boiling toluene; the solution was cooled to 100° and decanted from the crystallized product. At this point, the recrystallized glycol weighed 24 g. and melted at 160–163°. A final recrystallization from 350 ml. of toluene gave 22 g. of pure *cis*-2,2,4,4-tetramethyl-1,3-cyclobutanediol, m.p. 162.5–163.5°.

Acknowledgment. We are indebted to J. H. Chaudet, of these laboratories, for the determination and interpretation of the nuclear magnetic resonance spectra.

KINGSPORT, TENN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Ring Enlargement Produced by the Alkaline Fusion of ω-Bromocamphene

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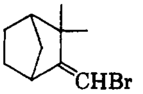
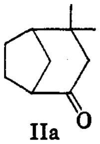
Received June 9, 1960

It is shown that "dicamphenyl ether," the major product produced by potassium hydroxide fusion of ω-bromocamphene (I), is a mixture composed largely of the ring expanded vinyl ethers (VIIIa) and (VIIIb). The "Schmelzketon," a minor product from the alkaline fusion of I, which was considered to be a single compound by earlier investigators is shown to be a mixture of 4,4-dimethylbicyclo[3,2,1]octan-2-one (IIa), 4,4-dimethylbicyclo[3,2,1]octan-3-one (IIb), and camphenilanaldehyde, whereas the "Oxidationketon" is a mixture of IIa, IIb, and carbocamphenilone (VI). The structures of IIa and IIb are suggested by a study of the NMR spectra of these ketones and their α-bromoderivatives. The reaction of I with potassium *t*-butoxide affords a mixture of the ring expanded enol ethers (XIX) and (XX). The formation of 2-butyne from 1,2-dibromo-2-methylpropane under similar conditions suggests that the cyclic acetylene (XXI) is an intermediate in the base induced ring enlargements of I.

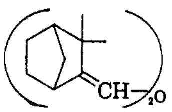
More than thirty years ago Lipp[1] observed that potassium hydroxide fusion of ω-bromocamphene (I) afforded, *in low yield*, a steam-volatile "Schmelzketon" which was assigned structure IIa, and named R-homocamphenilone, on the basis that it was converted by oxidation to camphenic acid (III) and was not affected by sodium amide.[2] The major product of the alkaline fusion of I, a nonvolatile oil, was represented as "dicamphenyl ether" (IV) since acid hydrolysis was alleged to give camphenilanaldehyde (V)[3] in quantitative yield. It was further claimed[1] that the oxidation of "dicamphenyl ether" with chromium trioxide produced an "Oxidationketon" which was identical with the "Schmelzketon."



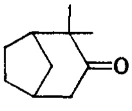
I



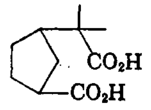
IIa



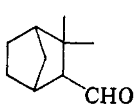
IV



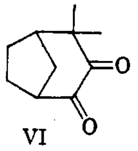
IIb



III



V



VI

Later, Hückel[4,5] described the conversion, by successive treatment with lead tetraacetate and alkali, of camphene (Ia) to a ketone which by reason of its conversion to camphenic acid (III) and carbocamphenilone (VI) was arbitrarily assigned structure IIb[5] and also given the name R-homocamphenilone. Hückel[5] made no reference to Lipp's work[1] and apparently overlooked a report[6] which recorded the identity of Hückel's ketone[4] with Lipp's "Schmelzketon." Matsubara[7] on the other hand, has recently stated that the "Schmelzketon" and "Oxidationketon" are different and only the latter substance is identical with Hückel's ketone. Moreover, Matsubara reversed the original structural assignments,[1,5] the "Schmelzketon" was shown to be 4,4-dimethylbicyclo[3,2,1]octan-3-one (IIb), while Hückel's ketone and the "Oxidation keton" were characterized as 4,4-dimethylbicyclo[3,2,1]octan-2-one (IIa).

In view of the conflicting statements in the literature and the interesting mechanistic consequences of these reactions we were led to reinvestigate this matter. It soon became apparent that the

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[1] P. Lipp, *J. Prakt. Chem.*, **105**, 50 (1922); P. Lipp, A. Gotzen, and F. Reinartz, *Ann.*, **453**, 1 (1927).

[2] A decision between structures IIa and IIb for the ketone on the basis of its stability toward sodium amide is invalid since both ketones possess active methylene groups adjacent to the carbonyl group and would be expected to form stable salts with sodium amide.

[3] Camphenilanaldehyde was identified by a positive Tollens test and by the melting point of a semicarbazone derivative. It is not clear whether the homogeneity of this derivative was established.

[4] W. Hückel and K. Hartmann, *Ber.*, **70**, 959 (1937).

[5] W. Hückel, *Ber.*, **80**, 41 (1947).

[6] M. Ishidate, N. Inoue, and H. Fukushima, *Bull. soc. chem. Japan*, **17**, 491 (1942).

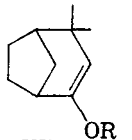
[7] Y. Matsubara, *Nippon Kagaku Zasshi*, **76**, 1088 (1955); *Chem. Abstr.*, **51**, 17827 (1957). Y. Matsubara and M. Morita, *Nippon Kagaku Zasshi*, **76**, 1101 (1955); *Chem. Abstr.*, **51**, 17831 (1957). Y. Matsubara, *Nippon Kagaku Zasshi*, **78**, 719, 723 (1957); *Chem. Abstr.*, **53**, 21716 (1959).

major reason for the discrepancies in the literature was that earlier investigators[1,6,7] had failed to demonstrate the homogeneity of their products; in our hands these products were shown to be mixtures. It is important also to note that the predominance of a ring expansion in the alkaline fusion of I has long been overlooked; it will be shown that "dicamphenyl ether,[9]" the major product from the alkaline fusion, is largely a mixture of ring expanded vinyl ethers.

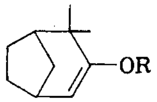
Our work began with a scrutiny of the products from the potassium hydroxide fusion of I.[1] The crude "Schmelzketon," isolated in 5–10% yield, contrary to the conclusions of the other investigators,[1,6,7] was shown by chromatography of its 2,4-dinitrophenylhydrazine derivative to be a mixture of ketones IIa, IIb[7,8] and aldehyde V in a ratio of approximately 8:20:1, respectively. In a single experiment the semicarbazone derivative of IIb was isolated directly from the "Schmelzketon." In all other instances mixtures of semicarbazone derivatives showing melting points concurring with those cited by Lipp[1] were obtained. It was further noted that the first crop in the preparation of the semicarbazone derivative was a mixture, whereas succeeding crops were largely IIb semicarbazone.

