Studies in the Oxepin Ring System. Stability and Spectral Properties of 3-Benzoxepin Derivatives

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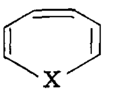
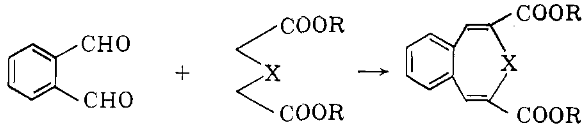
Several new 3-benzoxepin derivatives have been prepared. Structure confirmation of IV and V are made by proton magnetic resonance spectral measurements. The stability of IV and V is explained by the unfavorable electronic effect to acid cleavage exerted by the carboxyl and carbomethoxyl groups. The most likely protonation site is evaluated by means of basicity measurements.

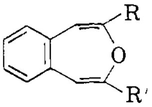
Seven-membered unsaturated heterocycles are of inherent interest in connection with the question of aromatic stability of other than $(4n + 2)$ electron containing ring systems,[2] since planarity, a chief requirement for resonance, appears feasible in these eight-electron ring systems. The parent ring compounds, oxepin (Ia), thiepin (Ib), and azepin (Ic), are not known and have eluded active preparative efforts.[3–6] A few complex derivatives of I have been reported[7] but are of uncertain structure assignment. Dibenzo derivatives of Ia, b, c have been prepared, but these compounds hardly qualify as true derivatives of I. The 3-benzoxepin derivatives, on the other hand, were considered suitable representatives of ring system I. A number of these 3-benzo derivatives have been reported, prepared from the condensation reaction of phthalaldehyde[8–10] (or substituted phthalaldehyde[11]) with the heterodiacetic acid II, to give derivatives of type III. (X = O, S, NCH_3, NC_6H_5; R = H, C_2H_5). Of particular interest[12] was the oxygen analog (III, X = O), resulting from this reaction when the ester of 2,2′-oxydiacetic acid (II, X = O) was employed.[8b,9] The two products obtained, IV and V, have been reported to possess a surprising degree of stability, incompatible with their representation as classical cyclic divinyl ether structures, and aromatic stability has been attributed, to the 3-benzoxepin ring system, for this reason. In view of this claim and because of the interesting chemical properties associated with this ring system, it was of interest to examine the chemistry of these compounds in greater detail. A number of new benzoxepin derivatives were prepared and these were employed for a more detailed characterization of the benzoxepin ring system and for a verification of the correctness of the structural assignments made for IV and V.

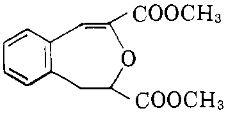


Ia, X=O
b, X=S
c, X=NH

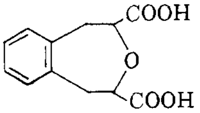


I II III





IX



X

IV. R,R′ = COOH
V. R,R′ = $COOCH_3$
VI. R,R′ = CH_2OH
VII. R,R′ = CH_2OCOCH_3
VIII. R = CH_2OH, R′ = CHO

The ester V was employed for the synthesis of derivatives VI, VII, VIII, and IX. The alcohol VI was obtained from the lithium aluminum hydride reduction of V under controlled conditions, or more conveniently, by employing a mixture of lithium aluminum hydride and aluminum chloride.

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(1) The author gratefully acknowledges a postdoctoral fellowship from the Public Health Service, Division of General Medical Sciences, 1959–1961.

(2) See, for example, A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, 1961, Chap. 10.

(3) J. Meinwald and H. Nozaki, *J. Am. Chem. Soc.*, **80**, 3132 (1958).

(4) J. Meinwald, D. W. Dicker, and N. Danieli, *ibid.*, **82**, 4087 (1960).

(5) E. E. Schweizer and W. E. Parham, *ibid.*, **82**, 4085 (1960).

(6) K. Dimroth and G. Pohl, *Angew. Chem.*, **73**, 436 (1961).

(7) G. Westoo, *Acta Chem. Scand.*, **13**, 604 (1959): A. A. Bothner-By and G. Traverso, *Ber.*, **90**, 453 (1957); F. Arndt, *ibid.*, **89**, 730 (1956); R. Huisgen, *Angew. Chem.*, **67**, 756 (1955); R. Huisgen, *et al.*, *Ber.*, **91**, 1, 12 (1958).

