The product was recrystallized several times from ethanol to yield material of m.p. 125–126°.

3,3-Dimethyl-1-butanol-1-^{14}C.—The reduction of 6.0 g. (0.052 mole) of 3,3-dimethylbutyric-1-^{14}C acid with 2.0. g. (0.053 mole) of lithium aluminum hydride gave 3.8 g. (72%) of 3,3-dimethyl-1-butanol-1-^{14}C, b.p. 142–143°. The same procedure was used to prepare inactive material of b.p. 144°, n^{20}D 1.4146 (lit.[19] b.p. 141–143°, n^{23}D 1.4160).

2,3-Dimethyl-2-butanol.—The reaction of methylmagnesium iodide with methyl isopropyl ketone gave a 71% yield of 2,3-dimethyl-2-butanol, b.p. 115–120°. The sample for infrared spectra had b.p. 118°, n^{25}D 1.4157 (lit.[20] b.p. 118.7°, n^{25}D 1.4151).

3,3-Dimethyl-2-butanol.—The reduction of 3,3-dimethyl-2-butanone (pinacolone) with lithium aluminum hydride yielded 78% of 3,3-dimethyl-2-butanol, b.p. 116–118°. Fractionation gave a center cut of b.p. 119.5°, n^{20}D 1.4160 (lit.[21] b.p. 120.4°, n^{20}D 1.4148).

2-Methyl-2-pentanol.—The reaction of *n*-propylmagnesium bromide with acetone gave 51% of 2-methyl-2-pentanol, b.p. 121–125°. Fractionation gave a center cut of b.p. 122°, n^{20}D 1.4130 (lit.[22] b.p. 119.3°, n^{25}D 1.4089).

Analysis of Alcohol Mixture from Diazotization.—Infrared spectra of 3,3-dimethyl-1-butanol (IV), 3,3-dimethyl-2-butanol (V), 2,3-dimethyl-2-butanol (VI) and 2-methyl-2-pentanol (VII) were compared with the infrared spectrum of the alcohol product from a cold run on the diazotization. The spectrum of V had strong peaks at 7.77 and 9.93 μ, which were absent in the spectrum of the mixture. Similarly, VII showed strong absorption at 11.18 and 11.34 μ, where the mixture showed no peaks. Calculations based on the above peaks showed that no more than a small percentage of V or VII could be present. Comparison of the spectra of IV and VI with that of the mixture gave an approximate composition of 60% IV and 40% VI. Three synthetic mixtures of IV and VI bracketing this composition were prepared and plots of optical density *vs.* composition at 10.05, 10.60, 10.96 and 11.71 μ made. The composition of the unknown was thus found to be 57.7 ± 1.7% IV.

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(19) R. C. Huston and A. H. Agett, *J. Org. Chem.*, **6**, 123 (1941).

(20) F. Hovorka, H. P. Lankelma and J. W. Bishop, THIS JOURNAL, **63**, 1097 (1941).

(21) F. C. Whitmore and P. L. Meunier, *ibid.*, **55**, 3721 (1933).

(22) F. H. Norton and H. B. Hass, *ibid.*, **58**, 2147 (1936).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Preparation and Geometry of *o,o'*-Bridged Biphenyls Containing Sulfur or Selenium in the Bridge

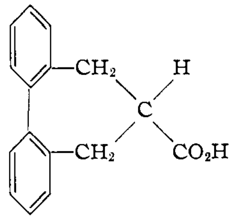
BY WILLIAM E. TRUCE AND D. D. EMRICK

RECEIVED JUNE 21, 1956

2,7-Dihydro-3,4-5,6-dibenzoheteropins (1-heterodibenzo[a,c] [3,5]-cycloheptadienes) have been prepared where the hetero function is represented by sulfide, selenide, sulfone, methylsulfonium and methylselenonium groups. As predicted from molecular models, these materials, with the exception of the sulfonium compound, show ultraviolet absorption maxima at shorter wave lengths than the corresponding carbocyclic and other seven-membered ring *o,o'*-bridged biphenyls, indicative of enhanced non-coplanarity and accompanying asymmetry in the biphenyl system. 2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2',3"-dicarboxylic acid has been obtained in optically active form. This is the first example of demonstrable activity in a seven-membered ring *o,o'*-bridged biphenyl not having auxiliary 6,6'-biphenylic hindering groups.

The fact that Bell could not resolve the seven-membered ring bridged biphenyl[1] I has left open the question of whether or not in a seven-membered ring bridged biphenyl auxiliary hindering groups in the biphenyl 6,6'-positions are necessary to obtain optical activity. Presumably, a seven-membered ring all carbon atom 2,2'-bridged biphenyl is sufficiently close to coplanarity so that relatively moderate bond stretching and bond angle distortion cause racemization.[2]

Fischer–Hirschfelder–Taylor molecular models indicate that the presence of large hetero atoms (sulfur or the even larger selenium) in 2,2'-bridged biphenyls would be more likely to develop enantiomorphism.[3] The increasing covalent radii[4] of carbon, sulfur and selenium, respectively, give a theoretical basis for this prediction. Accordingly, 2,7-dihydro-3,4-5,6-dibenzothiepin (1-thia[a,c][3,5]dibenzocycloheptadiene) (IIA), 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide (III), the methylsulfonium iodide (IVA) of the former, 2,7-dihydro-3,4-



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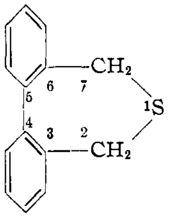
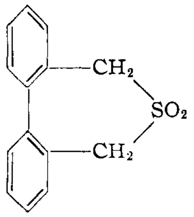
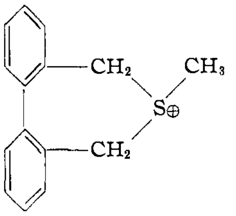


II A, S = sulfur
B, S = selenium



III



IV A, S = sulfur
B, S = selenium

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(1) F. Bell, *J. Chem. Soc.*, 5047 (1952). The inability of Bell to obtain activity in compounds of the dibenzo[a,c][3.5]cycloheptadiene type is being checked by current studies of Iffland and Siegel (University of West Virginia, private communication) involving optically active compounds of this type in which activity is maintained by auxiliary biphenylic 6,6'-diamino groups which are then subjected to deamination under very mild conditions. The latter studies should prove very illuminating.

(2) K. E. Howlett, D. M. Hall and E. E. Turner, *ibid.*, 1249 (1955).

(3) *Cf.* M. H. Beeby, F. G. Mann and E. E. Turner, *ibid.*, 1923 (1950).

(4) L. Pauling, *Proc. Natl. Acad. Sci.*, **18**, 292 (1932).