"Dicamphenyl ether," the *major* product from alkaline fusion of I, displayed an absorption maximum at 6.05 μ which corroborated the presence of a vinyl ether. "Dicamphenyl ether" was transformed into the 2,4-dinitrophenylhydrazine derivatives of its constituent carbonyl components and chromatographic analysis of the resulting derivatives demonstrated the presence of the dinitrophenylhydrazones of IIa, IIb, and V in a ratio of *ca.* 2:1:1. Consequently, "dicamphenyl ether," incorrectly assigned structure IV by Lipp,[1] can be best represented as a mixture of compounds VIIIa–VIIIc, *revealing that the alkaline fusion of I predominantly produces a unique ring expansion.*

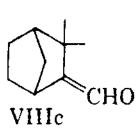
Attempts to separate the mixture of divinyl ethers into individual components were unsuccessful. Silica gel chromatography, for example, led to hydrolysis with the elution of aldehyde V contaminated with ketone IIb, followed by ketone IIa. A small amount of crystalline solid (IX), $C_{20}H_{30}O$, m.p. 92–94°, was isolated from the earliest fractions and appeared to be a vinyl ether since it displayed strong absorption at 6.02 μ. The fallacy of this assumption became apparent when IX failed to react, even after heating for forty hours, with Brady's reagent.[9] While the latter test also appears to eliminate the presence of a carbonyl group, independent evidence ruled otherwise. Lithium aluminum hydride reduction of IX afforded a solid whose infrared spectrum was free of absorption in the carbonyl region, but exhibited a weak, sharp maximum at 2.75 μ indicative of a hydroxyl group. The simple diagnostic test of converting this material with acetic anhydride–pyridine to an oil which displayed characteristic acetate absorption at 5.85 and 8.0 μ confirmed the presence of a hydroxyl group in the reduction product and, in turn, established the presence of a hindered carbonyl group in IX. The 6.02 μ band in the spectrum of IX demands that the carbonyl group be conjugated, a conclusion supported by the appearance of maximal absorption at 250 mμ, ε, 1010[10] in the ultraviolet.



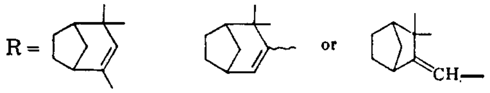
VIIIa

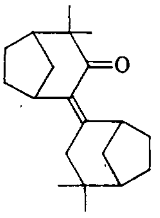


VIIIb

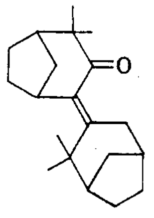


VIIIc

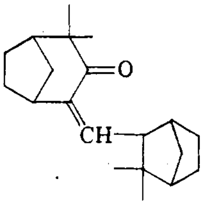




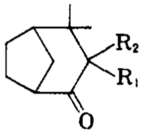
IXa



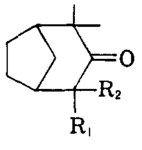
IXb



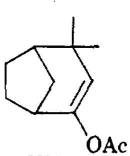
IXc



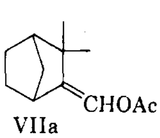
Xa. $R_1 = H$; $R_2 = Br$
XIa. $R_1 = R_2 = Br$



Xb. $R_1 = H$; $R_2 = Br$
XIb. $R_1 = R_2 = Br$



VII



VIIa

Application of these data, incorporating the probable genesis of IX from IIa, IIb, or V, leaves

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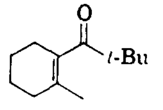
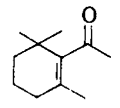
[8] Evidence for the correctness of these structural assignments will be found in succeeding paragraphs.

[9] O. L. Brady, *J. Chem. Soc.*, 756 (1931).

[10] It is instructive to note that the low intensity is in accord with the formulation of IX as a nonplanar α,β unsaturated ketone; *i.e.* ketones i (E. A. Braude and C. J. Timmons, *J. Chem. Soc.*, 3766 (1955)) and ii (H. B. Henbest and G. Woods, *J. Chem. Soc.*, 1150 (1952)) display absorption at 239 and 243 mμ, ε 1300 and 1400, respectively. Models of IXa suggest that noncoplanarity is probably a



i



ii

consequence of the chair conformation of the six-membered ring which introduces an angle of *ca.* 60° between the planes of the double bonds.

structures IXa–IXc to consider. A careful survey of the NMR spectrum of IX revealed signals at 245, 268, 272, 295 and 315 c.p.s. whose area, taking the first three signals together, varied in a ratio of 3:1:1. The absence of peaks characteristic of vinyl hydrogen atoms eliminated structure IXc. A decision between the remaining structures was achieved by ozonolysis of IX; ketone IIa was isolated as its 2,4-dinitrophenylhydrazone derivative, thereby establishing IXa as a minor product from the alkaline fusion of I.

Since "dicamphenyl ether" is a mixture of VIIIa–VIIIc its conversion to a ring expanded "Oxidationketon"[1] on treatment with chromium trioxide is not surprising since the acid present in this reaction would be expected to hydrolyze the vinyl ethers giving ketones IIa and IIb, which would be largely unaltered, and aldehyde V, which would be oxidized further. Accordingly *the "Oxidationketon" was shown to be a mixture of ketones IIa, IIb, and carbocamphenilone (VI), with ketone IIa predominating.* The acidic portion from the chromic acid oxidation yielded, after chromatoggraphy, a considerable amount of camphenic acid (III).

Attention was next directed to a re-examination of the oxidation of camphene with lead tetraacetate. The enol acetate (VII) (strong band at λ_{max} 5.73 μ) produced as described by Hückel[5] was transformed by basic hydrolysis and purification *via* the semicarbazone derivative to ketone IIa. While this ketone IIa was homogenous,[7] the enol acetate (VII) from which it was derived contained a small amount of enol acetate (VIIa) as shown by treatment with Brady's reagent[9]; the dinitrophenylhydrazones of IIa and V were isolated by chromatography on silica gel.

In order to characterize further ketones IIa and IIb, the corresponding mono- and dibromoderivatives were prepared. Monobromination of pure IIa afforded monobromo ketone Xa, m.p. 69–70°,[7] whereas monobromination of the "Schmelzketon" afforded a mixture, easily separated by chromatography, of monobromo ketone Xa and monobromoketone Xb, m.p. 109–111°.