(8) (a) K. Dimroth and H. Freyschlag, *ibid.*, **89**, 2602 (1956); **90**, 1628 (1957); (b) K. Dimroth and H. Freyschlag, *ibid.*, **90**, 1623 (1957); *Angew. Chem.*, **69**, 95 (1957): **68**, 518 (1956).

(9) R. Huisgen, E. Laschtuvka, I. Ugi, and A. Kammermeir, *Ann.*, **630**, 128 (1960).

(10) G. P. Scott, *J. Am. Chem. Soc.*, **75**, 6332 (1953); K. Dimroth and G. Lenke, *Ber.*, **89**, 2608 (1956); *Angew. Chem.*, **68**, 519 (1956).

(11) F. Dallacker, K. W. Glombitza, and M. Lipp, *Ann.*, **643**, 97 (1961).

(12) Molecular oribtal calculations predict that oxygen in oxepin (Ia), by virtue of its larger electronegativity, will exert a stabilizing effect on the antibonding orbital containing the fourth electron pair, lowering the energy of this orbital relative to that of azepin (Ib) and thiepin (Ic) so that it approaches a bonding orbital in energy. A. Streitwieser, Jr., personal communication.

TABLE I

NUCLEAR MAGNETIC RESONANCE SPECTRA[a,b]

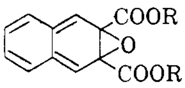
Compound	Aromatic hydrogen	"Benzylic" hydrogen	Other
V	2.75 (m)	2.90 (s)	—OCH_3, 6.10 (s)
VI	2.95 (m)	4.23 (s)	—CH_2, 5.90 (s) —OH, 5.60 (s)
VII	3.01 (m)	4.18 (s)	—CH_2O, 5.45 (s) —OCOCH_3, 7.90 (s)
VIII	2.80 (m)	3.37 (s) 4.17 (s)	—CHO, 0.75 (s) —CH_2OH, 5.92 (d)[c]
IX	2.83 (m)	3.02 (s)	—OCH_3, 6.15 (s), 6.36 (s) α-Hydrogen, 5.00 (t)[d] β(benzylic), 6.61 (d)[d]
XV	2.70 (m)	2.06 (s)	—OCH_3, 6.22 (s)

[a] All n.m.r. spectra were taken in deuteriochloroform and were recorded on a Varian Associates 60-Mc. spectrometer. Chemical shifts in τ, relative to tetramethylsilane as 10.00. Peaks are designated as follows: (s) singlet; (m) multiplet; (d) doublet; (t) triplet. [b] All proton signals were integrated and gave expected proton area ratios. [c] The oxygen bound proton overlaps with the methylenic hydrogens to give an unresolvable doublet. [d] The designation α and β refers to positions relative to the ether oxygen.

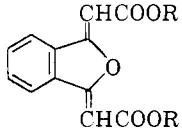
Under normal conditions, lithium aluminum hydride caused reduction of the double bonds. Manganese dioxide oxidation of VI gave the aldehyde VIII. Attempts to prepare the dialdehyde by further oxidation of VIII were unsuccessful.

Hydrogenation of IV and V over palladium-charcoal in ethanol proceeded in two stages; the first mole of hydrogen was consumed within fifteen minutes, yielding the dihydro derivative IX from V, while further hydrogenation over a period of twenty-four hours led to the uptake of a second mole of hydrogen.[13] The tetrahydro derivative X was prepared from IV in this manner.

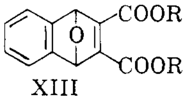
The n.m.r. spectra of compounds V–IX are reported in Table I. The interrelationships of the spectra of the various derivatives afford a full proof of the original structural assignment made of Dimroth and Huisgen. The proton magnetic resonance pattern obtained here clearly demonstrates that IV, V, VI, and VII have symmetrical structures; the absence of splitting of the methylenic hydrogens in the acetate VII eliminates any structures which possess α-hydrogens to the carboxyl group, such as XII[14] and the lack of symmetry in the the spectrum of the dihydro derivative IX disposes of alternative structures such as the naphthalene oxide structure XI or structure XIII. Thus, by means of a combination of spectral changes observed in the derivatives, a rigorous structural confirmation of IV and V was made possible.[15]



XI



XII



XIII

The ultraviolet and infrared spectra of the benzoxepin derivatives IV–X are reported in Table II. The successive bathochromic shifts observed in the ultraviolet spectrum in going from VI to IV, V and VIII suggest that the strong maximum in the vicinity of 240 mμ and the weaker absorption maximum in the 300-mμ region are characteristic spectral properties of the benzoxepin nucleus. A notable change occurs n the dihydro ester IX; with the destruction of the benzoxepin chromophore, the resulting spectrum is found to be consistent with a cinnamoyl chromophore carrying an α-alkoxy substituent.