TABLE I

RELATIVE PLANARITY OF BIPHENYLS AS DEDUCED FROM ULTRAVIOLET ABSORPTION SPECTRA

	Compound	λmax, mμ	εmax	θ[a]
1	Biphenyl (crystal, no solvent)	275[b]	. . . . .	0°[i]
2	4,5-Methylene-9,10-dihydrophenanthrene	*ca.* 272[c]	*ca.* 18,500	16.5°[i]
3	9,10-Dihydrophenanthrene	264[c]	*ca.* 18,000	*ca.* 31°[i]
4	Fluorene	261[d]	*ca.* 20,000	. .
5	9,10-Dihydro-4,5-dimethylphenanthrene	261[e,o]	16,000	. .
6	Dibenzo[a.c] [1,3]cycloheptadiene-6-one	252[f]	20,000	. .
7	2,7-Dihydro-3,4-5,6-dibenzoxepin (in hexane)	250[g]	16,500	47°
8	Dibenzo[a.c] [3,5]cycloheptadiene-1-carboxylic acid (I)	249[h]	16,800	. .
9	Dibenzo[a,c] [3,5]cycloheptadiene-1,1-dicarboxylic acid	249[h]	*ca.* 100,000	. .
10	Biphenyl (in ethanol)	249[g]	18,000	. .
	Biphenyl (in heptane)	247.5[i]	19,000	50°[i]
11	2,7-Dihydro-1-methyl-3,4-5,6-dibenzothiepinium iodide	249[j]	23,500	. .
12	2,7-Dihydro-3,4-5,6-dibenzazepinium-1-spiro-1′′′-piperidinium bromide (in water)	248[g]	15,000	49°[i]
13	2,7-Dihydro-3,4-5,6-dibenzoselenepin (IIB)	247[j]	6,250	. .
14	2,7-Dihydro-3,4-5,6-dibenzothiepin (IIA)	245[j]	10,000	. .
15	2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide (III)	243[j]	*ca.* 130,000	. .
16	2,7-Dihydro-4′,1″-dimethyl-3,4-5,6-dibenzoxepin	242[k,o]	11,000	. .
17	2,7-Dihydro-4′,1″,1,1-tetramethyl-3,4-5,6-dibenzazepinium bromide	242[k,o]	9,000	. .
18	2-Methylbiphenyl (in heptane)	235[i]	10,000	63°[i]
19	2,2′-Dimethylbiphenyl	*ca.* 227[l]	6,800	70°[i]
20	2,7-Dihydro-1-methyl-3,4-5,6-dibenzoselenepinium iodide (IVB)	218[j]	57,000	. .
21	2,7-Dihydro-1,1-dimethyl-3,4-5,6-dibenzoselenepinium diiodide (IX)	215[j]	. . . . .	. .
22	6-Iodo-6-arsa-1,2-3,4-dibenzocyclohepta-1,3-diene[m]	(*ca.* 224)[m]	(50,000)	(63°)[m]
23	Dibenzyl sulfone[n]	259[n]	480[n]	. .

[a] Estimated angle out of coplanarity by Suzuki[6]. [b] Suzuki;[6] A. R. Deb, *Ind. J. Phys.*, 305 (1953). [c] Suzuki[6]; R. N. Jones, THIS JOURNAL, **63**, 1658 (1941); **67**, 2127 (1945); *Chem. Revs.*, **32**, 1 (1943). [d] R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York. N. Y., 1951. [e] Not obtainable in active form, G. Wittig and H. Zimmerman, *Ber.*, **86**, 629 (1953). [f] Z. B. Papanastassiou, Ph.D. Thesis, University of West Virginia, 1954. [g] Not obtainable in active form, G. H. Beaven, D. M. Hall, M. S. Lesslie and E. E. Turner, *J. Chem. Soc.*, 854 (1952). [h] Prepared after Kenner[18] and Bell[1]; the ultraviolet absorption spectra of this and all other compounds determined in the course of this work were obtained using a Cary recording spectrophotometer at temperatures of 25–30°; *cf.* G. H. Beaven, *et al.*, *J. Chem. Soc.*, 2708 (1955). [i] Suzuki.[6] [j] Prepared in the course of this work. [k] Wittig and Zimmerman, footnote *e*, obtainable in active form. [l] Suzuki[6]; G. H. Beaven, *et al.*, *J. Chem. Soc.*, 131 (1954). [m] Beeby, *et al.*, *ibid.*, 1923 (1950); maximum estimated by extrapolation; true maximum may not exist or may exist at shorter wave length; angle θ is apparently non-molecular orbital estimate, presumably based upon models. [n] E. A. Fehnel and M. Carmack, THIS JOURNAL. **71**, 232 (1949); **72**, 1292 (1950); spectrum of dibenzyl sulfone resembles that of alkylbenzenes or diphenylmethane. [o] Direct comparison of the spectra of these bridged biphenyls having biphenylic 6,6′-auxiliary methyl groups with compounds not having such auxiliary methyl substituents may not be perfectly valid. Even though such alkyl groups as methyl substituents probably exhibit only small inductive and resonance interaction with the benzene rings of the biphenyl system, their over-all effect (including presumably insignificant solvent interaction differences), as deduced from ultraviolet absorption spectra, is not necessarily completely negligible. This is probably confirmed by the rather similar maxima of 264 and 261 mμ for 9,10-dihydrophenanthrene and 9,10-dihydro-4,5-dimethylphenanthrene, respectively; intuitively it might be expected that the *ortho* hindering methyl substituents of the latter should probably cause a somewhat larger shift to shorter wave lengths than that of only 3 mμ actually observed. Using the 4,4′-dimethylbiphenyls as a very rough basis, perhaps values as large as *ca.* 8 mμ should be subtracted from the absorption maxima of bridged biphenyls having auxiliary 6,6′-methyl groups in order to "correct" them for purposes of comparison to analogous bridged biphenyls not having such auxiliary groups. This of course should be considered mere speculation since the situation may be much more complex.

5,6-dibenzoselenepin (IIB) and the methylselenonium iodide (IVB) of the latter have been prepared. Ultraviolet absorption spectral data of these compounds are tabulated in Table I along with literature values of maxima for biphenyl and several 2,2′-bridged biphenyls reported previously (all solutions are in 95% ethanol, unless otherwise indicated).

Since all of the above bridged biphenyls contain the hetero function removed from the benzene rings by one methylene group, effects of any electronic or resonance interaction of the hetero function with the aromatic system are greatly minimized and the ultraviolet spectral data of these materials can be used, with proper reservations, as a criterion of biphenyl conjugation.[5,6] The spectral data indicate that the size of the hetero atom in the bridge does have an important effect upon the conjugation (and relative degree of asymmetry) of the biphenyl. From the shift in wave lengths toward shorter values as well as the decrease in the extinction coefficients of the maxima, it is concluded that the larger neutral selenium[7] (more polarizable than sul-

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(5) G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1947, p. 169; L. Doub and J. M. Vandenbelt, THIS JOURNAL, **71**, 2415 (1949), have shown that resonance interactions rather than inductive effects are primarily responsible for ultraviolet spectra.

(6) H. Suzuki, *Bull. Chem. Soc., Japan*, **27**, 597 (1954); a recent critical evaluation of ultraviolet absorption spectra as a criterion of 1,1-conjugation in biphenyls appears in W. Klyne, "Progress in Stereochemistry," Vol. I, Academic Press, Inc., New York, N. Y., 1954, pp. 140–144.

(7) G. Milazzo and E. Miescher, *J. phys. radium*, **15**, 401–2 (1954); *C. A.*, **48**, 12,552 (1954), report that the large size of selenium in selenophene produces deformation of the planar configuration in the ring. This inhibits homocyclic conjugation which results in an ultraviolet spectral shift to shorter wave lengths. A slight deformation is also indicated by Raman and infrared spectra of selenophene.

fur) and sulfur cause less 1,1′-biphenyl conjugation than the much smaller hetero oxygen atom in the oxepin compound (item 7 of Table I), the effect being greatest with selenium.[8]

Ultraviolet absorption spectra (Tables I and II) indicate that compounds having the basic structures II and III show less 1,1′-biphenylic conjugation than biphenyl and very much less conjugation than the more nearly coplanar fluorene.[9] Thus, the presumed enhanced non-coplanarity of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide (III) has considerable basis. Item 16 of Table I probably represents about the borderline in resolvability of seven-membered 2,2′-bridged biphenyls; hence, biphenyls (such compounds would be assumed to *not* contain attached groups of significant auxochromic influence, which would add to the resonance of the structures) which show ultraviolet absorption maxima at significantly higher wave lengths than the 242 mμ maximum of item 16 would not be expected to be very optically stable. These facts are consistent with the observation that an azepin compound (item 17), which can be obtained readily in active form, also has a maximum at 242 mμ. The fact that 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide (III) shows a maximum at 243 mμ (Table I) lends encouragement to the belief that this compound should probably be resolvable, although it may not be as optically stable as items 16 and 17 of Table I.