Monobromo ketones Xa and Xb were recovered following short treatment with bromine at 0°; however, with excess bromine at room temperature IIa or Xa and IIb or Xb gave dibromo ketone XIa, m.p. 198–199°, and dibromo ketone XIb, m.p. 48–50°, respectively.

Treatment of the "Oxidationketon" with excess bromine for a short period at 0° gave a complex mixture of products from which camphenic acid (III) was separated owing to its insolubility in petroleum ether. Chromatography of the neutral products afforded dibromo ketone XIb, monobromo ketone Xa, and carbocamphenilone (VI).

Justification for the structural assignments for the ketones produced by alkaline fusion of I and lead tetraacetate oxidation of camphene constitutes a challenging problem which Matsubara[7] has solved by a study of their oxidation with peracids. Our investigations, completed prior to the appearance of the abstract of Matsubara's latest publication,[7] also utilized the Baeyer-Villiger oxidation and in addition, was concerned with a study of the NMR spectra of these ketones and their bromo derivatives.

In the sequel ketone A will refer to the ketone produced by lead tetraacetate oxidation of camphene, which, in turn, is identical with the major component of the "Oxidationketon." Ketone B will designate the main constituent of the "Schmelzketon."

It is suggested that the introduction of a bromine atom *alpha* to a cyclic ketone may serve as an excellent technique for determining the location of neighboring methyl groups by reason of the electronegativity and large steric size of the bromine atom, as well as the possibility of local anisotropy of the C—Br bond,[11] producing affects on neighboring hydrogen atoms which are readily detected using NMR spectroscopy.

Inspection of molecular models of the two possible monobromo ketones Xb suggests that the equatorial isomer is thermodynamically favored; consequently, the bromine atom can not influence the neighboring *gem*-methyl group and accordingly, should have no affect on their chemical shifts in the NMR. An axial-axial bromine-methyl interaction is unavoidable in dibromo ketone XIb, and, therefore, the signal of one methyl group should be found at lower applied magnetic field, that is, shifted to the left. With monobromo ketone Xa, on the other hand, the bromine atom, regardless of its configuration, contacts the adjacent *gem*-methyl group and should produce a shift of at least one methyl signal, whereas, both methyl signals should be shifted to the left in dibromo ketone XIa.

Inspection of the NMR spectra of these compounds, presented in Table I, shows that the chemical shifts for the methyl groups in ketone B, 303 and 310 c.p.s., and monobromo ketone B, 300 and 307 c.p.s., are essentially identical, whereas in dibromo ketone B, 282 and 303 c.p.s., a single methyl peak is displaced to the left, suggesting, therefore, that ketone B has structure IIb.

On proceeding from ketone A, 309 and 312 c.p.s., to monobromo ketone A, 297 and 310 c.p.s., and then to dibromo ketone A, 285 and 292 c.p.s., first one methyl signal and then both methyl peaks shift to lower applied magnetic field, strongly supporting the identity of ketone A with structure IIa.

Additional chemical evidence for these assignments was provided by an examination of the

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[11] H. M. McConnell, *J. Chem. Phys.*, 27, 226 (1957); J. A. Pople, W. G. Schneider, and H. J. Bernstein, *High-resolution Nuclear Magnetic Resonance*, McGraw-Hill Book Company, Inc., New York, 1959, p. 176.

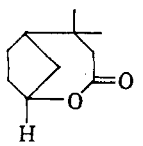
TABLE I

NMR SPECTRA OF KETONES A AND B AND RELATED COMPOUNDS[a]

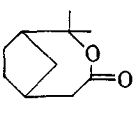
Compound	Shifts in c.p.s.[b]
Ketone A (IIa)	222, 240, 255, 263, 309, 312
Monobromo ketone A (Xa)	118, 203, 258, 263, 297, 310
Dibromo ketone A (XIa)	198, 250, 285, 292
Ketone B (IIb)	231, 248, 277, 303, 310
Monobromo ketone B (Xb)	94, 213, 277, 300, 307
Dibromo ketone B (XIb)	190,[c] 265, 282, 303
Carbocamphenilone (VI)	203, 260, 299
Camphene	104,[d] 258, 275, 309
ω-Bromocamphene (I)	37, 176, 236, 258, 275, 295
Isobornyl bromide	138,[e] 240, 294, 283, 300, 307, 315
2,10-Dibromocamphane	125,[e] 164,[e] 234, 250, 296, 314

[a] The spectrometer employed for these measurements was a Varian Associates V-4300-B high resolution spectrometer with associated 12" electromagnet system equipped with a super stabilizer. [b] All spectra were obtained at 56.4 megacycles/second in a magnetic field of approximately 13,300 gauss. The compounds were studied in *ca.* 10% solutions of carbon tetrachloride. The shift values of the *sharp bands* in the spectra were measured by the audiofrequency side band method in cycles per second using a sealed benzene capillary as an external reference. The shift values are reproducible to 1–2 c.p.s. [c] Center of a triplet. [d] Center of a doublet. [e] A quartet.

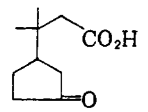
products from the Baeyer-Villiger oxidation of ketone A.[7] In view of the well established selectivity and stereospecificity of the Baeyer-Villiger oxidation,[12] ketones IIa and IIb should be transformed into lactones XIII and XIV, respectively. An exclusive feature of lactone XIII, which can be easily detected using NMR spectroscopy, is the H—C—O hydrogen atom at the bridgehead.



XIII



XIV



XV

Treatment of ketone A with pertifluoroacetic acid[13] afforded a product whose NMR spectrum displayed a weak quartet centered at 110 c.p.s. characteristic of a proton, *alpha* to a carbon atom bound to an electronegative oxygen atom, which is spin-spin coupled with adjacent methylene groups.[14] The area enclosed by this signal suggested that the lactone XIII constituted *ca.* 50% of the crude product. Unaltered ketone A, isolated in *ca.* 50% yield following alkaline hydrolysis of the crude product, accounted for the remainder of the mixture. The acidic fraction from alkaline hydrolysis, without further purification, was oxidized with chromic acid in acetone[15] and yielded a keto acid, presumably XV,[16] isolated as its 2,4-dinitrophenylhydrazone derivative. Incorporating the NMR data above with the formation of keto acid XV secures structure XIII for the lactone and structure IIa for ketone A.

