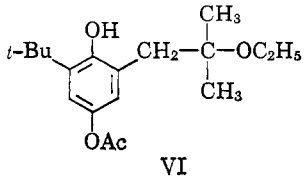
Oxidation of II at 25° with chromic acid in acetic acid[7] led to the quinone[6] VII as a liquid. The n.m.r. spectrum of VII was very similar to that of II except in the aromatic region: in place of the distinct AB quartet of II there appeared one signal (2 H) of complex pattern centered at τ 3.00. This complexity must be caused by additional coupling through long-range spin–spin interaction. In structure VII the methylene group should undergo allylic coupling with the nearer of the two aromatic protons which are mutually coupled through the ketone. In the alternative structure (corresponding to IIb) neither allylic nor homoallylic coupling (H—C—C=C—C—H) is feasible. Irradiation of the methylene signal at τ 7.20 caused the multiplet at 3.00 in the high-frequency side band to resolve into a quartet (AB pattern), whereas irradiation of the τ 3.00 signal with the same decoupling frequency caused a sharpening of the methylene peak at 7.20 in the low-frequency side band. This double resonance experiment shows that the methylene group is coupled (J < 1 c.p.s.) with one of the aromatic protons and thus supports the structure VII. The coupling between the two aromatic protons (J = 2.9 c.p.s.) is consistent with their *meta* relationship to each other. If the molecular rearrangement had involved the migration of the side chain from one nuclear

(1) (a) P. A. Leighton and G. S. Forbes, *J. Am. Chem. Soc.*, **51**, 3546 (1929); (b) A. Schönberg and A. Mustafa, *Chem. Rev.*, **40**, 181 (1947).
(2) (a) R. C. Cookson and J. Hudec, *Proc. Chem. Soc.*, 11 (1959); (b) E. Zavarin, *J. Org. Chem.*, **23**, 47 (1958); (c) R. C. Cookson, D. A. Cox, and J. Hudec, *J. Chem. Soc.*, 4499 (1961); (d) D. Bryce-Smith and A. Gilbert, *ibid.*, 2428 (1964).
(3) (a) D. Bryce-Smith and A. Gilbert, *Proc. Chem. Soc.*, 87 (1964); (b) D. Bryce-Smith and A. Gilbert, *Tetrahedron Letters*, 3471 (1964); (c) G. O. Schenck, I. Hartmann, and W. Metzner, *ibid.*, 347 (1965).
(4) Photolysis was carried out using a Pyrex vessel and a 275-w. G.E. sunlamp.
(5) C. D. Cook, R. G. Inskeep, A. S. Rosenberg, and E. C. Curtius, Jr., *J. Am. Chem. Soc.*, 77, 1672 (1955).
(6) Satisfactory microanalyses were obtained for this compound.
(7) C. F. Koelsch and S. Wawzonek, *J. Am. Chem. Soc.*, **65**, 755 (1943).

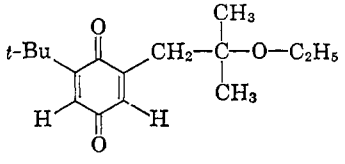
carbon to another, the two aromatic protons could not have been in a 1:3 position in the quinone VII.

The structure IIa is also supported by the mass spectrum of the rearranged product, which shows the base peak at *m/e* 87 corresponding to a scission of the side chain to produce the fragment A.

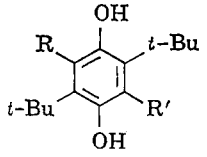
Before the completion of our investigation a report[8] appeared in which structures VIII and IX were assigned to two of the products from the photolysis of Ib in ethanol. We have repeated this photolysis experiment and examined the n.m.r. spectra of the products of m.p. 167–167.5° and 209–210°. The spectral data indicate that the structures for these two compounds are IV and V, respectively.



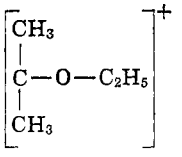
VI



VII



VIII, R = H; R′ = OC_2H_5
IX, R = R′ = OC_2H_5



A, *m/e* 87

There are a considerable number of naturally occurring compounds which possess the *p*-benzoquinone moiety.[9] An alkenylphenol has recently been shown to be a biosynthetic precursor of ubiquinone.[10] It would be of interest to ascertain the role, if any, of the photorearrangement of alkyl-*p*-benzoquinones to hydroquinones in the biogenesis of naturally occurring quinones. The scope and mechanism of the photorearrangement reported here is currently under investigation.

Acknowledgment. We thank Dr. M. S. Manhas for the mass spectrum, R. Tavares for the n.m.r. spectra, and Dr. E. R. Malinowski for the double resonance data.

(8) J. Petránek and O. Ryba, *Chem. Ind.* (London), 225 (1965).
(9) L. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1961, p. 863.
(10) R. K. Olsen, J. L. Smith, G. D. Daves, H. W. Moore, K. Folkers, W. W. Parson, and H. Rudney, *J. Am. Chem. Soc.*, **87**, 2298 (1965).