The split carbonyl stretching frequency observed for the ester V in carbon tetrachloride may be due to conformational effects, frequently observed in symmetrical dicarbonyl compounds[17,18]

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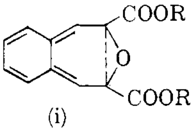
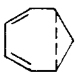
(13) This is another example of the reluctance with which addition to the second double bond takes place in these benzoxepin systems. Huisgen[9] reported that the ester V added only one mole of bromine.

(14) The chemical evidence presented by the authors[8b,9] did in no way exclude alternative structures such as XI, or less likely structures such as XII and XIII and a number of less symmetrical structures. Few chemical reactions were attempted on IV and V, and those reported appeared in conflict with the expected behavior for IV and V; for example, V was reported to add only one mole of bromine under forcing conditions and to undergo only slow oxidation with neutral permanganate; IV was reported to resist thermal decarboxylation. The products obtained from the copper-catalyzed thermal reaction of IV (2,3-naphthalenedicarboxylic acid and 2-naphthol-3-carboxylic acid) require an elaborate rearrangement scheme for their formation. A thorough structure clarification of IV and V thus appeared necessary.

(15) A fourth alternative, representing the structure of IV and V as (i) cannot be considered effectively without information about the planarity of the benzoxepin ring system and the magnitude of the resonance energy. This structure designates 1,6-overlap of the *p*-orbitals to give a planar *quasi* naphthalene oxide structure, a ten-electron system, expected to possess considerable aromatic stability. Similarly, cycloheptatriene has been formulated as the tropilidene structure (ii), on the basis of the resonance energy found to be contained.[16]



(i)

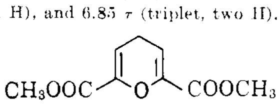


(ii)

(16) R. B. Turner, *et al.*, *J. Am. Chem. Soc.*, **79**, 4127 (1957); W. von E. Doering, *et al.*, *ibid.*, **78**, 5448 (1956); K. Conrow, *ibid.*, **83**, 2958 (1961).

(17) J. B. Rogan and D. J. Ellis, *J. Org. Chem.*, **26**, 5232 (1961).

(18) A very similar situation exists in 2,6-dicarbomethoxypyran (iii) which shows *both* a split carbonyl band (5.72 and 5.76 μ) and two double bond vibrations (5.93 and 6.05 μ) in carbon tetrachloride. [Unpublished results; the n.m.r. spectrum of this compound is consistent with structure (iii) giving signals at 3.90 τ (triplet, two H), 6.10 τ (singlet, six H), and 6.85 τ (triplet, two H).]



(iii)

NOTE ADDED IN PROOF. A recent publication, S. Masamune and N. T. Castellucci, *J. Am. Chem. Soc.*, **84**, 2452 (1962), reports the preparation of the parent system, 4-pyran. It is important to note that the pyran, as expected, was found to be extremely unstable. This finding supports the stability argument dealt with in detail below. Attention should be drawn to the similarities in infrared and n.m.r. spectra between 4-pyran and the dicarbethoxy derivative (iii). Both show two double bond vibrations in the 6-μ region. The allylic hydrogens in the simple pyran appear at 7.34 τ, but in contrast to the sharp triplet signals observed in (iii), they give rise to a complex multiplet. The vinyl hydrogens in the β-position appear at a very similar location, at 3.84 τ.

