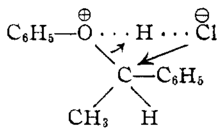
hydrogen halide in a non-polar solvent, the intermediate is an *oxonium ion-pair*. This may, as in the present instance, fall apart in such a way that halide ion becomes attached to the carbon atom undergoing C–O fission from the same side that the phenol molecule departs.



According to this view, the ion pair will give way to solvated ions if the solvent is made more polar. The stereochemical result may then be extensive racemization with some inversion due to shielding (S_N1); or, if the reagent is more nucleophilic and the involved carbon more susceptible to nucleophilic attack (for example, a primary carbon) the reaction course may be bimolecular nucleophilic displacement with inversion (S_N2).

These consequences are being tested by studying the influence of solvent, halide ion, kinetics and cleavage with other reagents.

Experimental

The ethers were synthesized as previously described,[3] and cleaved by passing dried (H_2SO_4) hydrogen chloride into the reaction mixture for a definite time at a given temperature. The mixture was then taken up in benzene or petroleum ether, and extracted with 20% alkali to remove the phenol produced. After drying the alkali-insoluble product over sodium sulfate and stripping the solvent, the residue was distilled *in vacuo*. All rotations are on the homogeneous material, l = 1 dm. at 25° unless otherwise indicated. The refractive index of the chloride samples was $n^{25}\mathrm{D}$ 1.525. The yield of cleavage products was excellent in all cases, and no uncleaved ether was recovered. Cleavage of racemic α-phenethyl phenyl ether proceeded smoothly in methanol and di-*n*-butyl ether, as well as in the solvents shown in Table I. The stereochemical results obtained with optically active ethers are summarized in the table.

TABLE I

STEREOCHEMISTRY OF CLEAVAGE OF α-PHENETHYL ARYL ETHERS BY HYDROGEN CHLORIDE

Aryl group	Wt. of ether, g.	$[\alpha]^{25}\mathrm{D}$ of ether	Time, min.	Temp., °C.	Solvent	$[\alpha]^{25}\mathrm{D}$ of α-phenethyl chloride
Phenyl	10	− 4.1°	60	50	Benzene, 39 g.	+ 0.40°
Phenyl	10	−16.58	10	50	None	+16.75
Mesityl	5	+37.25	10	50	None	+11.15
p-Tolyl	7.5	− 2.32[a]	20	55	Acetone, 45 g.	+ 1.12

[a] $[\alpha]^{27}\mathrm{D}$ in benzene, *c* 32.3.

The signs of rotation of α-phenethyl chloride and ethers of equivalent configuration are[3] (+)-chloride ≡ (−)-phenyl ether ≡ (+)-mesityl ether ≡ (−)-*p*-tolyl ether.

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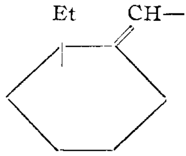
Dehydration of 1,2-Diethylcyclohexanol Over Alumina

BY J. V. KARABINOS AND A. T. BALLUN

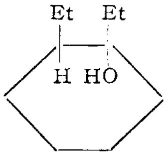
RECEIVED NOVEMBER 11, 1953

In a recent article a "1,2-diethylcyclohexene" was prepared[1] by dehydration of the corresponding cyclohexanol in the customary manner with iodine. We wish to record the dehydration of 1,2-diethylcyclohexanol over alumina catalyst in which case a single olefin was obtained which proved to be 1-ethyl-2-ethylidenecyclohexane (I) rather than one of the expected cyclohexenes, as shown by ozonolysis of the olefin to acetaldehyde and 2-ethylcyclohexanone. Since dehydrogenation of the olefin over chromia–alumina catalyst at 400–460°, conditions which usually favor the dehydrogenation of alkylcyclohexenes to alkylbenzenes, gave naphthalene in 30% yield with no evident formation of 1,2-diethylbenzene, the ethylidene structure for the olefin was substantiated further. Similar results had been reported by Ruzicka and Peyer[2] who obtained a 5 to 50% yield of naphthalene by dehydrogenation of crude "1,2-diethylcyclohexene" with selenium catalyst.

