2-Oxaspiranes and the Thorpe–Ingold Effect[1,2]

By Scott Searles, Eugene F. Lutz and Milton Tamres

A series of 2-oxaspiranes, $(CH_2)_nC(CH_2)_2O$ (I), with $n = 2$ (II), 3 (III), 4 (IV) and 5 (V), has been synthesized and studied to observe effects of small changes in bond angle deformation in the strained oxetane ring. Comparison was made of infrared spectra, hydrogen bonding abilities and ease of reductive cleavage with lithium aluminum hydride of these compounds, as well as of oxetane (VI) and 3,3-diethyloxetane (VII). The bathochromic shift of the 10 μ band characteristic of the oxetane ring was in the order expected for deformation of the oxetane ring by the Thorpe–Ingold effect: II > III > IV ~ V ~ VI > VII. The relative basicities, as measured by hydrogen bonding, were in the order IV > III > II > V ~ VI > VII, and the order with regard lithium aluminum hydride cleavage was IV > III > II > VI > VII ≫ V, reflecting the influence also of steric and electronic effects of the carbocyclic rings.

It is well known that many properties of cyclic compounds are markedly affected by the size of the ring involved. The causes of the effects are, however, uncertain, although there are several theories. It would seem that a handicap in elucidating the basic principles involved may be the restriction generally assumed of strained bond angles to the three sizes (60°, 90° and 108°) associated with symmetrical 3-, 4- and 5-membered rings. Obviously fractional ring sizes are impossible, but intermediate angles might be realized by distortion of rings due to appropriate substitution, according to the Thorpe–Ingold effect.

The principle known as the "Thorpe–Ingold effect" states that when the bond angle is distorted between one pair of substituents on a saturated carbon atom, the bond angle between the other pair of substituents will be distorted in the opposite manner.[3,4] It was first propounded in 1915[4] to explain the greater tendency observed for the formation of the cyclopropane or α-butyrolactone ring in cases possessing *spiro*-fusion with a cyclohexane, than in cases having analogous *gem*-dimethyl substitution.

Other evidence of a similar nature has been presented, the most systematic of which was a study of the base-catalyzed equilibrium between supposed β,β-dialkyl-α-ketoglutaric acids and their cyclic tautomers.[5] This appears to have been invalidated, however, by the recent report that two of these compounds were oxetanedicarboxylic acids.[6]

Other types of evidence, however, may be cited for the reality of the Thorpe–Ingold effect. The greater degree of internal hydrogen bonding associated with the presence of bulky groups on the carbinol carbon atoms may be attributed to such groups spreading the exterior angle of the 5-membered chelate ring, thus decreasing the internal CCO angle and stabilizing the ring.[7]

The most direct evidence on the validity of the Thorpe–Ingold theory should be measurement of bond angles in appropriate cases. There seems to be lack of sufficient data for non-cyclic cases,[8] but data on the molecular structure of small-ring compounds, such as listed in Table I, all support it. The correlation is only qualitative, but the accuracy of the data would not warrant more.

Table I

Bond Angles in Small-ring Compounds

Compound	Internal angle	External angle	Ref.
Cyclopropane	CCC 60°	HCH 118.2°, 120°	9, 10
1,1,2,2-Tetramethyl-cyclopropane	CCC 60°	MeCMe 114 ± 6°	11
Ethylene oxide	CCO 59.3°^{a}	HCH 116.7°	12
Ethylene sulfide	CCS 57.1°^{a}	HCH 116.0°	12
Cyclobutane	CCC 90°	HCH 114 ± 8°	13
Trimethylene oxide (oxetane)	CCC 88.5 ± 3° CCO 88.5 ± 3°^{a}	HCH 112°	14, 15

^{a} Calculated from literature data assuming planar ring.

Thus, it seems very likely that appropriate substitution is capable of altering bond angles in the manner of the Thorpe–Ingold effect, except where strong electrical forces may predominate. It should be possible, then, to distort deliberately the bond angles of small ring compounds to obtain unusual bond angles.