TABLE II

ULTRAVIOLET AND INFRARED SPECTRA

Compound	Infrared spectra, μ[a]	Ultraviolet spectra, mμ[b]
IV	3–4 (s), 5.80 (s), 5.93 (s) 6.10 (s), 6.40 (w)[c]	248 (30,150); 290 (2200)[d]
V	5.75 (s), 5.83 (s), 6.10 (m)[f]	258 (40,000); 325 (2160)[d]
VI	2.90 (s),[e] 5.93 (m), 5.85 (sh)	238 (37,200); 285 (1210)[d]
VII	5.78 (s), 5.95 (w)	
VIII	2.90 (w), 5.98 (s), 6.13 (m)	258 (34,800); 307 (3280)[d]
IX	5.66 (m), 5.78 (s),[e] 6.11 (m)	293 (20,200); 225 (9800)[d]
X	5.80 (s)[e]	Weak end absorption
XV	5.83 (s), 6.20 (m)	241 (28,800); 287 (17,200)

[a] Infrared spectra, unless stated otherwise, are taken in chloroform. [b] Ultraviolet spectra are taken in ethanol; values in parentheses refer to extinction coefficients. [c] Spectrum taken in potassium bromide. This compound showed different absorption in the 7–8-μ and 12–14-μ region, dependent on the crystalline form. [d] The long wave length maximum is ill-defined and the position recorded is subject to an error of approximately ±5 mμ. [e] Bands are broad. [f] Spectrum taken in carbon tetrachloride.

and α-substituted ketones.[19,20] Various rotational isomers are possible for V, differing in the alignment of the carbonyl and ring oxygen dipoles and being largely solvent dependent.[21]

The confirmation of structures IV and V demanded a re-examination of the question of stability of these compounds. The evidence for aromaticity reported in the literature is conflicting. On the one hand, IV and V are reported to enter, though somewhat reluctantly, into typical double bond reactions (bromination, permanganate oxidation, hydrogenation); on the other hand, they have been described as possessing dramatic stability toward strong acid treatment.[22] The latter property has been explained on the basis of formation of a protonated species in which the benzoxepin ring as a whole acts as the protonation site, giving rise to a resonating aromatic sextet.[8] Huisgen[9] criticized this proposal, but no alternative explanation for the remarkable stability of these compounds towards acid has been offered.

The following line of reasoning leads to the conclusion that the stability of IV and V is the consequence of the presence of the carboxyl and carbomethoxyl groups in the α-position to the ether oxygen. Thus, the derivatives VI, VII and VIII, which lack these substituents are found to be very unstable to acid treatment. On the other hand, the dihydro derivative IX, which lacks the benzoxepin nucleus, also is found to possess considerable resistance to acid, far above that expected for an enol ether of this type. For example, it is found not to add methanol under conditions under which enol ethers readily add methanol to give acetals.[23] Similarly, it is reported[24] that furan 2,5-dicarboxylic acid has an astounding stability to acids, in contrast to simple furans which are readily opened by mineral acids. Moreover, as a more pertinent example to the present argument, 2,6-pyrandicarboxylic acid is found to be stable to strong acid, while the simple parent system pyran is not known.[18] These facts are readily accommodated if the intermediate in the acid catalyzed ring opening or in the acetal formation is considered. Protonation of the double bond in every case leads to carbonium ions whose positive charge is unfavorably located α to a carbonyl group; it is to be expected that protonation will occur at a different site instead. In complete agreement with this conclusion, it was found that no deuterium was incorporated when V was dissolved in concentrated deuteriosulfuric acid. Deuterium incorporation in the position α to the benzene ring should have occurred, had carbonium ion XIVa been formed.

The stability of IV and V is, therefore, not a manifestation of aromatic character of the benzoxepin ring system. Some stability to ring opening in the benzoxepin system may be derived from the presence of a divinyl ether grouping in the ring; it has been reported,[25] for example, that divinyl ether is more stable to hydrolysis than vinyl ether by a factor of about 400. But by far the major contribution to the stability of IV and V appears to be derived from the unfavorable electronic effect exerted by the presence of carboxyl and carbomethoxyl groups in the α-position.[26]

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[19] P. Yates, S. Lipinsky, and D. Vossius, *Can. J. Chem.*, **39**, 1977 (1961).

[20] J. L. Adelfang, P. H. Hess, and N. H. Cromwell, *J. Org. Chem.*, **26**, 1402 (1961).