Assuming the likelihood of *trans* elimination of water[3] upon dehydration of 1,2-diethylcyclohexanol, it may be pointed out that a *cis*-1,2-diethyl structure is indicated for the cyclohexanol used in the dehydration step since a *trans*-1,2-diethylcyclohexanol should have given 1,2-diethylcyclohexene-1.



I



II

Experimental

1,2-Diethylcyclohexanol.—2-Chlorocyclohexanone,[4] $n^{28}\mathrm{D}$ 1.4800, was treated with one equivalent of ethylmagnesium bromide in ether followed by benzene treatment[5] to give 2-ethylcyclohexanone[6] in an over-all yield of 35% from cyclohexanone. To a Grignard reagent prepared from 2180 g. of ethyl bromide and 480 g. of magnesium turnings was added 2520 g. of 2-ethylcyclohexanone having $n^{20}\mathrm{D}$ 1.4557. After hydrolysis with 5% sulfuric acid, the solvent was removed from the dried ether layer and the residue was fractionated *in vacuo* on a column rated at 12 theoretical plates. After several fractionations there appeared to be no separation of isomers. Attempts to prepare derivatives from the various fractions either with phenyl isocyanate or 3,5-dinitrobenzoyl chloride resulted only in the formation of diphenylurea and 3,5-dinitrobenzoic acid, respectively. The yield of 1,2-diethylcyclohexanol amounted to 76%. A sample having $n^{20}\mathrm{D}$ 1.4665, $d^{20}{}_4$ 0.918 and b.p. 128° (59 mm.) was used for the dehydration.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.85; H, 12.90. Found: C, 76.78; H, 12.74.

Dice, *et al.*,[1] reported $n^{25}\mathrm{D}$ 1.4653 and $d^{25}{}_4$ 0.919 for their cyclohexanol.

Dehydration of 1,2-Diethylcyclohexanol.—By dehydration of 500 g. of 1,2-diethylcyclohexanol over alumina catalyst at 300°, followed by careful distillation on a column, rated at 80 theoretical plates, only one olefin was obtained in 90% yield, $n^{20}\mathrm{D}$ 1.4641, $d^{20}{}_4$ 0.8411 and b.p. 175° (750 mm.).

Anal. Calcd. for $C_{10}H_{18}$: C, 86.87; H, 13.13. Found: C, 86.70; H, 13.10.

The recorded constants[1] for "1,2-diethylcyclohexene" are b.p. 170–175° (747 mm.), $n^{25}\mathrm{D}$ 1.4598 and $d^{25}{}_4$ 0.831.

Ozonolysis of the above olefin (0.05 mole, $n^{20}\mathrm{D}$ 1.4641) was carried out according to the directions of Henne and

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[1] J. R. Dice, L. E. Loveless, Jr., and H. L. Cates, Jr., THIS JOURNAL, **71**, 3546 (1949).

[2] L. Ruzicka and E. Peyer, *Helv. Chim. Acta*, **18**, 676 (1935).

[3] C. C. Price and J. V. Karabinos, THIS JOURNAL, **62**, 1159 (1940).

[4] M. S. Newman and M. D. Farbman, *ibid.*, **66**, 1550 (1944).

[5] P. D. Bartlett and R. H. Rosenwald, *ibid.*, **56**, 1990 (1934).

[6] M. L. Bouveault and F. Chereau, *Compt. rend.*, **142**, 1986 (1906).

Hill.[7] The ozonide was reduced with zinc dust and acetic acid, and the acetaldehyde formed was collected in a solution[8] of 2,4-dinitrophenylhydrazine. The phenylhydrazone weighed 2.5 g. (22%) and gave m.p. 164–166°. Admixture with authentic acetaldehyde 2,4-dinitrophenylhydrazone of m.p. 165–166° showed no depression in melting point. The recorded[9] value for this derivative is 168°. The residual material resulting from the decomposition of the ozonide was purified in the previously described[7] manner and 3.4 g. (54%) of 2-ethylcyclohexanone, $n^{20}D$ 1.4555, was obtained, the 2,4-dinitrophenylhydrazone of which gave a melting point of 133–134°.