An example of such appears to be found in *spiro*pentane, in which the internal bond angles on the central carbon atom are reported to be

(1) We wish to thank the National Science Foundation for a research grant which supported this investigation.

(2) Abstracted from the Ph.D. Thesis of Eugene F. Lutz, Kansas State University, 1959; presented before the Division of Organic Chemistry, American Chemical Society, at the 135th National Meeting, Boston, Mass., April 9, 1959 (Abstracts, p. 63-O).

(3) J. W. Baker, "Tautomerism," Rutledge, London, 1934, p. 179.

(4) R. M. Beesley, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, 107, 1080 (1915).

(5) S. S. Deshapande and J. F. Thorpe, *ibid.*, 121, 1430 (1922); L. Bains and J. F. Thorpe, *ibid.*, 123, 1206 (1923); J. W. Baker, *ibid.*, 127, 1678 (1925); summarized by C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, p. 538.

(6) K. B. Wiberg and H. W. Holmquist, *J. Org. Chem.*, 24, 578 (1959).

(7) L. P. Kuhn, This Journal, 74, 2492 (1952); 80, 5950 (1958). In the latter paper an alternative explanation is suggested, involving bent bonds between the carbinol carbon atoms.

(8) Except halogen-substituted alkanes, which generally do not fit the Thorpe–Ingold principle. Such exceptions should not be of great concern to us here, however, as they can be explained by various electrical effects which may be quite strong in such compounds. Two electron diffraction studies of propane have indicated a CCC angle of approximately 114° and 111.5°, but the HCH angle which the Thorpe–Ingold theory would predict to be less than tetrahedral, was not measured. The data are well summarized in "Tables of Interatomic Distances and Configuration in Molecules and Ions," ed. by L. E. Sutton, Spec. Publ. No. 11, The Chemical Society, London, 1958.

(9) O. Hassel and H. Viewoll, *Acta Chem. Scand.*, 1, 149 (1947).

(10) H. H. Gunthard, R. C. Lord and T. K. McCubbin, Jr., *J. Chem. Phys.*, 25, 768 (1956).

(11) H. P. Lemaire and R. L. Livingston, *Acta Cryst.*, 5, 817 (1952).

(12) G. L. Cunningham, A. W. Boyd, R. J. Meyers, W. D. Gwinn and W. I. Levan, *J. Chem. Phys.*, 19, 676 (1951).

(13) J. D. Dunitz and V. Schomaker, *ibid.*, 20, 1703 (1952).

(14) W. Shand in P. W. Allen and L. E. Sutton, *Acta Cryst.*, 3, 46 (1950).

(15) J. Fernandez, R. J. Meyers and W. D. Gwinn, *J. Chem. Phys.*, 23, 758 (1955).

approximately 61.5° instead of 60°.[16] This result suggested study of compounds having a four-membered ring spiro to a small or medium ring. As a four-membered ring is not a rigid architectural unit, its internal angles should be more susceptible to modification by the Thorpe–Ingold effect than those of the cyclopropane ring.

Among 4-membered rings, the oxetane ring seemed to possess unique advantages for this type of study, because of its susceptibility to a number of reactions and interactions that could be studied to give information on the chemical effects of the changes in bond angles. *Spiro* fusion at position 3 on the oxetane ring seemed preferable, because the electrical and steric effects of the *gem*-substituents would be minimized and the compounds would be symmetrical, di-primary ethers. Therefore, a program was undertaken to synthesize a series of 2-oxaspiranes (I).
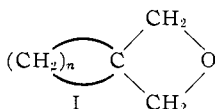
No general method of synthesis was found for the 2-oxaspiranes, as the double strain in the lower members presented special problems. It would be predicted by the Thorpe–Ingold principle, of course, that closure of a second, strained ring *spiro* to another strained ring would be difficult, due to spreading of the atoms that must be joined to form the new ring.