For purposes of attempted optical resolution, a structure with carboxylic acid "handles" placed in non-buttressing positions was prepared in fair overall yield by the following sequence of reactions. Previously reported dimethyl 4,4′-dibromodiphenate[10] was prepared for the first time by Ullmann reaction from methyl 2-iodo-5-bromobenzoate in good yield. Subsequent reduction with lithium aluminum hydride gave 4,4′-dibromo-2,2′-bis-(hydroxymethyl)-biphenyl; this dialcohol was converted to 4,4′-dibromo-2,2′-bis-(bromomethyl)-biphenyl, which was cyclized with alcoholic sodium sulfide to V. Peroxide oxidation gave the corresponding sulfone VI, which was converted by the Rosenmund–von Braun nitrile synthesis[11] to VII; the dinitrile was hydrolyzed to the diacid VIII. Attempts to resolve VIII as the neutral cinchonine salt gave amorphous crystals deposited from a gummy concentrated solution. Intractable gums were obtained with both the neutral quinidine and quinidine hydrogen salts of VIII. Beautifully formed crystals were obtained with strychnine, and *levo*-α-phenylethylamine, completely homogenous crystals being obtained in the initial and final crystalline fractions in both cases. Decomposition of these initial and final fractions with hydrochloric acid followed by dissolving the free, washed, recovered acid in 0.5 *N* NaOH gave absolutely no evidence of activity for the sodium salt.

TABLE II

ULTRAVIOLET ABSORPTION SPECTRA OF *para*-SUBSTITUTED BIPHENYLS AND *o,o*′-BRIDGED BIPHENYLS

		Compound[a]	$\lambda_{max.}$, mμ
A.	1	2-Nitrofluorene	330^{b}
	2	4-Nitrobiphenyl	$307^{b,d}$
	3	2,7-Dihydro-2′-nitro-3,4-5,6-dibenzothiepin-1-dioxide (XA)	290^{d}
B.	1	2,7-Dinitrofluorene	331^{e}
	2	4,4′-Dinitrobiphenyl	306^{e}
	3	2,7-Dihydro-2′,3″-dinitro-3,4-5,6-dibenzothiepin-1-dioxide (XB)	290^{d}
C.	1	Biphenyl-4,4′-dicarboxylic acid (methyl ester)	280^{f}
	2	2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic acid (ethyl ester) (*cf.* VIII)	269^{d}
D.	1	2,7-Dibromofluorene	$277^{d,i}$
	2	4,4′-Dibromobiphenyl	262^{f}
	3	2,7-Dihydro-2′,3″-dibromo-3,4-5,6-dibenzothiepin (V)	258^{d}
	4	2,7-Dihydro-2′,3″-dibromo-3,4-5,6-dibenzothiepin-1-dioxide (VI)	257^{d}
E.	1	2-Aminofluorene hydrochloride (in 0.100 *N* HCl)	$261^{d,j}$
	2	4-Aminobiphenyl hydrochloride (in 0.100 *N* HCl)	249^{c}
	3	2′-Amino-2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide hydrochloride (in 0.100 *N* HCl)	$243^{d,g}$
F.		(for comparison)	
	1	Fluorene	$261^{h,d}$
	2	Biphenyl	$249^{h,d}$
	3	2,7-Dihydro-3,4-5,6-dibenzoxepin (in hexane)	250^{h}
	4	2,7-Dihydro-3,4-5,6-dibenzothiepin (IIA)	$245^{h,d}$
	5	2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide (III)	$243^{h,d}$

[a] All solutions in 95% ethanol, unless otherwise indicated. [b] E. D. Bergmann, *et al.*, *Bull. soc. chim.*, *France*, 705 (1952). [c] M. Pestemer and E. Mayer-Pitsch, *Monatsh.*, **70**, 104 (1937); confirmed during this work. [d] Prepared in connection with this work. [e] Sandin, *et al.*[9] [f] B. Williamson and W. H. Rodebush, THIS JOURNAL, **63**, 3019 (1941). [g] Obtained by reducing 2,7-dihydro-2′-nitro-3,4-5,6-dibenzothiepin-1-dioxide followed by purification through the acetyl derivative, hydrolysis of the latter and dissolution of the purified amine in cold 0.100 *N* hydrochloric acid. [h] See Table I. [i] Prepared by bromination of fluorene in chloroform solution followed by recrystallization to constant m.p. 166.5–167°; lit. m.p. 166–167°, A. Pictet and L. Ramseyer, *Ber.*, **44**, 2491 (1911). [j] Prepared by recrystallizing stock 2-aminofluorene to constant m.p. 127–127.5°; lit. m.p. 127.5–129°, A. H. Blatt, "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 448; O. Diels, *Ber.*, **34**, 1758 (1901).

The material did show definite evidence of resolution when the brucine salt was crystallized very carefully, but all fractions of the salt, upon decomposition with 0.5 *N* ammonia and extraction of the liberated brucine by means of chloroform, gave no evidence of activity as the ammonium salt. Compound VIII was obtained in active form by the rather easily accomplished crystallization of the acid cinchonine salt from aqueous ethanol, followed by decomposition of the moist salt with cold 2 *N* hydrochloric acid and washing successively with cold 3 *N* hydrochloric acid and several changes of ice-water. Dissolution of the cold moist precipitated acid in cold 0.5 *N* ammonia in 5% aqueous urea solution gave an observed specific rotation of +3.1° for the acid obtained from the more-dextrorotatory more-soluble mother-liquor fractions of the cinchonine hydrogen salt; its levorotatory antipode could not be obtained.

The parent compound of this study, 2,7-dihydro-3,4-5,6-dibenzothiepin (IIA), was obtained in nearly quantitative yield by cyclization of 2,2′-

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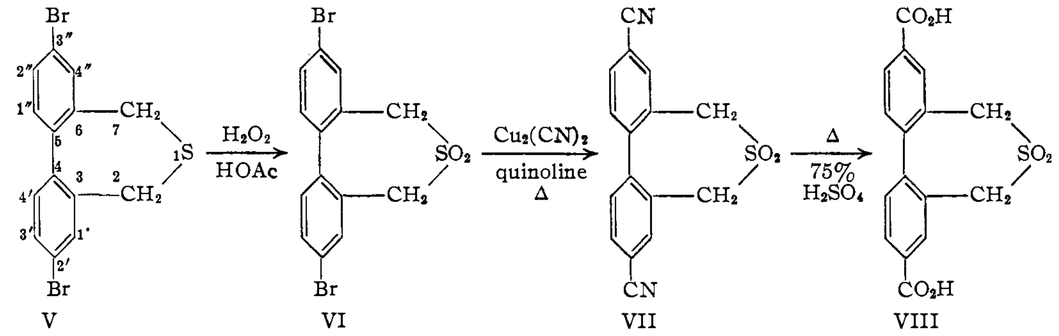
[8] J. D. McCullough and R. E. Marsh, THIS JOURNAL, **72**, 4556 (1950); E. Goldish, K. Hedberg, R. E. Marsh and V. Schomaker, *ibid.*, **77**, 2948 (1955).

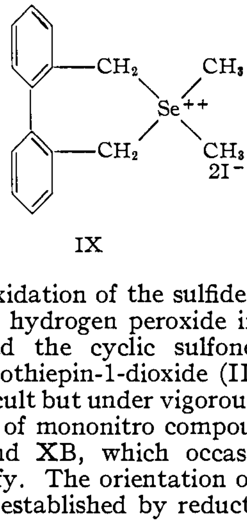
[9] D. W. Sherwood and M. Calvin, *ibid.*, **64**, 1350 (1942); R. B. Sandin, R. Melby, A. S. Hay, R. N. Jones, E. C. Miller and J. A. Miller, *ibid.*, **74**, 5073 (1952).

[10] R. J. W. LeFevre and H. Vine, *J. Chem. Soc.*, 970 (1938).