After determining the nature of the products produced by alkaline fusion of I, the mechanism by which these substances were produced remained to be considered. Prior to the realization that the alkaline fusion predominantly involved a ring expansion it appeared remotely possible that the "Schmelzketon" may have arisen from a ring expanded impurity in bromide I. Consequently, the preparation of I was examined carefully.

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[12] R. B. Turner, *J. Am. Chem. Soc.*, **72**, 878 (1950); W. von E. Doering and L. Speers, *J. Am. Chem. Soc.*, **72**, 5515 (1950); K. Mislow and J. Brenner, *J. Am. Chem. Soc.*, **75**, 2318 (1953).

[13] W. D. Emmons and G. B. Lucas, *J. Am. Chem. Soc.*, **77**, 2287 (1955); W. F. Sager and A. Duckworth, *J. Am. Chem. Soc.*, **77**, 188 (1955).

[14] J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958).

[15] K. Bowden, I. M. Heibron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[16] This keto acid is probably identical with the keto acid Matsubara[7] isolated from pervanadic acid oxidation of ketone A.

[17] (a) O. Wallach, *Ann.*, **230**, 235 (1885); **357**, 79 (1907); (b) A. Reychler, *Ber.*, **29**, 900 (1896); (c) E. Junger and A. Klages, *Ber.*, **29**, 544 (1896); (d) Godlewski, *Ber.*, **32**, 2303 (1899); (e) F. W. Semmler, *Ber.*, **33**, 3425 (1900); (f) G. Langlois, *Ann. chim.*, [9] **12**, 265 (1919).

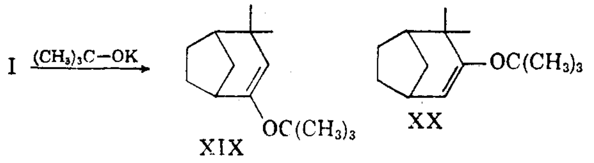
[18] While the camphane skeleton has been adequately established in XVI,[17e] the position of the bromine atoms has never been demonstrated unequivocally. An insight into the location of the halogen atoms in XVI was gained by comparing its NMR spectrum with the spectra of isobornyl bromide and α,α'-dibromocamphor (W. D. Kumler, J. N. Shoolery, and F. V. Brutcher, *J. Am. Chem. Soc.*, **80**, 2533 (1958)). α,α'-Dibromocamphor exhibits peaks at 293, 299, and 306 c.p.s. assigned, respectively, to the *gem*-methyl group which contacts the bromine atom, the methyl group at C_1, and the *gem*-methyl group which does not contact the halogen atom. The corresponding peaks in isobornyl bromide, see Table I, fall at 300, 307, and 315 c.p.s., a uniform shift to the right, for each signal, of *ca.* 7–9 c.p.s. which can be attributed to the absence of the magnetic anisotropy of the carbonyl group. Assuming that the interaction of the bromine atom with the *gem*-methyl group is identical in both compounds, the peaks at 300 and 315 c.p.s., in isobornyl bromide can be assigned to the *gem*-methyl group, whereas the signal at 306 c.p.s. can be attributed to the methyl group at C_1. The methyl groups in XVI are found at 296 and 314 c.p.s. suggesting that the methyl group at C_1 is absent, thus favoring its formulation as 2,10-dibromocamphene.

Another extremely interesting feature of the spectrum of XVI is the unsymmetrical quartet centered at 164 c.p.s. The area enclosed by this quartet is double that of the quartet at 125 c.p.s. which is attributed to the proton at C_2 spin-spin coupled with an adjacent methylene group. The peaks at 164 c.p.s. must be assigned to the two protons at C_{10} which, in addition to displaying the chemical shift of the bromine atom, are nonequivalent and thus, spin-spin coupled with one another. The nonequivalence of these protons is possible if rotation about the C_1C_{10} bond is hindered, a conclusion supported by an examination of molecular models of XVI [*cf.* P. M. Nair and J. D. Roberts, *J. Am. Chem. Soc.*, **79**, 4565 (1957)].

Addition of bromine to camphene,[1,17] in ether solution, afforded, in addition to a lower boiling fraction, 2,10-dibromocamphane (XVI)[18] in 72% yield. Vapor phase chromatography and the infrared spectrum of the lower boiling fraction suggested it was composed of I and isobornyl bromide.

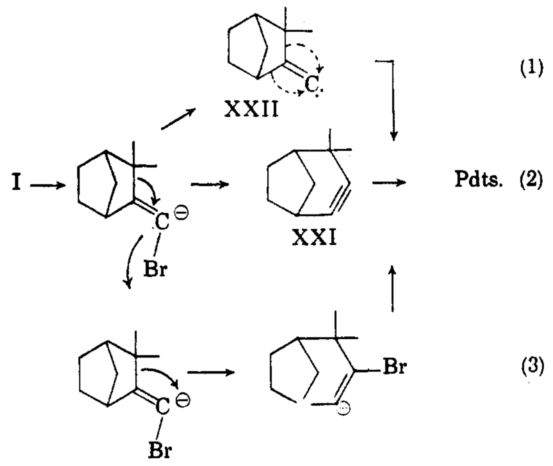
Pure XVI was smoothly converted into ω-bromocamphene (I) by digestion with dimethylaniline at 180°. The I obtained in this manner was a colorless liquid, remaining colorless after prolonged storage, which crystallized on cooling f.p. −36 to −38°, and displayed a single band on vapor phase chromotography. With the homogeneity and structure of I[17e,f] established it was concluded that the ring expansion could not have occurred during the addition of bromine to camphene or the subsequent dehydrobromination of XVI.

In view of the vigorous nature of the potassium hydroxide fusion it became desirable to determine whether the ring expansion could be initiated by other strong bases. Heating I with potassium *t*-butoxide in toluene gave, in essentially quantitative yield, a mixture of enol ethers (XIX) and XX, in a ratio of approximately 2:1 as shown by treatment with Brady's reagent[9] and chromatography of the resulting derivatives on silica gel. Only a trace of the dinitrophenylhydrazone of V was found, demonstrating that potassium *t*-butoxide exhibits greater specificity in promoting ring expansion than does potassium hydroxide.



Several expressions, Equations 1–3, appear capable of accounting for the unusual ring expansion produced by the reaction of strong bases with I. Equation 3 appears to be the least attractive since examples of carbanionic migration of alkyl groups are unknown.[19] Equations 1 and 2, on the other hand, are analogous to mechanisms proposed for the base initiated formation of tolanes from 1,1-diaryl-2-bromoethylenes,[20] however, examples of alkyl migration in the latter reaction are unknown.