For the first member of the series, 2-oxaspiro-[3.2]hexane (II), the Freund reaction was used to close the cyclopropane ring after the oxetane ring had been closed. The details of this synthesis and the proof of structure of the compound have been described in an earlier paper.[17]
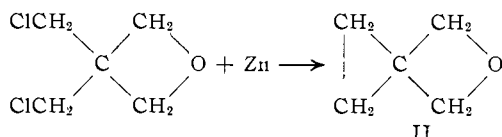

Several attempts were made to synthesize 2-oxaspiro[3.3]heptane (III) before success was realized. In the first route employed, the cyclobutane ring was formed successfully after the oxetane ring by condensing sodiomalonic ester with 3,3-bis-(chloromethyl)-oxetane in a manner similar to that described by Campbell.[18] Hydrolysis of the diester proceeded readily, but the second stage of decarboxylation could not be achieved without breaking the ring system and forming polymer. Alternatively, the silver salt of the monoacid was formed and added to bromine in carbon tetrachloride, with the intention of replacing the carboxyl group by a bromine atom, which could perhaps be replaced subsequently by hydrogen by means of the Grignard reaction.[19] Only polymeric product, however, could be ob-

tained from the reaction of the silver salt with bromine.

These difficulties may have been due to unusual ease of ring opening in this doubly-strained system in the presence of acidic reagents, as was demonstrated for 2-oxaspiro[3.2]hexane.[17] Therefore, it seemed more promising to close the oxetane ring under non-acidic conditions after forming the cyclobutane ring. The internal Williamson reaction on 1-bromomethyl-1-cyclobutanemethanol, however, gave no III[20]; but fortunately a recently discovered method of catalytically decomposing 1,3-carbonate esters to form oxetanes was available.[21]

By this reaction a 10% yield of 2-oxaspiro[3.3]-heptane was obtained under the best conditions found, which involved heating the cyclic carbonate of the corresponding diol with a catalytic amount of potassium propionate at 245–280°. Its structure was confirmed by its analysis, its infrared spectrum and its reduction by lithium aluminum hydride to 1-methylcyclobutanemethanol. An alcohol and an aldehyde were also formed from the cyclic carbonate ester. These were tentatively identified as 1-cyclopentenemethanol, due to Demjanov ring enlargement of the cyclobutane ring, and 1-methylcyclobutanecarboxaldehyde, which could arise by a 1,3-hydride shift, as observed in the decomposition of other cyclic carbonates.[21,22]
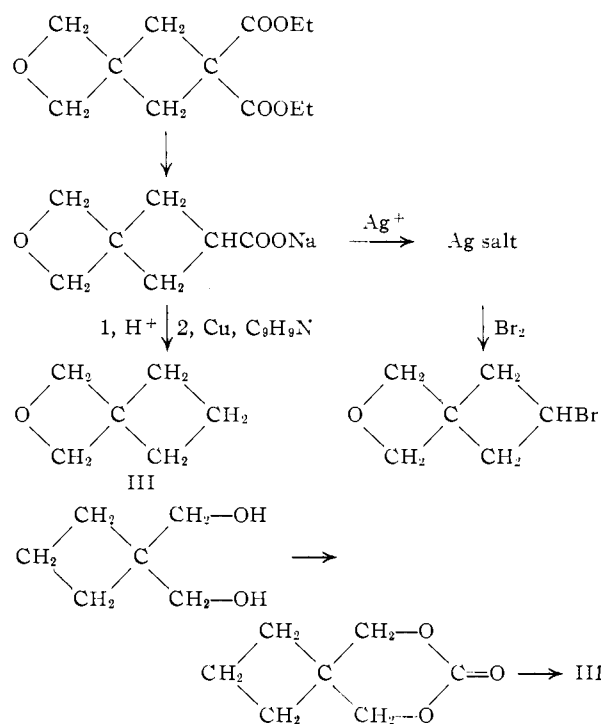
The two other members of the series studied here, 2-oxaspiro[3.4]octane (IV) and 2-oxaspiro[3.5]nonane (V) were prepared in a smooth fashion, the intramolecular Williamson reaction being used to close the oxetane ring in the final step in each

(16) J. Donohue, G. L. Humphrey and V. Schomaker, THIS JOURNAL, **67**, 332 (1945).