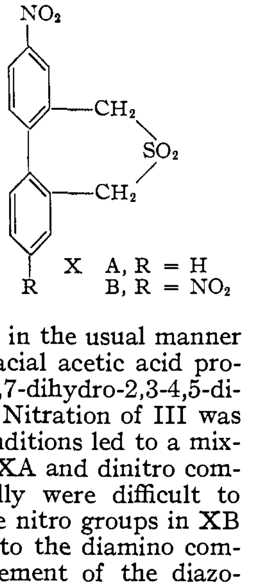
[11] C. F. Koelsch and A. G. Whitney, *J. Org. Chem.*, **6**, 795 (1941); D. T. Mowry, *Chem. Revs.*, **42**, 207 (1948).



bis-(bromomethyl)-biphenyl[12] with sodium sulfide in methanol, again illustrating the ease of forming seven-membered ring bridged biphenyls.[13-15] The corresponding selenide was obtained in the same manner from the dibromide employing potassium selenide in methanol. Alkylation of IIA with a mixture of absolute ethanol and methyl iodide gave in good yield the methylsulfonium salt IVA. While alkylation of IIB with methyl iodide in the absence of other solvent yielded the methylselenonium salt IVB, alkylation with a mixture of methyl iodide and methanol yielded the unique quaternary compound, 2,7-dihydro-1,1-dimethyl-3,4-5,6-dibenzoselenepinium diiodide (IX). The ability of the selenide to form a quaternary salt, whereas sulfides do not, may be ascribed to the larger size of selenium.[16]



IX



X A, R = H
B, R = NO$_2$

Oxidation of the sulfide IIA in the usual manner with hydrogen peroxide in glacial acetic acid produced the cyclic sulfone, 6,7-dihydro-2,3-4,5-dibenzothiepin-1-dioxide (III). Nitration of III was difficult but under vigorous conditions led to a mixture of mononitro compound XA and dinitro compound XB, which occasionally were difficult to purify. The orientation of the nitro groups in XB was established by reduction to the diamino compound, tetrazotization, replacement of the diazonium groups with cuprous cyanide and hydrolysis of the resulting dinitrile to the diacid VIII, which was identified by comparing its diethyl ester with an authentic sample. The orientation obtained in this nitration parallels that obtained in the nitration of biphenyl, 4-nitrobiphenyl[17] and fluorene.

The maximum at 249 mμ in the ultraviolet spectrum of IVA suggests that IVB should be much more amenable to resolution as indicated by the great shift of its maximum to much shorter wave lengths (in fact, the selenonium compound does not show any of the spectral maximum "characteristic" for 1,1-conjugated biphenyls. The band actually observed (218 mμ) is probably of simple benzenoid origin. The *d*-camphoric acid salts of both IVA and IVB could not be crystallized readily and hence could not be used for attempted resolution. The *d*-camphorsulfonic acid salt of the sulfonium compound showed no sign of diastereoisomerism and the perfectly homogeneous salt had the calculated specific rotation for a simple non-asymmetric cationic salt. The neutral *d*-tartrate salt and the hydrogen *d*-tartrate salt of the sulfonium compound were homogeneous, showed no signs of diastereoisomerism, and had the calculated specific rotation one would expect of simple non-asymmetric cationic salts. However, the neutral *d*-tartrate and *d*-camphorsulfonate salt of the selenonium compound showed some evidence of diastereomeric fractionation into crops of somewhat different activity; the hydrogen *d*-tartrate salt showed definite evidence of two different diastereomeric fractions of different solubility, physical appearance and specific rotation. Unfortunately, conversion of the two diastereomeric fractions back to the selenonium iodide XIVB showed no signs of activity in ethanol. This is, however, in accord with the confirmed observations that active tetrahedral selenonium salts of the type $RR'R''Se^+Z^-$ are completely racemized when reconverted back to iodide complexes.[18] Conversion of the mother liquor fraction of the selenonium hydrogen *d*-tartrate to the chloroplatinate did give signs of faint activity, but the results were hardly beyond experimental error (Balfe and Phillips[18] noted that their active selenonium chloroplatinates racemized readily at room temperature).

Experimental

2,7-Dihydro-3,4-5,6-dibenzothiepin (IIA).—A mixture of 1600 ml. of methanol, 80 ml. of water, 30.0 g. (0.088 mole) of 2,2′-bis-(bromomethyl)-biphenyl[12] and 63.6 g. (0.265 mole) of sodium sulfide nonahydrate was refluxed with vigorous stirring for 24 hours. After distilling off the methanol and treating the residue with ice-water, the crude product was filtered off and recrystallized from 240 ml. of ethanol with treatment with 1.0 g. of Norite decolorizing

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(12) D. M. Hall, M. S. Lesslie and E. E. Turner, *J. Chem. Soc.*, 711 (1950).

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(16) C. R. Noller, "Chemistry of Organic Compounds," W. B. Saunders Co., Philadelphia, Pa., 1951, p. 272.

(17) H. C. Gull and E. E. Turner, *J. Chem. Soc.*, 491 (1929).

(18) W. J. Pope and A. Neville, *ibid.*, **81**, 1552 (1902); M. P. Balfe and H. Phillips, *ibid.*, 127 (1933).

charcoal; yield 17.4 g. (93%) of white crystals, m.p. 89–90°; molecular weight (naphthalene eutectic method) 195 (calcd. 212).

Anal. Calcd. for $C_{14}H_{12}S$: C, 79.20; H, 5.70. Found: C, 79.46; H, 5.52.

The mercuric chloride coördination complex was made by mixing hot solutions of 1.00 g. of mercuric chloride and 0.80 g. of the cyclic sulfide in absolute ethanol; white crystals, m.p. 182.5–183.5°.

2,7-Dihydro-1-methyl-3,4-5,6-dibenzothiepinium Iodide (IVA).—Five grams (0.024 mole) of 2,7-dihydro-3,4-5,6-dibenzothiepin, 90 g. (0.63 mole) of methyl iodide and 30 ml. of absolute ethanol were refluxed for 24 hours. Most of the excess methyl iodide was evaporated off by means of an air jet and the resulting crystals were recrystallized twice from absolute ethanol after treatment with decolorizing charcoal; yield of pure white cubical crystals was 5.2 g. (62%), m.p. 139.5–140.5°.

Anal. Calcd. for $C_{15}H_{15}SI$: I, 35.8. Found: I, 36.1.

2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide (III).—Ten grams (0.047 mole) of 2,7-dihydro-3,4-5,6-dibenzothiepin, 50 ml. of 30% hydrogen peroxide (*ca.* 0.46 mole) and 100 ml. of glacial acetic acid were refluxed for 90 minutes and then cooled to −5° overnight. The resulting white needles were filtered off, washed with cold acetic acid and recrystallized from a minimum of ethanol; yield 10.9 g. (95%), m.p. 209–210°.

Anal. Calcd. for $C_{14}H_{12}SO_2$: C, 68.82; H, 4.95. Found: C, 69.06; H, 4.99.

2,7-Dihydro-2′-nitro-3,4-5,6-dibenzothiepin-1-dioxide (XA) and 2,7-Dihydro-2′,3″-dinitro-3,4-5,6-dibenzothiepin-1-dioxide (XB).—To a solution of 5.0 g. (0.020 mole) of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide in 30 ml. of hot glacial acetic acid, was added a cold mixture of 1.16 ml. (0.018 mole) of concentrated nitric acid (sp. gr. 1.43) and 10 ml. of concentrated sulfuric acid with stirring. The temperature was maintained at 100° for 45 minutes. A mixture of 10 ml. of glacial acetic acid and 10 ml. of water was added and the mixture was allowed to spontaneously cool to room temperature for 12–14 hours. The crude crystals, which were deposited, were recrystallized from 50:50 ethanol–benzene to give white crystals, which melted at 220°, resolidified and then remelted at 230.5°. Recrystallization from toluene gave crystals melting at 230.5°. The yield of recrystallized 2,7-dihydro-2′-nitro-3,4-5,6-dibenzothiepin-1-dioxide was 3.2 g. (54%).

Anal. Calcd. for $C_{14}H_{11}SNO_4$: N, 4.84. Found: N, 5.06.