In order to establish the feasibility of an alkyl group migration and, in turn, provide evidence for the intermediary existence of endo-camphyne (XXI),[21] a preliminary experiment was conducted with a simpler system. Heating 1,2-dibromo-2-methylpropane with two equivalents of potassium *t*-butoxide in *p*-cymene afforded 2-butyne contaminated with a small amount of 1,2-butadiene.



The formation of 2-butyne establishes the possibility of an alkyl group migration in this type of rearrangement[22] and suggests that endocamphyne (XXI)[23] is a likely intermediate in the rearrangement of I.

Although Bothner-By[24] has excluded a carbene intermediate in the tolane synthesis by demonstrating the migration of an aryl group *trans* to the departing bromine atom, the lack of data correlating the base induced ring expansion of I with the formation of tolanes from 1,1-diaryl-2-bromoethylenes makes a choice between carbene XXII and the concerted rearrangement, equation 2, impossible at the present time. Further work directed toward extending and elucidating the proper sequence of these rearrangements is planned.

EXPERIMENTAL[25]

Addition of bromine to camphene. To a stirred and cooled solution of 385 g. (2.85 moles) of camphene in 500 ml. of dry ether was slowly added 453 g. (2.83 moles) of bromine. The ether was removed and the residue distilled rapidly *in vacuo* affording the following fractions: (*a*) camphene, b.p. 39–70° (1.0–5.0 mm.), which was removed from the system before proceeding further; (*b*) 220 g. of a yellowish liquid, b.p. 79–100° (0.7–2.4 mm.); and (*c*) 519 g. of a liquid which solidified immediately, b.p. 116–134° (1.4–3.8 mm.).

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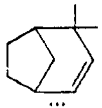
(19) H. E. Zimmerman and F. J. Smentowski, *J. Am. Chem. Soc.*, 79, 5455 (1957).

(20) T. L. Jacobs, *Org. Reactions*, 5, 40 (1949).

(21) The name endocamphyne is suggested by analogy to the use of endocamphene for compound iii.[1]



iii

(22) D. Y. Curtin and J. W. Crump, *J. Am. Chem. Soc.*, 80, 1922 (1958).

(23) Direct evidence for cyclohexyne as a reaction intermediate has been provided by F. Scardiglia and J. D. Roberts, *Tetrahedron*, 1, 343 (1957). A related cyclooctyne intermediate has been proposed by D. Y. Curtin and W. H. Richardson, *J. Am. Chem. Soc.*, 81, 4719 (1959).

(24) A. A. Bothner-By, *J. Am. Chem. Soc.*, 77, 3293 (1955).

(25) All boiling and melting points are uncorrected. Infrared spectra were determined by Mrs. M. Dilling on a Perkin-Elmer double beam spectrometer, model 21. The microanalyses were performed by Dr. C. S. Yeh and Mrs. I. Groton.

Recrystallization of a portion of *fraction c* from ethanol gave white crystals, m.p. 90–91°. Reported for 2,10-dibromocamphane (XVI), m.p. 90–91°.[19a–f]

Redistillation of *fraction b* afforded, after a forerun of 20 g. of yellowish liquid, b.p. 69–84° (5.5 mm.), 130 g. of a mixture of I and isobornyl bromide, b.p. 88–89.5° (5.5 mm.), n_D^{18} 1.5183. The still residue solidified on standing and yielded an additional 20 g. of XVI.

Atmospheric distillations of purified *fraction b* led to a copious evolution of hydrogen bromide and a distillate whose infrared spectrum was identical with that of camphene.

ω-Bromocamphene (I). Pure XVI, 25 g., was digested at 180° with 100 ml. of dimethylaniline. The resulting black solution was taken up in ether and washed repeatedly with water and 1:1 hydrochloric acid until the washings were distinctly acidic. After drying, the ether was removed and distillation gave 15 g. of I, b.p. 87–88° (5 mm.), n_D^{21} 1.5221, f.p. −36° to −38°.

Using crude XVI there was obtained a colorless liquid, which gradually turned yellow and then orange on standing, b.p. 87–90° (5 mm.), n_D^{18} 1.5212.

A solution of 0.4 g. of I in 10 ml. of acetic anhydride was ozonized at −70° for 1 hr. and then the resulting ozonide was decomposed by stirring with a slurry of zinc dust and water. Brady's reagent[9] was added to the resulting solution. Extraction with ether–petroleum ether (b.p. 35–37°) afforded a yellow-orange solid showing m.p. 155–157° when recrystallized from ethanol. Reported for camphenilone 2,4-dinitrophenylhydrazone, m.p. 152°,[26] 159–160°,[27] 161°.[28]

Fusion of I *with potassium hydroxide*. Potassium hydroxide,[29] 18 g., was heated in a nickel crucible for 20 min. using a bunsen burner. The molten alkali was poured into a round bottom flask and then 15 g. of I was added cautiously. The resulting mixture, with intermittent swirling, was heated with a burner until the organic layer became very viscous (10–20 min.). Several fusions were combined and steam distilled affording a distillate containing the "Schmelzketon" and a distilland composed of "dicamphenyl ether."

The "Schmelzketon." A portion of the steam-volatile liquid produced by alkaline fusion of I, *ca.* 1.9 g. from 15 g. of I, was treated with Brady's reagent[9] affording an orange solid, m.p. 118–120°. This derivative was chromatographed on a column prepared using a slurry of 35 g. of silica gel (Davison, 200 mesh) in chloroform. The adsorbant was washed with 100 ml. of chloroform and 100 ml. of petroleum ether (b.p. 35–37°) and then 203 mg. of the dinitrophenylhydrazone mixture in 10 ml. of benzene was placed on the column. The following fractions were collected using 4% diethyl ether in petroleum ether as an eluent: (*a*) 211 mg. of the yellow 2,4-dinitrophenylhydrazone of IIb, m.p. 117.5–119.5°; (*b*) 11 mg. of the yellow 2,4-dinitrophenylhydrazone of V, m.p. 137–142°; and (*c*) 81 mg. of the orange 2,4-dinitrophenylhydrazone of IIa, m.p. 134–136°.

The 2,4-dinitrophenylhydrazone derivative of ketone IIb showed m.p. 117.5–119.5° when recrystallized from ethanol.

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07. Found: C, 58.00; H, 6.32.