(17) S. Searles and E. F. Lutz, *ibid.*, **81**, 3674 (1959).

(18) T. W. Campbell, *J. Org. Chem.*, **22**, 1029 (1957).

(19) A similar procedure has been used successfully in the cyclobutane series by J. Cason and R. L. Way, *ibid.*, **14**, 31 (1949).

(20) S. Searles, R. G. Nickerson and W. K. Witsiepe, *ibid.*, **24**, 1839 (1959).

(21) S. Searles, D. G. Hummel, S. Nukina and P. E. Throckmorton, THIS JOURNAL, **82**, 2928 (1960).

(22) S. Searles and P. E. Throckmorton, unpublished data.

case. The use of alcoholic potassium hydroxide was found to give much better yields than that of aqueous potassium hydroxide, used previously.[20] The much better yield obtained with the cyclohexane derivative than with the cyclopentane derivative (68%, compared with 25%), as well as the complete failure of the reaction with the cyclobutane derivative (see above) might be considered a manifestation of the Thorpe–Ingold effect, but of course other steric factors may be involved.

IV, n = 2   V, n = 3
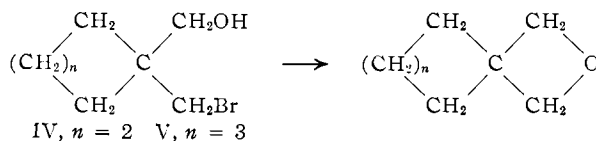
The 2-oxaspiranes were all reasonably stable compounds. In Table II are summarized the physical properties, including position of the characteristic oxetane band in the infrared spectrum, for each and for some comparable monocyclic oxetanes.

TABLE II

PHYSICAL PROPERTIES OF CERTAIN OXETANES

Compound	B.p. °C.	Mm.	n^{20}D	I.r. band, μ
Oxetane	48			10.15
3,3-Dimethyloxetane	77–79			10.20
3,3-Diethyloxetane	78–80	106		10.20
2-Oxaspiro[3.2]hexane	97		1.4371	10.35
2-Oxaspiro[3.3]heptane	120		1.4439	10.23
2-Oxaspiro[3.4]octane	138–142		1.4527	10.17
2-Oxaspiro[3.5]nonane	100–103	81	1.4602	10.14

The variations in boiling points and refractive indices are in agreement with expectations based on relative molecular weight. The bathochromic shifts in the position of the 10 μ absorption band is of particular interest, as the shift becomes greater as the ring system becomes more strained. This band has been assigned to a ring vibration, probably a ring-twisting vibration[23]; and one may speculate that the greater ease of distorting the oxetane ring in the most strained cases is due to the tendency for the oxetane methylenes, distorted already by the Thorpe–Ingold effect, to return to their normal positions. At any rate, the order of the bathochromic shift is in the order of the expected Thorpe–Ingold distortion of the methylenes.

The relative basicities of the oxaspiranes and related oxetanes were measured by means of their hydrogen bonding ability, using the shift of the O–D band in the infrared spectrum of CH_3OD solutions as the criterion. The method has been used widely in hydrogen bonding studies, including those of other cyclic ethers,[24] and has been found to give a measure of electron density on oxygen in cyclic ethers which is in agreement with results obtained from study of iodine complexes[25] and from nuclear magnetic resonance studies.[26] Such hy-

(23) R. F. Zürcher and H. H. Günthard, *Helv. Chim. Acta*, **38**, 849 (1955); **40**, 89 (1957).

(24) S. Searles and M. Tamres, THIS JOURNAL, **73**, 3704 (1951).

(25) M. Brandon, M. Tamres and S. Searles, *ibid.*, **82**, 2129 (1960).