C. M. Orlando, Jr.
Kay-Fries Chemicals, Inc.
West Haverstraw, New York

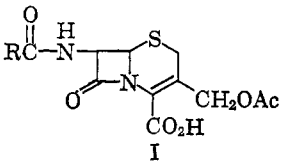
Ajay K. Bose
Department of Chemistry and Chemical Engineering
Stevens Institute of Technology
Hoboken, New Jersey

Received June 11, 1965

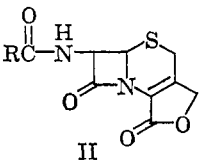
Total Synthesis of the Cephalosporin Antibiotics. I. The Dihydrothiazine System of Cephalosporin C_c.

Sir:

The outstanding antibacterial properties of many of the antibiotics related to cephalosporin C (I, R = $(CH_2)_3CH(NH_2)CO_2H$),[1] together with their remarkable lack of toxicity,[2] have established their importance in medicine. Of no less interest to the organic chemist has been the challenge presented by their molecular architecture which embodies within a single six-membered ring the features of an enamide, an α,β-unsaturated carboxyl, an allylic alcohol, and an allylic sulfide. Although much progress has been made recently toward the construction of substituted 3,6-dihydro-2H-1,3-thiazines,[3] the synthesis of the actual dihydrothiazine system found in cephalosporin C, or in cephalosporin C_c (II, R as in I), has not yet been successful.

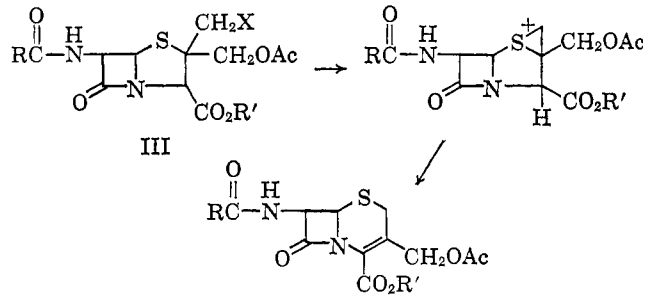


I



II

We wish to report a solution to this problem which we believe to be a general one. It occurred to one of us some years ago that a suitably substituted penicillin derivative (*cf.* III) could be constructed which might be transformed into the cephalosporin C system. This scheme is



III

Since methods for the construction of the penicillin ring system are well worked out,[4] the crucial part of the synthesis is the postulated formation of the properly substituted dihydrothiazine by ring expansion of a thiazolidine.

We have now been able to put this synthetic scheme to the test and are able to report its success.

Addition of hydrogen sulfide in methanol solution[5] to the known 2-phenyl-4-(2-acetoxy-1-acetoxymethylethylidene)-2-oxazolin-5-one,[6] followed by heating of the resulting thiazoline with a 1:2:4 mixture of hydrochloric acid, water, and acetic acid for 45 min. at 100°, gave the bicyclic thiazoline lactone V, obtained as its monohydrate, m.p. 52°, from aqueous ethanol. *Anal.* Found: C, 53.80; H, 4.72; N, 5.40. The substance had λ_{max}^{MeOH} 246 mμ (log ϵ 4.28) and $\nu_{max}^{CHCl_3}$ 1780,

(1) E. P. Abraham and G. G. F. Newton, *Biochem. J.*, **79**, 377 (1961); D. C. Hodgkin and E. N. Maslen, *ibid.*, **79**, 393 (1961).
(2) *Cf.*, *inter alia*, W. E. Wick and W. S. Boniece, *Appl. Microbiol.*, **13**, 248 (1965); E. V. Heyninger, *J. Med. Chem.*, **8**, 22 (1965).
(3) R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, and S. L. Andrews, *J. Am. Chem. Soc.*, **85**, 1896 (1963); D. M. Green, A. G. Long, P. J. May, and A. T. Turner, *J. Chem. Soc.*, 766 (1964); G. C. Barrett, V. V. Kane, and G. Lowe, *ibid.*, 783 (1964); G. C. Barrett, S. H. Eggers, T. R. Emerson, and G. Lowe, *ibid.*, 788 (1964); E. Galantay, H. Engel, A. Szabo, and J. Fried, *J. Org. Chem.*, **29**, 3560 (1964); S. H. Eggers, V. V. Kane, and G. Lowe, *J. Chem. Soc.*, 1262 (1965).
(4) *Cf.* J. C. Sheehan and K. R. Henery-Logan, *J. Am. Chem. Soc.*, **84**, 2983 (1962), and earlier references therein.
(5) *Cf.* J. W. Cornforth in H. T. Clarke, *et al.*, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 737.
(6) E. Galantay, A. Szabo, and J. Fried, *J. Org. Chem.*, **28**, 98 (1963).