The 2,4-dinitrophenylhydrazone derivative of aldehyde V crystallized in several polymorphic forms, *i.e.*, long stout rods, m.p. 150.5–151.5°; fluffy needles, m.p. 150.5–153.5°, which on standing with ethanol transformed into sharp, fine needles, m.p. 159–161°. The NMR spectrum of this derivative, using a 10% solution in methylene chloride, displayed a peak at −144 c.p.s., relative to water, characteristic of a —CH=N— proton.[30]

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07. Found: C, 57.75; H, 6.32.

The 2,4-dinitrophenylhydrazone derivative of ketone IIa displayed m.p. 137.5–139° when recrystallized from ethanol.

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07. Found: C, 57.96; H, 6.41.

Ketone IIb. The "Schmelzketon" was kept overnight with an aqueous-methanol solution of semicarbazide hydrochloride and sodium acetate and then water and petroleum ether (b.p. 35–37°) were added. The solid which collected at the interphase was separated and showed m.p. 200–203°. A second and a third crop, m.p. 210–213° and 211–214°, were collected after standing 1 week. The latter crops were recrystallized from methanol affording a white solid, m.p. 224–227°, depressed to m.p. 203–208° when mixed with the semicarbazone derivative of ketone IIa.

A mixture of the purified semicarbazone derivative and aqueous oxalic acid was steam distilled affording crude ketone IIb, m.p. 33–35°. Pure IIb, obtained by sublimation *in vacuo*, showed m.p. 40.5–42°.

Divinylethers VIIIa–VIIIc. The distilland from steam distillation of the products from alkaline fusion of I was taken up in ether, the ether was removed, and distillation afforded a viscous, light yellow oil, b.p. 122–128° (0.35 mm.).

A portion, 301 mg., of the orange solid, m.p. 116–119°, which was obtained by treatment of the divinyl ether mixture with Brady's reagent[9] was chromatographed on a silica gel column and afforded the following fractions: (*a*) 86 mg. of the 2,4-dinitrophenylhydrazone of IIb, m.p. 116.5–119° from ethanol; (*b*) 80 mg. of the 2,4-dinitrophenylhydrazone of V, m.p. 151–153° from ethanol; and (*c*) 160 mg. of the 2,4-dinitrophenylhydrazone of IIa, m.p. 137–138.5° from ethanol.

The "Oxidationketon." Three grams of VIIIa–VIIIc and 2.0 g. of chromium trioxide in 20 ml. of acetic acid were heated on a steam bath for 1 hr. Potassium carbonate was added to the green solution and the mixture was steam distilled. The distillate was extracted with ether affording a yellow oil. A portion of this product was converted to a 2,4-dinitrophenylhydrazone with Brady's reagent. A portion, 196 mg., of the resulting solid was chromatographed on silica gel and gave the following fractions: (*a*) 45 mg. of the 2,4-dinitrophenylhydrazone of IIb, m.p. 118–119.5° from ethanol; (*b*) 88 mg. of the 2,4-dinitrophenylhydrazone of IIa and the mono-2,4-dinitrophenylhydrazone of diketone VI; and (*d*) 12.0 mg. of the mono-2,4-dinitrophenylhydrazone of VI, m.p. 183–187°.

The mono 2,4-dinitrophenylhydrazone derivative of diketone VI, m.p. 188.5–190°, crystallized in long, yellow needles from ethanol.

Anal. Calcd. for $C_{16}H_{18}N_4O_5$: C, 55.48; H, 5.24; N, 16.18. Found: C, 55.58; H, 5.76; N, 16.48.

The acidic fraction recovered from the chromic acid oxidation was dissolved in chloroform and placed on a column containing 125 g. of silica gel. Elution with chloroform gave a trace of solid, whereas elution with 10% methanol in chloroform afforded 600 mg. of a brown semisolid. The latter solid was dissolved in boiling water; the water was decanted from an insoluble brown oil and cooled yielding 250 mg. of white crystals, m.p. 134–136°, whose infrared spectrum was identical with that of camphenic acid (III).

Unsaturated ketone IX. A solution of 2 g. of the vinyl ether mixture VIIIa–VIIIc in petroleum ether (b.p. 00–00°) was placed on a column containing 135 g. of silica gel. Elution with 2% methylene chloride–benzene gave 300 mg. of a white solid (IX) m.p. 71–76°. Succeeding fractions using 1:1 methylene chloride–benzene and then methylene chloride displayed distinct aldehyde bands at 3.7 μ and were composed of aldehyde V and ketone IIb. Elution with 20% methanol-chloroform gave 1.0 g. of a brown oil whose infrared spectrum was identical with that of ketone IIa.

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(26) G. Clement, *Compt. rend.*, **232**, 2106 (1951).

(27) D. P. Archer and W. J. Hickinbottom, *J. Chem. Soc.*, 4197 (1954).

(28) W. J. Hickinbottom and D. G. M. Wood, *J. Chem. Soc.*, 1906 (1953).

(29) It is instructive to note that reagent potassium hydroxide, 87% by weight, had no affect on I.

(30) D. Y. Curtin, J. A. Gourse, W. H. Richardson, and K. L. Rinehart, *J. Org. Chem.*, **24**, 93 (1959).

IX was recrystallized three times from petroleum ether at $-70°$ and showed m.p. 92–94°, $\lambda_{max}^{isooctane}$ 250 mμ, ε 1010.

Anal. Calcd. for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.85; H, 10.51.

Lithium aluminum hydride reduction of 21.3 mg. of IX gave, after sublimation, a white solid, m.p. 72–98°. This solid was kept in acetic anhydride–pyridine overnight and then the volatile reactants were removed and the residue sublimed at 0.3 mm. and 50°. The resulting colorless oil displayed strong infrared bands at 5.85 and 8.0 μ characteristic of an acetate group.

Ozonolysis of IX. Ozone was bubbled through a Dry Ice–trichloroethylene cooled solution of 21 mg. of IX in acetic anhydride until the solution became blue. The ozonide was decomposed with a slurry of zinc and water, the zinc was removed by filtration, and Brady's reagent was added to the filtrate. Extraction with ether–petroleum ether afforded a solid which was chromatographed on 5 g. of silica gel affording several fractions comprised of yellow-orange crystals, m.p. 128–130°. The melting point was raised to 136–138° by recrystallization from ethanol and was undepressed when mixed with the 2,4-dinitrophenylhydrazone derivative of ketone IIa.