(26) H. S. Gutowsky, R. L. Rutledge, M. Tamres and S. Searles, *ibid.*, **76**, 4242 (1954).

drogen bonding is, of course, relatively free from steric effects.

The data are presented in Table III. It may be noted first that 3,3-diethyloxetane, which is an analog of the 2-oxaspiranes, appears to be a somewhat poorer electron donor in hydrogen bonding than oxetane itself, while the reverse is true for 2,2-diethyloxetane. The latter case may be explained by the inductive effect of the ethyl groups increasing the electron density on the oxygen atom, but in the former case some other factor is evidently operating. This may be the Thorpe–Ingold effect, the *gem*-diethyl structure widening the external angle at position 3, thereby decreasing both the internal angle there and the internal COC angle directly across the ring. A sufficient decrease in the COC angle can cause a decrease in the electron availability, since ethylene oxides are much poorer electron donors than other cyclic ethers.[27]

TABLE III

SOME CHEMICAL PROPERTIES OF CERTAIN OXETANES

Oxetane	O–D shift, CH_3OD soln., cm.$^{-1}$	Reductive cleavage with LAH,[a] % yield
Oxetane	120	65
3,3-Dimethyloxetane		32[b]
3,3-Diethyloxetane	115	43[c]
2-Oxaspiro[3.2]hexane	122	66
2-Oxaspiro[3.3]heptane	128	76
2-Oxaspiro[3.4]octane	135	80
2-Oxaspiro[3.5]nonane	120	0
2,2-Diethyloxetane	125[d]	42[e]

[a] Standardized conditions, including 7 hours refluxing with tetrahydrofuran as solvent, except as noted below. [b] Same, except 20 hours refluxing. [c] Same, except 40 hours refluxing. [d] Ref. 24. [e] Ref. 28.

In 2-oxaspiro[3.2]hexane the oxetane ring should be distorted in the opposite manner to that in 3,3-diethyloxetane, since the spiro fusion with a cyclopropane ring imposes an external angle of about 60° at the carbon atom of the oxetane ring opposite the oxygen atom. The COC angle then should be considerably greater than its value of 94.5° in oxetane.[14] The electron donor ability, however, is but slightly greater than for oxetane itself. This might be due to the well-known electronegativity of the cyclopropane ring, or to the COC angle being now greater than optimum for electron donor ability. The latter explanation seems to be favored by the observation that the O–D shift does increase as the size of the spirocarbocyclic ring increases from three to four to five atoms.

On this basis one would not expect much further change when the carbocyclic ring is expanded to six members, and so the large drop in the O–D shift for 2-oxaspiro[3.5]nonane is surprising and suggests an additional factor. Molecular models here suggest that steric interaction between the axial hydrogen atoms of the cyclohexane ring and the hydrogen atoms of a methylene group in the oxetane ring. This may result in distorting the oxetane ring such that the COC angle is less than

(27) For example, the O–D shift for propylene oxide in methanol-*d* is 99 cm.$^{-1}$ (ref. 24).

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Table IV

Identification of Cleavage Products
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Alcohol is 1-Methylcyclo-	B.p., °C.	n^{20}D	Deriv.[a]	M.p., °C.	Lit., m.p., °C.
-Propanemethanol	122–125.5	1.4312[b]	DNB	85.5–87	85.2–85.3[c]
-Butanemethanol	132–142	1.4310	PU	90–91[d]	....
-Pentanemethanol	161–166	1.4540	PU	83.5–84.5[e]	....

[a] DNB signifies 3,5-dinitrobenzoate; PU signifies phenylurethan. [b] Index of refraction taken at 19°. [c] S. Siegel and C. B. Bergstrom, This Journal, **72**, 3815 (1950). [d] *Anal.* Calcd. for $C_{13}H_{17}O_2N$: N, 6.39. Found: N, 6.61. [e] *Anal.* Calcd. for $C_{14}H_{19}O_2N$: N, 6.00. Found: N, 6.18.

it is in oxetane itself and less than optimum for hydrogen bonding.