Treatment of 5.0 g. (0.020 mole) of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide in 30 ml. of hot glacial acetic acid with a mixture of 3 ml. (sp. gr. 1.50) of fuming nitric acid (0.064 mole) and 10 ml. of concentrated sulfuric acid, at 100° for 90 minutes, followed by cooling, gave a crude crystalline product. Recrystallization first from benzene and then twice from 90% acetic acid gave white to pale-yellow crystals, melting at 287–288° (Fischer block). The yield of highly purified 2,7-dihydro-2′,3″-dinitro-3,4-5,6-dibenzothiepin-1-dioxide was 1.9 g. (26%).

Anal. Calcd. for $C_{14}H_{10}SN_2O_6$: N, 8.38. Found: N, 8.11.

Reworking of the mother liquors gave very difficultly separable mononitro compound, dinitro compound and mixtures of the two (m.p. 214–217°). The orientation of the nitro groups in the above 2,7-dihydro-2′,3″-dinitro-3,4-5,6-dibenzothiepin-1-dioxide was elucidated as follows. The dinitro compound was reduced with zinc and hydrochloric acid in the usual manner to give 2,7-dihydro-2′,3″-diamino-3,4-5,6-dibenzothiepin-1-dioxide. This material had a melting point above 310° (with decomposition) and could not be crystallized readily from most common organic solvents. The diamine was diazotized in the usual manner, the resulting tetrazonium salt solution was filtered off from a considerable quantity of undiazotized amine, treated with urea to remove excess nitrous acid, cautiously neutralized with sodium carbonate and then slowly added to a cuprous cyanide solution in potassium cyanide in the usual Sandmeyer manner[19] to give the expected dinitrile in only fair yield. Hydrolysis of the dinitrile by refluxing several hours with 75% (by volume) sulfuric acid gave a very crude dicarboxylic acid which was considerably purified by recrystallization from 70% dimethylformamide (in water). The purified dicarboxylic acid was converted to the diacid chloride by refluxing with thionyl chloride and then esterified by treatment with excess absolute ethanol. Recrystallization from ethanol gave nearly white crystals of the diethyl ester of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide 2′,3″-dicarboxylic acid. The over-all yield was about 0.1 g. of ester from 1.0 g. of starting dinitro compound. The m.p. of this ester was 200–201° and it did not depress the m.p. of the diethyl ester made from the authentic dicarboxylic acid as indicated later.

Anal. Calcd. for $C_{20}H_{20}SO_6$: C, 61.84; H, 5.16. Found: C, 61.45; H, 5.17.

2,7-Dihydro-3,4-5,6-dibenzoselenepin (IIB).—Ferrous selenide was prepared by heating to redness an intimate mixture of equimolar quantities of powdered selenium and 60 mesh iron filings. Hydrogen selenide gas was generated by the action of warm 25% sulfuric acid upon powdered ferrous selenide and was filtered by means of glass wool to remove entrained acid. Potassium selenide solution was prepared as follows: 13.1 g. of C.P. potassium hydroxide pellets dissolved in 60 ml. of water was saturated (under cooling) with excess hydrogen selenide gas. This was followed by the addition of a cold solution of 13.1 g. of potassium hydroxide pellets in 20 ml. of water. The resulting potassium selenide solution (*ca.* 80–90 ml., *ca.* 0.22 mole) was mixed with 1600 ml. of absolute methanol (99.85%) and 20.0 g. (0.059 mole) of 2,2′-bis-(bromomethyl)-biphenyl and then refluxed with rapid stirring for 24 hours. At the end of the 24-hour reflux period, about 1400 ml. of methanol was distilled off; 400 g. of ice was added to the residue and the white plastic selenide was mechanically removed from the excess potassium selenide with its suspension of amorphous selenium. After agitation with water, separation and drying, the crude cyclic selenide solidified, upon standing overnight, to give pasty white crystals. The yield of crude product was nearly the theoretical. A small amount of the crude product was recrystallized from petroleum ether and was found to melt at 65–66°.

Anal. Calcd. for $C_{14}H_{12}Se$: Se, 30.5. Found: Se, 30.5 (macro detn.).

A small quantity (0.21 g.) of the selenide, dissolved in 15 ml. of boiling absolute ethanol, was poured with rapid stirring into a boiling solution of 0.22 g. of mercuric chloride dissolved in 15 ml. of absolute ethanol; upon cooling, white crystals of a mercuric chloride coördination complex of the selenide settled out; these crystals sintered and nearly melted at 101° but appeared to solidify and slowly decompose upon heating to 260° without really ever completely melting.

2,7-Dihydro-1-methyl-3,4-5,6-dibenzoselenepinium Iodide (IVB).—A mixture of 14 g. of crude 2,7-dihydro-3,4-5,6-dibenzoselenepin and 50 ml. of methyl iodide was gently refluxed for 36 hours in the dark. The resulting slurry of crystals was decanted into an open beaker and about 80% of the excess methyl iodide was evaporated off on a steam-cone. To the resulting slurry was added 80 ml. of methanol with stirring and the resulting mixture was then cooled to −5° for 4 hours. The yellowish-white crystals of selenonium iodide were filtered off and washed with cold methanol; yield of crude crystals was 12.5 g. (58%), m.p. 123–125° dec.

Anal. Calcd. for $C_{15}H_{15}SeI$: I, 31.6. Found: I, 31.4.

2,7-Dihydro-1,1-dimethyl-3,4-5,6-dibenzoselenepinium Diiodide (IX).—This preparation was exactly the same as that described above for the preparation of 2,7-dihydro-1-methyl-3,4-5,6-dibenzoselenepinium iodide except that 2,7-dihydro-3,4-5,6-dibenzoselenepin was alkylated with a mixture of methanol and methyl iodide. Two recrystallizations from methanol gave massive hexagonal-shaped crystals of the quaternary dimethylselenonium compound, m.p. 97–98°.

Anal. Calcd. for $C_{16}H_{18}SeI_2$: I, 46.8. Found: I, 46.6.

Dimethyl 4,4′-Dibromodiphenate.—Ninety-two grams (0.27 mole) of methyl 5-bromo-2-iodobenzoate (b.p. 133–134° (1 mm.))[20] was heated to 180°, by means of an oil-

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(19) H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I, 2nd edition, John Wiley and Sons, New York, N. Y., 1951, p. 514.

(20) H. Hirtz, *Ber.*, **29**, 1407 (1896).

bath. In five portions, 23 g. (0.36 g. atom) of No. 44F copper bronze powder was added over a period of one hour, heating to 220° after each addition and allowing to cool to 180° before adding another portion of the copper powder. After all the copper powder had been added, the mixture was stirred at 220–230° for another hour to ensure completeness of reaction. The cooled product was extracted with several portions of boiling methanol to dissolve out the desired ester. After filtering, the combined methanol solutions were concentrated down to *ca.* 300 ml. and then cooled to −10°. Nearly white crystals of the desired dimethyl 4,4′-dibromodiphenate were obtained upon filtering off and washing with cold methanol; yield 43 g. (75%), m.p. 121–122°; recrystallization from methanol gave m.p. 123–124°; reported[10] 124° (prepared by different method).

4,4′-Dibromo-2,2′-bis-(hydroxymethyl)-biphenyl.—The procedure employed was an adaptation of the method of Hall, *et al.*,[12] for the reduction of dimethyl diphenate.

A solution of 42.5 g. of dimethyl 4,4′-dibromodiphenate, dissolved in a mixture of 400 ml. of absolute ethyl ether and 400 ml. of purified dimethyl ether of diethylene glycol, was added slowly over a period of one hour to a stirred suspension of 6.0 g. of lithium aluminum hydride in 200 ml. of absolute ether. The mixture became quite thick and very difficult to stir but was, nevertheless, refluxed with stirring for 3.5 hours more, after which time the mixture became more mobile. The excess lithium aluminum hydride was decomposed with ethyl acetate and then 200 ml. of 6 *N* sulfuric acid was added with stirring. The ether was distilled off and the residual mixture was poured into 1200 ml. of cold water and allowed to stand at 0° for 24 hours. The crude precipitate was filtered off and recrystallized from 200 ml. of 60:40 benzene–toluene mixture to give white crystals; yield 28 g. (76%), m.p. 128–133°. Further recrystallization from toluene gave m.p. 134–135°; a third recrystallization from 65% ethanol gave m.p. 136–137°.