Oxidation of camphene with lead tetraacetate.[5] A solution of 33 g. (0.24 mole) of camphene and 100 g. (0.23 mole) of lead tetraacetate in 400 ml. of acetic acid was kept at 80–90° for 5 hr. Water and ether were added, the layers were separated, and the ether layer was washed with water and aqueous sodium carbonate until free of acid. The ether solution was dried, the ether removed, and distillation at 5 mm. gave, after a forerun of camphene, 22 g. of VII and VIIa, b.p. 90–100°, n_D^{20} 1.4761, λ_{max} 5.73 and 8.25 μ.

Ketone IIa. A solution of 10 g. of enol acetates VII and VIIa and 2.3 g. of sodium hydroxide in methanol was kept at room temperature overnight and then an aqueous solution containing 6 g. of semicarbazide hydrochloride and 8 g. of sodium acetate was added. The semicarbazone derivative, 10 g., which began to separate immediately was collected after standing overnight. Recrystallization from methanol afforded the semicarbazone derivative of ketone IIa, m.p. 219–221°. A second crop showed m.p. 218–220°.

Steam distillation of a suspension of 10 g. of the semicarbazone derivative in water containing 25 g. of oxalic acid gave 5 g. of ketone IIa, b.p. 85–87° (6 mm.), which solidified immediately, m.p. 32–35°.

The *2,4-dinitrophenylhydrazone* of ketone IIa crystallized as fine yellow-orange needles from ethanol, m.p. 137.5–139°.

Treatment of 1.0 g. of the enol acetate with Brady's reagent gave 1.59 g. of an orange solid, m.p. 114–119°. Chromatography of 203 mg. of this solid on silica gel gave the following fractions: (*a*) 12.4 mg. of crude 2,4-dinitrophenylhydrazone of V; (*b*) 8.0 mg. of relatively pure dinitrophenylhydrazone of V, m.p. 151–154°; (*c*) 14.1 mg. of a mixture of the 2,4-dinitrophenylhydrazones of V and IIa; and (*d*) 120 mg. of the 2,4-dinitrophenylhydrazone of IIa, yellow-orange needles from ethanol, m.p. 136–138°.

Baeyer-Villiger oxidation of ketone IIa. To a magnetically stirred and cooled mixture of 0.4 g. of ketone IIa, 25 ml. of methylene chloride and 5.0 g. of anhydrous sodium hydrogen phosphate was slowly added a methylene chloride solution containing 0.08 ml. of 99% hydrogen peroxide and 0.5 ml. of trifluoroacetic anhydride. After stirring for 30 min. the mixture was filtered, washed with water and aqueous sodium carbonate, and the methylene chloride removed *in vacuo*. The resulting oil displayed a strong carbonyl band at 5.84 μ in addition to a weak band at 5.65 μ. Attempts to purify this product by distillation gave an oil whose infrared spectrum in the finger-print region was identical with that of the crude product, but whose carbonyl region was markedly altered.

The crude oxidation product was kept in methanol with 200 mg. of potassium hydroxide. Water and ether were added, ether layer was separated, dried, and the ether removed affording 190 mg. of an oil whose infrared spectrum was identical with that of ketone IIa.

The alkaline solution was acidified and extracted with methylene chloride. The methylene chloride extract was evaporated and the residue dissolved in pure acetone. Jones reagent[15] was added to the cooled solution until the color remained a definite orange. After 15 min. a few drops of isopropyl alcohol were added and the mixture was filtered. The filtrate was washed with water and then the solvent was removed. The residue was taken up in ethanol and treated with Brady's reagent[9] affording 290 mg. of the yellow 2,4-dinitrophenylhydrazone of XV, m.p. 193–194° after recrystallization from benzene.

Anal. Calcd. for $C_{17}H_{20}N_4O_6$: C, 52.74; H, 5.53. Found: C, 53.05; H, 5.77.

Monobromo ketone Xa. To a cold solution of ketone IIa in carbon tetrachloride was added 1.2 g. of bromine. The color of bromine was immediately discharged and hydrogen bromide was evolved. The solvent was removed under a stream of nitrogen. The residue was taken up in petroleum ether (b.p. 35–37°) and cooled to $-70°$ affording large, white blocks, m.p. 66.5–68°, which after several recrystallizations from petroleum ether at $-70°$ and then sublimation *in vacuo* showed m.p. 69–70°; reported,[7] m.p. 72°.

Anal. Calcd. for $C_{10}H_{15}BrO$: C, 51.96; H, 6.54. Found: C, 51.96; H, 6.27.

Dibromo ketone XIa. A carbon tetrachloride solution containing 89 mg. of ketone IIa and 0.5 g. of bromine was kept at room temperature overnight. The solvent was removed and the residue recrystallized from petroleum ether at $-70°$ and then sublimed at 70° and 0.3 mm. to yield 79 mg. of a white solid, m.p. 198–199° (subliming at 90–100°, block) m.p. 186–188° (sealed capillary).

Anal. Calcd. for $C_{10}H_{14}Br_2O$: C, 38.74; H, 4.55. Found: C, 38.76; H, 4.87.

Addition of excess bromine to monobromo ketone Xa, 45 mg., afforded 20.7 mg. of dibromo ketone XIa.

Monobromination of the "Schmelzketon"; monobromo ketone Xb. The crude "Schmelzketon," 730 mg., and 700 mg. of bromine in carbon tetrachloride was kept for 15 min. at 0°. The solvent was removed and a petroleum ether solution of the residue was placed on a column containing 20 g. of alumina. Elution with 1% ether–petroleum ether gave crude monobromo ketone Xb, m.p. 102–105°, raised to 109.5–112° by recrystallization from petroleum ether at $-70°$ and sublimation (reported,[1,7] m.p. 112–113°).[7] Elution with 20% ether–petroleum ether yielded monobromo ketone Xa, m.p. 67–68°.

Dibromo ketone XIb. A solution of 18.6 mg. of monobromo ketone Xb and 400 mg. of bromine was allowed to stand at room temperature overnight. The resulting oil afforded 12 mg. of white buttons, m.p. 49.5–50.5° from petroleum ether at $-70°$.

Anal. Calcd. for $C_{10}H_{14}Br_2O$: C, 38.74; H, 4.55. Found: C, 38.74; H, 4.43.