Lithium aluminum hydride reduction of these compounds was also studied.[28] The relative ease of reductive cleavage may be estimated from the yields obtained, since the reactions were carried out under standardized conditions and the main factor lowering the yields appeared to be incomplete reaction. The yields are given in Table III.

It will be noted that the yields observed correlate rather closely with the hydrogen bonding data, except for 2-oxaspiro[3.5]nonane, which failed to give any detectable reaction. This may be due to additional steric hindrance from the axial hydrogens toward the bulky aluminum hydride ion. The correlation of the two sets of data for the other compounds seems rather surprising in view of the quite different factors involved and indicates that coördination of the lithium ion is very important in the reductive cleavage process. Further work is planned on other reactions.

Experimental[29]

2-Oxaspiro[3.2]hexane was prepared as previously described[18]; b.p. 97°, n^{20}D 1.4371.

1,1-Bis-(hydroxymethyl)-cyclobutane.—To 149.3 g. (0.747 mole) of 1,1-dicarbethoxycyclobutane[30] in 1.8 liters of ether was added 35.5 g. (0.935 mole) of lithium aluminum hydride in 700 cc. of dry ether. When the hydride addition was complete, the reaction mixture was worked up in the usual manner.[28] A 76% yield of 1,1-bis-(hydroxymethyl)-cyclobutane, b.p. 132–140° (22 mm.), n^{20}D 1.4778 (reported[31] b.p. 147° (20 mm.), n^{20}D 1.4758), was obtained.

2,4-Dioxaspiro[5.3]nonan-3-one.—A mixture of 62.1 g. (0.536 mole) of 1,1-bis-(hydroxymethyl)-cyclobutane, 63.2 g. (0.536 mole) of diethyl carbonate and a few flakes of sodium was refluxed until the pot temperature dropped to a minimum according to the method of Pattison.[32] After ethyl alcohol was removed by distillation, the crude cyclic carbonate was taken up in chloroform, washed with water and then distilled; b.p. 130–163° (0.35–0.9 mm.). After recrystallization from carbon tetrachloride, 40.0 g. (52.6%) of cyclic carbonate ester, melting at 66–68°, was obtained. Further recrystallization gave a melting point of 67°.

Anal. Calcd. for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 59.38; H, 6.65.

2-Oxaspiro[3.3]heptane.—Ten grams (0.0704 mole) of 2,4-dioxaspiro[5.3]nonan-3-one and a catalytic amount of potassium propionate were placed in a flask arranged for distillation and heated at 245–280° until the volatile product no longer distilled. The crude product amounted to 5.7 g. This procedure was repeated until 48.2 g. of the crude product was collected. After fractionation over sodium through a 6-inch, glass helices-packed column, 6.5 g. (10%) of 2-oxaspiro[3,3]heptane, b.p. 110–116°, n^{20}D 1.4422, was obtained. Further purification was effected by distilling the oxetane from phenyl isocyanate; b.p. 120° (738 mm.),

n^{20}D 1.4439. The infrared spectrum showed the characteristic oxetane absorption[33] at 10.23 μ and no bands that were inconsistent with the assigned structure.

Anal. Calcd. for $C_6H_{10}O$: C, 73.43; H, 10.27. Found: C, 73.20; H, 10.31.

Side-products from 2-Oxaspiro[3.3]heptane Preparation.—A forerun in the above described fractional distillation, b.p. 63–105° n^{20}D 1.3995, appeared to be an azeotrope of water, an alcohol and probably other substances. Attempts to isolate the pure alcohol were not successful, but three derivatives of it were prepared from this fraction: an α-naphthylurethan, m.p. 120°; a p-nitrobenzoate, m.p. 90.5–91.8°; and a 3,5-dinitrobenzoate, m.p. 88–89°. Analysis of the 3,5-dinitrobenzoate gave 47.38% carbon and 3.83% hydrogen (Calcd. for $C_{13}H_{11}O_6N_3$: C, 46.30; H, 3.29). The ratio of C/H of 12.5/12 gives some support for 1-cyclopentenemethanol as the structure.