Anal. Calcd. for $C_{14}H_{12}O_2Br_2$: C, 49.19; H, 3.25. Found: C, 45.11; H, 3.42.

4,4′-Dibromo-2,2′-bis-(bromomethyl)-biphenyl.—The procedure employed was like that used for preparing 2,2′-bis-(bromomethyl)-biphenyl.[12]

Twenty-five grams of 4,4′-dibromo-2,2′-bis-(hydroxymethyl)-biphenyl was refluxed with 1800 g. of 48% hydrobromic acid with vigorous stirring for 4 hours. After cooling the resulting mass at 0° for 24 hours, the crude crystals were filtered off using a sintered glass funnel. After washing with water, drying and recrystallizing the crude crystals from 125 ml. of 50:50 benzene–petroleum ether (b.p. 90–100°) mixture, nearly white crystals were obtained; yield 24 g. (74%), m.p. 144–146°.

Anal. Calcd. for $C_{14}H_{10}Br_4$: C, 33.77; H, 2.03. Found: C, 34.05; H, 2.10.

2′,3″-Dibromo-2,7-dihydro-3,4-5,6-dibenzothiepin (V).—Twenty-three grams of 4,4′-dibromo-2,2′-bis-(bromomethyl)-biphenyl was refluxed with vigorous stirring for 48 hours with 33 g. of sodium sulfide nonahydrate, 1200 ml. of methanol and 30 ml. of water. The excess methanol was distilled off on a steam-cone and the residue was stirred with 300 ml. of cold water. The crude product was filtered off, washed with water and dried. Upon recrystallizing from a minimum of 60:40 benzene–toluene mixture, nearly white crystals were obtained; yield 13.5 g. (75%), m.p. 191–192°.

Anal. Calcd. for $C_{14}H_{10}Br_2S$: C, 45.4; H, 2.72. Found: C, 45.42; H, 2.65.

2′,3″-Dibromo-2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide (VI).—A mixture of 33 ml. of 30% hydrogen peroxide, 19 ml. of acetic anhydride, 90 ml. of glacial acetic acid and 11.6 g. of 2′,3″-dibromo-2,7-dihydro-3,4-5,6-dibenzothiepin was refluxed for 3.5 hours. Upon filtering off the beautiful white crystals and washing first with acetic acid and then with water, 12.4 g. of material was obtained (98% yield); the material seemed not to exhibit a melting point and was quite insoluble in most organic solvents.

Anal. Calcd. for $C_{14}H_{10}Br_2SO_2$: C, 41.81; H, 2.51. Found: C, 41.97; H, 2.52.

2′,3″-Dicyano-2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide (VII).—The bromine atoms of the above compound were replaced by nitrile groups employing the Rosenmund–von Braun nitrile synthesis.[11] A mixture of 6.0 g. of the above 2,3″-dibromo-2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide, 8.02 g. of cuprous cyanide, 5 drops of benzonitrile, 0.25 g. of anhydrous cupric sulfate and 19.5 ml. of quinoline was refluxed for 3 hours. The resulting molten mass was cautiously poured into 200 ml. of 20% hydrochloric acid contained in a good hood with adequate ventilation. The resulting mixture was heated with stirring at 100° for one hour to decompose completely all cuprous cyanide. The crude humin-like precipitate was used in the next hydrolysis step without further treatment. A sample was still brown after one recrystallization with Norit, but a second recrystallization from 50% aqueous dimethylformamide, again with charcoal treatment, gave a light tan precipitate, which did not melt at 300° and which was rather insoluble in the more common organic solvents but readily soluble in nitriles, amines and dimethylformamide. The material was purified for analysis by further recrystallization from a mixture of acetic acid and benzonitrile (followed by washing with acetic acid and water).

Anal. Calcd. for $C_{16}H_{10}SO_2N_2$: N, 9.51. Found: N, 9.48.

2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic Acid (VIII).—Five grams of the above crude, humin-like dinitrile was refluxed for 10 hours with 7 ml. of water and 30 ml. of concentrated sulfuric acid. Upon pouring the crude mixture onto 60 g. of ice, filtering and washing, a coal-black precipitate of the crude acid was obtained. The black precipitate was dissolved in 4 g. of sodium bicarbonate, the solution treated with 1 g. of decolorizing charcoal and filtered. Upon acidifying the filtrate, a light-brown, fine-particled precipitate was obtained, which tended to pass through filter paper unless coagulated by digestion in water at 100°. Although the material was slightly soluble in glacial acetic acid, it could not be crystallized out, forming amorphous-like jells on cooling hot saturated solutions (in acetic acid). White crystals could be obtained by dissolving the light brown crystals in a *very large* volume of hot water, treating with charcoal, filtering and concentrating down to about one-tenth of the original volume. A more convenient method of obtaining pure white crystals was recrystallization from a minimum of dimethylformamide, after treatment with charcoal, and washing the crystals from the dimethylformamide purification first with dilute hydrochloric acid and then with water to ensure complete removal of dimethylformamide (the crystals dissolved in dimethylformamide with considerable heat of solution). The final yield of white crystals was 1.8 g. The white material did not appear to melt (it should be pointed out that biphenyl-4,4′-dicarboxylic acid has been reported as not melting and as not being soluble in organic solvents) and was virtually insoluble in ordinary organic solvents; equivalent weight 168 (calcd. 166).

Anal. Calcd. for $C_{16}H_{12}SO_6$: C, 57.76; H, 3.66. Found: C, 57.57; H, 3.84.

The preparation of the diethyl ester (m.p. 200–201°) and the analysis for this compound are given in one of the previous preparations.

Attempted Optical Resolution of 2,7-Dihydro-1-methyl-3,4-5,6-dibenzothiepinium Salts.—The optical rotations reported in this work were determined with a Schmidt and Haensch precision polarimeter. This polarimeter gives readings directly to 0.01° but estimates to 0.005° are readily obtained and are quite reproducible when crystal clear solutions (filtered through fine sintered glass filters) are employed. Regular (macro) polarimeter tubes having a cross-section of 1 cm. were used in all of these studies. The tubes were either 2 dm. or 4 dm. in length, as indicated. Twenty individual readings were taken and the average of these 20 readings was employed for each reported rotation.

Conversion of the 2,7-dihydro-1-methyl-3,4-5,6-dibenzothiepinium iodide to the corresponding neutral *d*-camphorate and hydrogen *d*-camphorate salts gave only intractable non-crystalline gums. Conversion to the neutral *d*-tartrate (m.p. 130–131°), hydrogen *d*-tartrate (m.p. hydrate 103.5–104.5°, anhydrous 153–155°) and *d*-camphorsulfonate (m.p. 225–226.5°) gave salts having molar rotations[21,22]

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(21) H. Landolt, "The Optical Rotating Power of Organic Substances and Its Practical Applications," English Translation by J. H. Long, The Chemical Publishing Co., Easton, Pa., 1902, pp. 221, 548–9.

(22) W. J. Pope and C. S. Gibson, *J. Chem. Soc.*, **97**, 2214 (1910); J. I. Graham, *ibid.*, **101**, 748 (1912); W. J. Pope and S. J. Peachey, *ibid.*, **75**, 1085 (1899).

corresponding to non-asymmetric monovalent cationic salts of the respective acid. In no case was there any detectable diastereomerism or mutarotation observed between fractions of a particular salt.