[21] In chloroform solution only an unresolved broad band was observed; in potassium bromide the carbomethoxyl absorptions appeared at 5.77 and 5.88 μ with the intensities reversed from those in carbon tetrachloride. The acid IV also gives rise to two reasonably sharp bands in the carbonyl region. Similarly, the dihydro ester IX may exist in more than one rotational form, but in each solvent measured, the broad band due to the unsaturated carbomethoxyl group at *ca.* 5.80 μ could not be resolved.

[22] The acid IV is reported to be recovered unchanged after standing in 80% concentrated sulfuric acid for several weeks, and after reflux with 50% sulfuric acid.[8,9] This dramatic stability was confirmed in the present investigation. In addition, IV was found to remain unchanged after prolonged reflux in dilute ethanolic hydrochloric acid solution, and V was stable towards anhydrous methanolic hydrogen chloride.

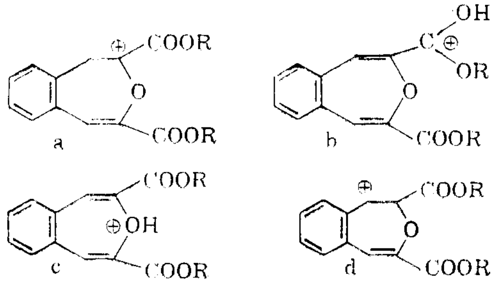
[23] R. K. Summerbell and G. J. Lestina, *J. Am. Chem. Soc.*, **79**, 6219 (1957); F. Korte and H. Machleidt, *Chem. Ber.*, **88**, 136, 1676 (1955).

[24] H. Gilman and R. V. Young, *Rec. trav. chim.*, **51**, 761 (1932).

[25] A. Skrabal and R. Skrabal, *Z. physik. Chem.*, **A181**, 449 (1938).

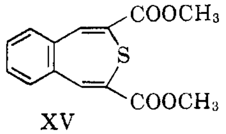
[26] Dimroth[6] recently has synthesized the parent 3-benzoxepin system by a route different from that employed for the synthesis of IV and V. He reports that 3-benzoxepin has some stability to mild acid treatment. This behavior is in line with and supports the argument above.

It was also of interest to determine the protonation site in IV and V. Four possible carbonium ions XIV a–d might be formed upon protonation. XIVa has been ruled out on the basis of lack of deuterium incorporation. A determination of the basicity of IV and V was expected to yield some information which would allow a choice among the other three possibilities, XIVb, c, and d, to be made. The pK_{BH^+} values were obtained by spectral measurement in 95% sulfuric acid–5% dioxane solution, to overcome solubility difficulties. Employing Geissman's method[27] for treatment of the data, a value of -5.30 ± 0.10 was obtained, within experimental error identical for both the acid IV and the ester V. This value is much more basic than that expected, were protonation to take place on the carbonyl group as in XIVb. Cinnamic acid has a pK_{BH^+} of approximately -6.3 ± 0.2[28] and the presence of oxygen in the α-position is expected to decrease the stability of XIVb, leading to a more negative pK_{BH^+} value for IV and V. On the other hand, the observed basicities, the unusual stability of the ester to acid hydrolysis and the relatively small spectral shifts observed on protonation, are consistent with a scheme by which the ether oxygen acts as the protonation site, as in XIVc. This species, although not capable of resonance stabilization, does not possess a ready pathway for further reaction. Carbonium ion XIVd might be favored on the basis of stability, but in view of the observed resistance to acid-catalyzed decarboxylation[8,9] under conditions which cause decarboxylation in cinnamic acid,[28] this species is not to be preferred to XIVc.



XIV

Finally, because of its close relationship to V, the n.m.r. spectrum of dimethyl 3-benzthiepin-2,4-dicarboxylate (XV)[10] was determined. Although to a much lesser extent, this compound also is reported to possess a surprising degree of stability toward acids. Toward a variety of other reagents, however, XV proved to be considerably less stable than V. The n.m.r. spectrum of XV is recorded in Table I, and, clearly, can be seen to be in agreement with its proposed structure.[29] It is interesting to note the large deshielding effect on the 'benzylic' hydrogens which is observed in this system. These signals are found at a lower field than those of the aromatic hydrogens, and analogous to the case of thiophene,[30] they are found at lower field from those in the corresponding oxygen heterocycle. The ultraviolet spectrum (Table II) also is considerably modified from that of its oxygen analog V.