The crude pyrolysis product above reduced Fehling solution and its infrared spectrum showed the characteristic C—H and C=O absorption bands for an aldehyde. The 2,4-DNP was prepared from the crude pyrolysate; m.p. 182–183°. On analysis it was found to contain 56.00% carbon and 5.41% hydrogen, corresponding to a C/H ratio of 6/7, as in the 2,4-DNP of 1-methylcyclobutane carboxyaldehyde ($C_{12}H_{14}O_4N_4$, for which the theory is 51.79% C and 5.07% H).

2-Oxaspiro[3.4]octane and 2-oxaspiro[3.5]nonane were prepared as previously described[20] with the exception that alcoholic potassium hydroxide was used to effect cyclization of the oxetane ring rather than aqueous potassium hydroxide. This resulted in a 28.4% yield of 2-oxaspiro[3,4]octane, b.p. 138–142° (735 mm.), n^{20}D 1.4527 (reported[20] b.p. 149–150°, n^{20}D 1.4539) and a 68.3% yield of 2-oxaspiro[3,5]nonane, b.p. 100–103° (81 mm.), n^{20}D 1.4602 (reported[20] b.p. 69–70° (20 mm.), n^{25}D 1.4584).

Lithium Aluminum Hydride Reductions.—The hydride reductions were carried out as previously described,[28] using tetrahydrofuran as the solvent and refluxing the reaction mixture for 7 hours for each reduction. In each case a 2.75% solution of lithium aluminum hydride in tetrahydrofuran was used to effect the reduction.

The following example was typical: A solution of 5.06 g. of 2-oxaspiro[3.3]heptane in 23 ml. of dry tetrahydrofuran was added in 30 minutes to a cooled, stirred solution of 0.98 g. of lithium aluminum hydride in 54 ml. of tetrahydrofuran. After the mixture was refluxed gently for 7 hours, it was hydrolyzed with 20% sodium carbonate solution. The decanted solution (plus three washings of the precipitate with ether) were dried over potassium carbonate and then fractionally distilled, giving 3.0 g. of 1-methylcyclobutanemethanol, b.p. 141–142°, n^{20}D 1.4310. There was also 0.9 g. of column hold-up with identical infrared spectrum and refractive index (thus, the yield was 3.9 g. or 76%), and about 0.5 ml. of an intermediate fraction containing both the product and tetrahydrofuran.

Purification of Samples for O–D Shift Determinations.—3,3-Diethyloxetane and 2-oxaspiro[3.2]hexane were fractionated through a 6-inch, glass helices-packed column over sodium, and pure middle cuts, as determined by their infrared spectra, were collected. 2-Oxaspiro[3.3]heptane, 2-oxaspiro[3.4]octane and 2-oxaspiro[3.5]nonane were distilled over sodium to remove carbonyl impurities and then over phenyl isocyanate[34] and a few drops of quinoline to remove hydroxyl impurities. In all cases the purity of the samples used for the O–D measurements was checked by infrared spectrum.

(28) S. Searles, K. A. Pollart and E. F. Lutz, This Journal, **79**, 951 (1957).

(29) All melting and boiling points are uncorrected. Elemental microanalyses were performed by Weiler and Strauss, Oxford, England, and by Micro-Tech Laboratories, Skokie, Ill.

(30) J. Cason and C. F. H. Allen, *J. Org. Chem.*, **14**, 1038 (1949).

(31) N. D. Zelinsky and M. N. Ujedinov, *Ber.*, **46**, 1093 (1913).

(32) D. B. Pattison, This Journal, **79**, 3455 (1957).

(33) G. M. Barrow and S. Searles, *ibid.*, **75**, 1175 (1953).

(34) α-Naphthyl isocyanate was used in the case of 2-oxaspiro[3.5]nonane.

Method of Determining O–D Shifts.—The method used was identical to that used by Searles and Tamres[24] in studying the hydrogen bonding abilities of ethers. A Perkin– Elmer model 12C double pass spectrometer, equipped with a lithium fluoride prisms was used for the determinations.