Evidence for the Resolution of 2,7-Dihydro-1-methyl-3,4-5,6-dibenzoselenepinium Ion.—2,7-Dihydro-1-methyl-3,4-5,6-dibenzoselenepinium iodide was converted to the hydrogen *d*-tartrate and produced diastereomeric fractions. The trapezoidal, less-soluble hydrogen *d*-tartrate had m.p. 116–117°, after drying over phosphorus pentoxide in a vacuum for several days, and $[\alpha]^{24}\mathrm{D}$ +8.5° (*c* 1.393 g., water) while the more-soluble, rosette-like fraction had m.p. 91–93° and $[\alpha]^{24}\mathrm{D}$ +12.7° (*c* 1.272 g., water) under the same conditions.

However, all attempts to demonstrate activity in recovered 2,7-dihydro-1-methyl-3,4-5,6-dibenzoselenepinium iodide regenerated from the initial trapezoid fraction and the final rosette-like fraction failed. Likewise, chloroplatinates prepared from the initial and final crops showed only traces of possible activity (not beyond experimental error). In a similar manner, the selenonium neutral *d*-tartrate, hydrate m.p. 116–117° dec., anhydrous m.p. 131–133° dec., was readily obtained in crystalline form. Again, although evidence for some diastereomerism was observed during fractionation of the neutral *d*-tartrate, the evidence was less conclusive than with the hydrogen *d*-tartrate.

Likewise, 2,7-dihydro-1-methyl-3,4-5,6-dibenzoselenepinium iodide was converted to the *d*-camphorsulfonate salt and was found to give some evidence for diastereomerism. Thus, the least-soluble fraction, after drying *in vacuo* over phosphorus pentoxide for several days at room temperature, had m.p. 190–191°, with decomposition, $[\alpha]^{28}\mathrm{D}$ +10.3° (*c* 2.884 g., water); $[M]^{28}\mathrm{D}$ +5210°. The hydrate had $[\alpha]^{27}\mathrm{D}$ 9.1° (*c* 2.1676 g., water). The more soluble fraction, after similar drying, had m.p. 199–200° dec., $[\alpha]^{28}\mathrm{D}$ +10.8° (*c* 2.4213 g., water); $[M]^{28}\mathrm{D}$ +5455°.

However, as with the selenonium hydrogen *d*-tartrate fractions, conversion of initial and tail *d*-camphor sulfonate fractions back to the selenonium iodide or chloroplatinate gave no significant indication of activity (the recovered chloroplatinate did show slight evidence of activity, but results were hardly beyond possible experimental error). Again, as above, the results may be taken as evidence for the non-asymmetric nature of the selenonium ion of this study, or the divergent molar rotation of the hydrogen *d*-tartrate and *d*-camphorsulfonate fractions may be merely unusual anomalies (non-additive anomalous activities of salts are not unusual with alkaloids, etc.); such anomalies could be rationalized as being caused by an enhanced tendency of the large selenonium to complex with the anionic resolving agent. On the other hand, in view of the known relative instability of most selenonium salts, the inactivity, or very slight activity, of the regenerated selenonium iodides and chloroplatinates, may merely be caused by ready racemization of the selenonium ion during the conversion as Balfe and Phillips[18] have observed in their previous work with asymmetric selenonium compounds.

Repeated attempts to obtain crystalline fractionation of 2,7-dihydro-1-methyl-3,4-5,6-dibenzoselenepinium neutral *d*-camphorate or hydrogen *d*-camphorate have been unsuccessful. Although the hydrogen *d*-camphorate eventually crystallizes when dried, all attempts at seeding solutions with such crystals have failed.

Attempts to Resolve 2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic Acid. (A).—*l*-Strychnine (1.610 g.) was dissolved in a minimum of chloroform and to the resulting solution was added 0.802 g. of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic acid and 100 ml. of boiling ethanol. The resulting solution was allowed to evaporate spontaneously at room conditions for several days until crystals appeared and then for 24 hours more. Beautiful small needles of the neutral *l*-strychnine salt were deposited. Initial, middle and mother liquor fractions were collected. All three fractions had identical physical appearance (fine needles) under the microscope. Initial crystals had $[\alpha]^{25}\mathrm{D}$ −3.5° (*l* = 2 dm.; *c* 4.17 g., chloroform) while mother liquor crystals had $[\alpha]^{25}\mathrm{D}$ −4.0° (*l* = 2 dm.; *c* 1.24 g., chloroform). When both fractions were decomposed with excess acid and the resulting precipitated acid washed and dissolved in cold 0.5 *N* sodium hydroxide, no trace of activity was observed for the sodium salt.

(B).—Likewise, when 1.000 g. of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic acid and 0.703 g. of (−)-α-phenylethylamine were dissolved in 30 ml. of hot water and allowed to evaporate spontaneously, beautiful crystals were obtained. All fractions were physically and optically homogeneous (m.p. 208–214° dec.) and no evidence for activity was observed for the sodium salt of the regenerated acid from initial or mother liquor salt fractions.

(C).—Attempts to obtain a crystalline neutral *d*-cinchonine salt of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic acid and all attempts to obtain crystalline neutral *d*-quinidine and hydrogen *d*-quinidine salts gave intractable oils or gums in 95% ethanol and aqueous ethanol.

(D).—Positive evidence of diastereomerism was observed during the crystallization of the neutral *l*-brucine salt of the dicarboxylic acid. In 100 ml. of boiling chloroform, 1.625 g. of *l*-brucine and 0.680 g. of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic acid were dissolved. The resulting solution was evaporated down to 20–30 ml. and then treated with 150 ml. of hot absolute ethanol. The resulting hot solution was covered with a watch-glass and allowed to cool in a pre-heated glass wool-insulated container without disturbance of any kind. White, rosette-like clusters of crystals were deposited, which were filtered off and air-dried. When 0.148 g. of this brucine salt was dissolved in a minimum of chloroform, the solution filtered from colloidal matter, diluted to 25 ml. and then examined in a 2 dm. polarimeter tube, $a^{23}\mathrm{D}$ +0.07° was obtained; this corresponds to $[\alpha]^{23}\mathrm{D}$ +5.9° (*c* 0.592 g., chloroform). Such *dextrorotary* brucine salts are very unusual and this was the first slight encouragement that diastereomerism might be observed.

Mother liquors from the above initial crystalline fractions were evaporated to about half their original volume and then allowed to slowly cool completely undisturbed as before. White cubical-like crystals were deposited in great abundance, m.p. 225–230° (dec., sinters 215–217°). When 0.680 g. of this second fraction of crystals was dissolved in a minimum of chloroform, filtered from a tiny trace of colloidal material, and diluted to 25 ml., examination in a 2 dm. polarimeter tube gave $a^{28}\mathrm{D}$ −0.09°; this corresponds to $[\alpha]^{28}\mathrm{D}$ −1.65° (*c* 2.72 g., chloroform).

Mother liquors from the above second fraction were allowed to evaporate spontaneously at room conditions to give a third fraction of crystalline clusters. When 0.414 g. of these third fraction crystals was dissolved to 25 ml. with chloroform and examined in a 2 dm. polarimeter tube, $a^{23}\mathrm{D}$ −0.14° was obtained; this corresponds to $[\alpha]^{23}\mathrm{D}$ −4.22° (*c* 1.656 g., chloroform). Although this evidence indicated diastereomerism in the brucine salt, decomposition of the initial and third (mother liquor) fractions with cold 3 *N* hydrochloric acid, washing the free liberated acid with two portions of cold 3 *N* acid, then with several portions of cold water, and then dissolving the dicarboxylic acid in cold 0.5 *N* ammonia gave no sign of activity when observed in a 2 dm. polarimeter tube.

Anal. Calcd. for $C_{16}H_{12}SO_6 \cdot 2C_{23}H_{26}N_2O_4 \cdot 3C_2H_5OH$: C, 64.84; H, 6.57; N, 4.46. Found: C, 65.08; H, 6.87; N, 4.62; $[\alpha]^{28}\mathrm{D}$ −1.65°.