XV

Experimental[31]

3-Benzoxepin-2,4-dicarboxylic Acid (IV).—The preparative method of Dimroth, *et al.*,[8] was employed. The acid was found to crystallize from acetic acid in three different forms, ranging in color from white to pale green. These crystalline modifications possessed different infrared spectra in potassium bromide, but had identical ultraviolet spectra and identical melting properties, m.p. 262–265° dec. (lit.,[8] m.p. 258–260°). Calcd. for $C_{12}H_{12}O_5$: neut. equiv., 116. Found: neut. equiv., 115.

Dimethyl 3-Benzoxepin-2,4-dicarboxylate (V).—The ester of IV was prepared by diazomethane treatment of IV as in the original preparation,[8] m.p. 110.5–111° (lit.,[8] 108–109°). Calcd. for $C_{14}H_{12}O_5$: mol. wt., 260. Found: mol. wt., 250 (Rast).

This compound was surprisingly stable to hydrolysis by mineral acids. It was recovered unchanged from 75% sulfuric acid after 30 min. at room temperature.

Upon dissolution in concentrated deuteriosulfuric acid, the recovered ester showed no change in the infrared and n.m.r. spectra, indicating that no deuterium was incorporated in the molecule.

2,4-Bis(hydroxymethylene)-3-benzoxepin (VI).—The ester V (260 mg., 1.0 mmole) in ether (30 ml.) was cooled to −5° and lithium aluminum hydride (40 mg., 1.05 mmole) in ether (10 ml.) was added dropwise while maintaining the temperature. After addition was complete, the solution was allowed to warm to room temperature and was stirred at that temperature for 30 min. The reaction solution was extracted with ether after destruction of the excess lithium aluminum hydride with water. The extracts were dried over anhydrous sodium sulfate and evaporated to give 0.20 g. (98%) of VI. Three recrystallizations from benzene afforded yellow plates, m.p. 89.5–90.5°.

Anal. Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.48; H, 5.84.

More conveniently, the alcohol was prepared by the following procedure.[32] The ester V (300 mg., 1.15 mmoles) in ether solution was added to a previously prepared solution of lithium aluminum hydride (200 mg., 5.3 mmoles) and

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[27] C. T. Davis and T. A. Geissman, *J. Am. Chem. Soc.*, **76**, 3507 (1954).

[28] F. Kirby, private communication.

[29] This structure has been disputed by Schoenberg. [A. Schoenberg and M. B. E. Fayez, *J. Org. Chem.*, **23**, 104 (1958). On the basis of the ready conversion which this compound undergoes to 2,3-naphthalenedicarboxylic acid, he prefers the naphthalene sulfide structure analogous to XI.]

[30] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, 1959, p. 64.

[31] Melting points are uncorrected; microanalyses were performed by V. Tashinian, Microchemical Laboratory, University of California, Berkeley.

[32] This method for prevention of double bond reduction is the subject of a forthcoming publication.

aluminum chloride (300 mg., 2.5 mmoles) which corresponded to the presence of 7 mmoles of aluminum hydride and 0.8 mmole of aluminum chloride. The solution was refluxed for 2 hr. Wet ether was added to destroy excess hydride followed by cold water. The ether layer upon work-up afforded 190 mg. (81%) of VI.

The infrared and ultraviolet spectra of VI are recorded in Table II. The alcohol VI underwent very facile decomposition when heated with a trace of mineral acid in ethanol.

2,4-Diacetoxy-3-benzoxepin (VII).—The acetate of VI was prepared by the use of acetic anhydride and pyridine.[33] The oil which was obtained from this preparation was purified by chromatography on neutral Woelm alumina, activity grade III. Benzene eluted the acetate as a yellow band moving down the column. Evaporation of the solvent afforded an oil, which crystallized on standing. Recrystallization from pentane at low temperatures afforded glistening off-white leaflets, m.p. 45–46°, after two recrystallizations. The infrared spectrum is recorded in Table II.

Anal. Calcd. for $C_{16}H_{10}O_5$: C, 66.65; H, 5.59. Found: C, 66.26; H, 5.34.