Bromination of the "Oxidationketon." A solution of 0.84 g. of the crude "Oxidationketon" and 1.2 g. of bromine in carbon tetrachloride was kept at 0° for 15 min. and then the solvent was removed under a stream of nitrogen. The residue was taken up in petroleum ether, whereupon a white solid precipitated, m.p. 131–133°, raised to 137–139.5° from water and undepressed when mixed with an authentic sample of camphenic acid.[31]

After removing the camphenic acid, the petroleum ether solution was placed on a column containing 20 g. of alumina and elution afforded the following fractions: (*a*) 77 mg. of a slowly crystallizing oil using 5% ether–petroleum ether; (*b*) 44 mg. of a white solid, m.p. 64–67° employing 1:1 ether–petroleum ether; (*c*) 101 mg. of a yellow oil with 10% methanol-chloroform.

Fraction a afforded white buttons from petroleum ether

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(31) O. Aschan, *Ann.*, 383, 52 (1911).

at −70°, m.p. 48–50°. This melting point was not depressed when mixed with dibromo ketone XIb.

Recrystallization of *fraction b* from petroleum ether at −70° gave monobromo ketone Xa, m.p. 67–69°.

Fraction c, after recrystallization from petroleum ether and sublimation *in vacuo* yielded yellow crystals, m.p. 50–53°. Reported for carbocamphenilone (VI), m.p. 58–59°,[32] 56–59°.[4]

The reaction of I *with potassium t-butoxide.* Potassium *t*-butoxide, 8.2 g., was added to 350 ml. of toluene and 100 ml. of toluene was removed by distillation. Compound I, 7.4 g., was added slowly to the resulting clear solution, a precipitate formed immediately. After heating for 4 hr., the mixture was allowed to cool and was filtered. The toluene solution was washed with water and then the toluene was removed. Distillation afforded 7.0 g. of XIX and XX, b.p. 46.5–47° (0.3 mm.), n_D^{20} 1.4730, λ_{max} 6.05 μ.

Anal. Calcd. for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.39; H, 11.34.

One gram of the enol ether mixture was treated with Brady's reagent[9] affording 1.58 g. of an orange solid, m.p. 125–127°. A portion of this solid, 229 mg., was chromatographed on silica gel and afforded the following fractions: (*a*) 57.2 mg. of the 2,4-dinitrophenylhydrazone of ketone IIb, m.p. 117–119° from ethanol; (*b*) 5.0 mg. of the 2,4-dinitrophenylhydrazone of aldehyde V; and (*c*) 125.5 mg. of the 2,4-dinitrophenylhydrazone of ketone IIa, m.p. 136–138° from ethanol.

2-Butyne. To a solution of 19.5 g. of potassium *t*-butoxide, dried at 170° *in vacuo*, in 150 ml. of *p*-cymene heated to 160° was added 18.5 g. of 1,2-dibromo-2-methylpropane at such a rate that the exothermic reaction which ensued did not cause *t*-butyl alcohol to distill from the system. A volatile product, 3 g., crystallizing as long white needles, was collected in a Dry Ice–trichloroethylene cooled trap. There followed the distillation of a colorless liquid, b.p. 80–82°, whose infrared spectrum was identical with that of *t*-butyl alcohol. The infrared spectrum of the volatile product, in a gas cell, displayed all the maxima characteristic of 2-butyne. In addition, a weak band at 5.10 μ and a strong band at 11.20 μ suggested the presence of a small amount of 1,2-butadiene.

Addition of bromine to the volatile product afforded a white solid, m.p. 228–230° from petroleum ether. Reported for 2,2,3,3-tetrabromobutane, m.p. 230°,[33] 237°.[34]

Acknowledgment. This work was supported in part by a grant from the Purdue Research Foundation. The author is deeply indebted to Mr. William E. Baitinger for determining the NMR spectra.

LAFAYETTE, IND.

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(32) S. V. Hintikka, *Ber.*, **47**, 512 (1914).

(33) A. Faworsky, *J. prakt. Chem.*, [2] **42**, 145 (1890).

(34) W. Dilthey, *Ber.*, **34**, 2119 (1901).

[CONTRIBUTION FROM THE DEPARTAMENTO DE QUÍMICA, FACULDADE DE FILOSOFIA, CIENCIAS E LETRAS, UNIVERSIDADE DE SÃO PAULO]

Synthesis of 6,8-Diphenoxyoctanoic Acid

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6,8-Diphenoxyoctanoic acid has been synthesized from the γ-butyrolactone by two different routes.

In our studies of homologation of the fatty acids chain[1a,1b] we were looking for substituting groups would emerge unaltered from the intermediate reactions. Dibenzylthio groups proved to be unsuitable for this purpose, since it was observed that 3,5-dibenzylthiopentanoic acid failed to undergo the Kolbe reaction and that the use of 2,4-dibenzylthiobutyric acid afforded secondary products in several steps of the chain homologation reactions.[2] Phenoxy groups which are less reactive deserved our attention. This paper describes a synthesis of 6,8-diphenoxyoctanoic acid.

γ-Butyrolactone was converted into 2,4-dibromobutyric acid by the modified Plieninger procedure.[3,4]

In order to avoid the elimination of hydrogen bromide which would lead to the formation of α-bromo-γ-butyrolactone, the crude reaction product was converted immediately into the corresponding methyl ester by treatment with methanol saturated with hydrogen chloride. The reaction of methyl 2,4-dibromobutyrate with sodium phenolate yielded methyl 2,4-diphenoxybutyrate. This compound was reduced to 2,4-diphenoxybutanol with lithium aluminium hydride in cold tetrahydrofuran, which by treatment with phosphorus tribromide gave 1-bromo-2,4-diphenoxybutane. The condensation of the latter compound with methyl sodiomalonate, followed by alkaline hydrolysis and decarboxylation, produced 4,6-diphenoxyhexanoic acid, which was characterized by conversion into the *S*-benzylisothiouronium salt. When the ethyl sodiomalonate was used, difficulties were found during the purification of the intermediate diethyl ester.

4,6-Diphenoxyhexanoic acid was submitted to electrolysis in the presence of an excess of benzyl hydrogen succinate. The benzyl ester, then formed by crossed coupling, could be either separated from the methyl ester of the starting acid by fractional

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(1) (a) B. Wladislaw, *J. Chem. Soc.* 4227 (1955).

(1) (b) B. Wladislaw, *Chem. & Ind.* 263 (1957).

(2) This aspect of the problem is under study.

(3) H. Plieninger, *Ber.* **83**, 265 (1950).

(4) A. F. Wagner, E. Walton, C. H. Hoffman, L. H. Peterson, F. W. Holly, and K. Folkers, *J. Am. Chem. Soc.* **77**, 5140 (1955).