Resolution of 2,7-Dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic Acid *via* its Hydrogen *d*-Cinchonine Salt.—In about 150 ml. of ethanol 1.380 g. of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic acid and 1.221 g. of *d*-cinchonine were dissolved and the resulting solution was evaporated down to about 70 ml. About 80 ml. of hot water was added and the mixture was allowed to cool slowly and crystallize spontaneously for a period of 48 hours. Fine crystalline masses were deposited. The initially deposited crystals were filtered off and the mother liquors were allowed to crystallize spontaneously for 48 hours at room conditions to give a second fraction of crystals. In like manner, third and fourth fractions of crystals were obtained. These four fractions had the following respective specific rotations: (1) $[\alpha]^{23}\mathrm{D}$ +90.0° (*l* = 2 dm.; *c* 1.510 g., ethanol); [2] $[\alpha]^{30}\mathrm{D}$ +93.7° (*l* = 2 dm.; *c* 0.7652 g., ethanol); (3) $[\alpha]^{29}\mathrm{D}$ +98.8° (*l* = 2 dm.; *c* 0.7748 g., ethanol); (4) $[\alpha]^{25}\mathrm{D}$ +121° (*l* = 4 dm.; *c* 0.1832 g., ethanol). By recrystallization and consolidation of these fractions from 20–30% ethanol (in water) fractions were obtained, which were subjected to decomposition with hydrochloric acid. For a period of 75 minutes a pulverized sample (0.830 g.) of the less dextrorotatory sample of the cinchonine hydrogen salt was stirred and intimately mixed with 90 ml. of cold 2 *N* hydrochloric acid at -5 to $-10°$. The mixture was filtered (sintered glass funnel) and the residual dicarboxylic acid was macerated with an additional 100 ml. of cold 2 *N* hydrochloric acid at $-5°$ for a period of 15–20 minutes. Filtration was followed by washing the cold residue with an additional 100 ml. of cold 3 *N* hydrochloric acid and then with three successive 100-ml. portions of cold water (0°). The residual cold dicarboxylic acid was then dissolved in 25 ml. of cold (-5 to 0°) 0.5 *N* ammonia in 5% aqueous urea solution and filtered. The resulting solution of the ammonium salt of 2,7-dihydro-3,4-5,6-dibenzothiepin-1-dioxide-2′,3″-dicarboxylic acid when examined in a 2 dm. polarimeter tube, had α^{29}D $+0.14°$; this corresponds to $[\alpha]^{29}$D $+1.81°$ (*l* 4 cm.; *c* 1.936 g., diammonium salt, 0.5 *N* ammonia in 5% aqueous urea) for the diammonium salt of the acid.

In exactly the same manner as that just described, the more dextrorotatory fraction (0.860 g.) gave a diammonium salt in 25 ml. of 0.5 *N* ammonia and 5% urea having α^{25}D $+0.225°$ when examined in a 4 dm. macro polarimeter tube; this corresponds to $[\alpha]^{25}$D $+3.1°$ (*l* 4 dm.; *c* 1.828 g., 0.5 *N* ammonia in 5% aqueous urea) for the acid, or expressed in respect to the diammonium salt, $[\alpha]^{25}$D $+2.85°$ (*l* = 4 dm.; *c* 1.98 g., diammonium salt; 0.5 *N* ammonia in 5% aqueous urea).

Since there is abundant evidence that in most simple cinchonine salts optical activity is relatively additive,[23] it would appear that the material is extensively racemized during the conversion of the cinchonine acid salt to the ammonium salt. This is confirmed by the difficulty in obtaining an active acid from the brucine salt (see above), by the fact that, effectively, only one (the dextrorotary) antipode can be isolated from recrystallization of the acid cinchonine salt.

Anal. Calcd. for $C_{19}H_{22}N_2O \cdot C_{16}H_{12}SO_6 \cdot 2H_2O$: C, 63.42; H, 5.78; N, 4.23. Found: C, 63.70; H, 5.50; N, 4.28; $[\alpha]^{23}$D $+90°$.

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(23) H. Landolt, ref. 21, p. 681; A. C. Oudemans, *Ann.*, **182**, 55 (1876). Anomalous activities are sometimes observed with alkaloid salts, especially salts, of unsaturated acids. *cf.* T. P. Hilditch, *J. Chem. Soc.*, **93**, 1388 (1908); **95**, 335, 1570 (1909); **99**, 224 (1911).

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Reactions of Carbon Monoxide at High Temperature. I. A New Synthesis of Phthalic Anhydrides

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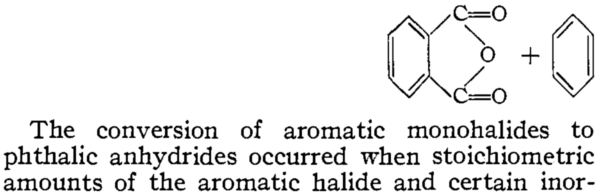
RECEIVED JUNE 27, 1956

A mixture of benzoic anhydride, phthalic anhydride and benzene is formed by the reaction of bromo- or chlorobenzene, carbon monoxide and alkali metal carbonates or orthophosphates in the presence of nickel tetracarbonyl. Under optimum conditions, phthalic anhydride is obtained in 75% conversion. Benzoic anhydride may be the immediate precursor of phthalic anhydride, as shown by its conversion to phthalic anhydride and benzene by heating with nickel carbonyl and carbon monoxide at 250–375° and 300–600 atm. Certain substituted phthalic anhydrides have been prepared from substituted aromatic halides and from aromatic acid anhydrides. Under similar conditions N-phenylphthalimide and benzene are formed from N,N-dibenzoylaniline.

During an investigation of high-temperature reactions of carbon monoxide with aromatic halides, it was found that chlorobenzene, carbon monoxide and nickel carbonyl gave traces of benzoyl chloride, a small amount of benzoic anhydride and much tar. When anhydrous sodium fluoride was added in molar amounts, the product contained benzoyl fluoride in up to 27% conversion and tar formation was suppressed.[1] An attempt to extend this reaction to the synthesis of tribenzoyl phosphate, by substituting dry trisodium phosphate for the sodium fluoride, resulted in a mixture of benzoic anhydride, phthalic anhydride and benzene. Since the conversion of a monosubstituted aromatic nucleus to an aromatic dicarboxylic acid derivative was an unexpected result, the reaction was studied in detail.



The conversion of aromatic monohalides to phthalic anhydrides occurred when stoichiometric amounts of the aromatic halide and certain inorganic salts were heated at 250–375°, under carbon monoxide pressure, in the presence of nickel carbonyl.[2] The nature of the inorganic salt was very important, since good yields of phthalic anhydride were obtained only with the alkali metal carbonates and orthophosphates. Traces of phthalic anhydride were formed with calcium phosphate and sodium fluoride.

Nickel tetracarbonyl appeared to be necessary for the synthesis of phthalic anhydride, since no phthalic anhydride was obtained from bromobenzene, carbon monoxide and sodium carbonate with either iron or cobalt carbonyl. Precursors of nickel carbonyl such as Raney nickel and nickel chloride were equivalent to the carbonyl.

The reaction of chloro- or bromobenzene with carbon monoxide and sodium carbonate was sufficiently exothermic to cause the temperature of the reaction mixture to exceed 400°. The products from such overheated reactions were black and difficult to purify. Dilution of the aromatic halide with three times its weight of an inert diluent such as toluene or cyclohexane not only eliminated this flash to extreme temperatures, but also increased the ratio of phthalic to benzoic anhydride in the product from 1:1 in the undiluted system to 15:1. The amount of non-distillable tarry by-products in the diluted system was only 0.3% of the weight of bromobenzene.

Nearly stoichiometric ratios of alkali metal to halide must be present in the reaction mixture to obtain maximum yields. Variation of the carbon

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(1) W. W. Prichard, U. S. Patent 2,696,503, Dec. 7, 1954.

(2) W. W. Prichard, U. S. Patent, 2,680,751, June 8, 1954.