The acetate was found to be very unstable, a pure sample decomposed after a few weeks of room temperature.

2-Aldehydo-4-hydroxymethylene-3-benzoxepin (VIII).—Compound VI (100 mg., 0.49 mmole) in chloroform (100 ml.) was stirred with manganese dioxide (2.0 g.) for 12 hr. Filtration of the suspension and evaporation of the solvent afforded 90 mg. (91%) of the aldehyde VIII. It crystallized from benzene–pentane in yellow-orange plates, m.p. 122–124° after two recrystallizations. The infrared and ultraviolet spectra are recorded in Table II.

Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.28; H, 4.99. Found: C, 70.98; H, 4.93.

A longer reaction period led only to lowered yield of VIII, no dialdehyde could be obtained.

Dimethyl 1,2-Dihydro-3-benzoxepin-2,4-dicarboxylate (IX).—The ester V (85 mg., 0.33 mmole) in ethanol (10 ml.) was hydrogenated over palladium–charcoal. Within 15 min. a total of 9.0 ml. of hydrogen (7.8 ml. at S.T.P., 1.1 molar equivalents) had been consumed, and rapid hydrogenation stopped. After filtration and evaporation of the solvent, an oil was obtained which solidified on standing. Two recrystallizations from methanol at low temperatures afforded white rosettes, m.p. 76–77.5°. The infrared and ultraviolet spectra of this compound are recorded in Table II.

Anal. Calcd. for $C_{14}H_{14}O_5$: C, 64.11; H, 5.38. Found: C, 64.52; H, 5.06.

A solution of this ester in 1 *N* methanolic hydrogen chloride was found to be stable over a period of 120 hr. at 45°. The ultraviolet spectrum of such a solution did not change with time and was identical to that in methanol.

1,2,4,5-Tetrahydro-3-benzoxepin-2,4-dicarboxylic Acid (X).—When IV was hydrogenated over palladium–charcoal in ethanol, a total of 2 moles of hydrogen were absorbed over a period of 24 hr. Filtration and evaporation of the solvent afforded an oil which solidified on standing. Recrystallization from methanol–chloroform gave white crystals, m.p. 196–198°. The infrared spectrum of this compound is recorded in Table II.

Anal. Calcd. for $C_{12}H_8O_5$: C, 61.01; H, 5.12. Found: C, 60.90; H, 5.35.

Dimethyl 3-Benzthiepin-2,4-dicarboxylate (XV).—The acid 3-benzthiepin-2,4-dicarboxylic acid was synthesized by the method of Dimroth, *et al.*[9] The ester was obtained from treatment of this acid with diazomethane and by purification of the resulting oil by chromatography on neutral Woelm alumina, activity grade III. Recrystallization from methanol gave orange prisms, m.p. 89–90° (lit.,[9] m.p. 95–97°).

Basicity Measurements.—Because of low solubility in aqueous solutions, a 95% sulfuric acid–5% dioxane medium was employed. The H_0 values for this mixed solvent system have been determined up to 70% acid[34] and additional values were determined in the higher concentration region. Because of the small spectral shifts which occurred on protonation, it was important to determine the optimum pair of wave lengths for measuring the optical density, since very ill-defined titration curves are obtained by an improper choice of wave lengths. The choice of wave lengths was made from a plot of (optical density at 80%–optical density at 50%) against wave length; the resulting plot had a well defined maximum and minimum, and these wave lengths were employed for measurement. The optical solutions were prepared by diluting 5-ml. aliquots of dioxane solutions of IV and V to 100 ml. with the requisite concentration of sulfuric acid. All measurements were made on the Beckman DU spectrophotometer at 25°. The values for the pK_{BH+} were obtained by employing a Geissman treatment of the data, employing 275 and 255 mμ as the wave length pair for the acid IV, and 275 and 250 mμ in the case of the ester V; a value of 5.30 ± 0.10 was obtained for both compounds. This value was in accord with approximate solubility measurements of the acid IV; the acid was insoluble in 50% sulfuric acid, dissolved completely in 80% sulfuric acid, and dissolved partially in 68% sulfuric acid.

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[33] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, 1948, p. 165.

[34] D. S. Noyce and M. J. Jorgenson, *J. Am. Chem. Soc.*, **83**, 2525 (1961), and unpublished results.