Reactions of Free Radicals with Aromatics. III. Isotope Effects in the Arylation of Deuterated Benzenes. The Mechanism of Arylation[1]

By Ernest L. Eliel, Seymour Meyerson,[2a] Zoltan Welvart[2b] and Samuel H. Wilen

Isotope effects have been determined for the free-radical arylation and alkylation of benzene-d and of benzene–benzene-d_6 mixtures with a variety of peroxides. In most cases isotope effects calculated from product deuterium content are in excess of unity. The benzene–benzene-d_6 mixture recovered from a chlorophenylation experiment (product isotope effect 1.3) is, however, unchanged in isotopic composition, indicating that the addition of the chlorophenyl radical to benzene to form an arylcyclohexadienyl radical is not freely reversible under the conditions of arylation. The product isotope effect is, therefore, ascribed to a competition between arylcyclohexadienyl radicals which go on to product biaryl and radicals which are diverted into side products (such as dimers), this competition being subject to isotopic discrimination. DeTar and Long (ref. 12) have shown that arylcyclohexadienyl radicals may disproportionate, at least in dilute solution, into arylbenzenes and aryldihydrobenzenes. In accordance with this it has now been shown that the apparent product isotope effect in biphenyl obtained from benzene-d and benzoyl peroxide in dilute solution is higher when the biphenyl is carefully separated from the dihydrobiphenyl than when the dihydrobiphenyl is allowed to be air-oxidized to biphenyl which becomes commingled with the primary biphenyl product. Biphenyl isolated under the latter circumstances contains biphenyl-d_2, as expected. Biphenyl-d_2 is formed also in the decomposition of benzoyl peroxide in benzene-d in relatively concentrated solutions, indicating that even under these conditions some biphenyl is formed by disproportionation of the phenylcyclohexadienyl intermediate, followed by dehydrogenation, rather than by direct hydrogen loss from the intermediate radical.

Introduction

The reaction of an aromatic compound with an aryldiazo acetate or hydroxide to give a biaryl was discovered almost simultaneously by Kühling[3] and by Bamberger.[4] Convenient experimental procedures for the reaction were developed by Gomberg and Bachmann[5] after whom the reaction is often named. A variation of the reaction in which the aromatic compound is allowed to react with an aroyl peroxide instead of a diazonium derivative was discovered by Gelissen and Hermans[6]; it is this variation which was studied exclusively in the present work. The free-radical character of the reaction was first recognized by Hey and Waters[7] whose school has contributed much fundamental information regarding the mechanism of the reaction.[8] Reference to their work and other pertinent publications through 1956 is found in recent reviews of the subject.[9,10] Several important papers have appeared since these reviews went to press.[8,11–13]

The sequence of events when benzoyl peroxide is decomposed in benzene has usually been considered to be the one shown in Fig. 1.

The first step in this reaction sequence is rate determining.[14] At low peroxide concentrations, this step is unimolecular, but at higher peroxide concentrations the reaction order increases, indicating the incursion of chain processes involving induced decomposition of peroxide.[14] That the second step is not concomitant with the first has been demonstrated by trapping the benzoate radicals generated in step one.[15] The third and fourth step represent the most interesting part of free-radical aromatic substitution since they are the steps which may be common to substitution reactions with such diverse radical sources as diaroyl peroxides, diazotates and nitrosoacetanilides. The finding that the isomer distribution (ortho–meta–para ratio) in the arylation of monosubstituted benzenes appears to be nearly independent of the nature of the radical source[9,16] suggests that step 3 is the same for all these arylations. This speaks against the possibility, sometimes suggested, that steps 2 and 3 are concomitant (extrusion of CO_2 during arylation).

The mechanism suggested above for the arylation reaction may be termed the "addition-abstraction mechanism." Two other mechanisms have been considered,[9b] namely the "abstraction-addition mechanism" and the "synchronous mech-

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