Anal. Calcd. for $C_{14}H_{18}O_4N_4$: C, 54.89; H, 5.92; N, 18.29. Found: C, 55.21; H, 5.68; N, 18.60.

Since the melting point of the 2,4-dinitrophenylhydrazone differed from that reported in the literature[10] (166°) this derivative was prepared from authentic 2-ethylcyclohexanone, derived from 2-chlorocyclohexanone, and this phenylhydrazone also gave a melting point of 133–134°. A mixed melting point with the derivative prepared from the ozonolysis product was unchanged. It would appear that 2-ethylcyclohexanone 2,4-dinitrophenylhydrazone exists in two forms.

The isolation of acetaldehyde and 2-ethylcyclohexanone, in fair yield, from the dehydration product of 1,2-diethylcyclohexanol of $n^{20}D$ 1.4665 indicates the structure of the olefin to be 1-ethyl-2-ethylidenecyclohexane rather than one of the expected cyclohexenes.

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[7] A. L. Henne and P. Hill, THIS JOURNAL, **65**, 752 (1943).

[8] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," Third Edition, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

[9] Reference 8, p. 229.

[10] F. E. King, J. A. Barltrop and R. J. Walley, *J. Chem. Soc.*, 277 (1945).

RESEARCH LABORATORIES
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The Isolation of Reserpine from *Rauwolfia canescens* Linn

BY M. W. KLOHS, M. D. DRAPER, F. KELLER AND F. J. PETRACEK

RECEIVED DECEMBER 18, 1953

The isolation of reserpine[1] from *Rauwolfia serpentina* Benth and the subsequent report of its sedative and hypotensive activity[2] has created widespread interest in this compound. In a search for other possible plant sources[3] of this alkaloid we have recently isolated reserpine, by the method previously employed in our investigation of *Rauwolfia serpentina*,[4,5] from the "oleoresin fraction" of *Rauwolfia canescens* Linn.

An earlier investigation of the alkaloidal fraction of *Rauwolfia canescens* by A. Chatterjee yielded one crystalline alkaloid, rauwolscine,[6] to which the hypotensive activity of the crude drug has been ascribed.[7] It now appears that there are at least two hypotensively active alkaloids present in this species.

Experimental

The Isolation of Reserpine from the "Oleoresin Fraction."—The "oleoresin fraction" from the ground dried roots of *Rauwolfia canescens*[8] was obtained in the same manner as previously described for fraction I in our investigation of *Rauwolfia serpentina*.[5] Ten grams of this fraction was dissolved as much as possible in 2% methanol–chloroform (50 ml.). The solution was filtered and the filtrate was applied to a chromatographic column (5.5 × 25 cm.) containing silicic acid–celite 3:1. The column was developed with the same solvent system until the most rapid moving band had reached the bottom of the column. The adsorbent was then extruded and examined under ultraviolet light and with the aid of spot tests using Fröhdes reagent. A colorless zone in the lower section of the column, which exhibited blue fluorescence and the characteristic Fröhdes color reaction (yellow → yellow-green → light blue) for reserpine, was removed by sectioning and washed thoroughly with methanol (150 ml.). The methanol was concentrated *in vacuo* to approximately 10 ml. On the addition of several drops of ammonium hydroxide reserpine separated as flat needles (150 mg.). The material was recrystallized several times from methanol by dissolving in an excess and concentrating on the steam-bath; m.p. 254° dec., $[\alpha]^{24}D$ $-121.8°$ (c 1.03 in $CHCl_3$). A mixed melting point with an authentic sample gave no depression. The infrared and ultraviolet absorption spectra were identical. For analysis the sample was dried to constant weight at 110° (2 mm.).

Anal. Calcd. for $C_{33}H_{40}O_9N_2$[9]: C, 65.11; H, 6.62; mol. wt., 608.67. Found: C, 65.13; H, 6.70; mol. wt., 611,[12] 614.[13]

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[1] J. M. Müller, E. Schlittler and H. J. Bein, *Experientia*, **8**, 338 (1952).

[2] H. J. Bein, *ibid.*, **9**, 107 (1953).

[3] The isolation of reserpine from *Rauwolfia heterophylla* Roem. and Schult. has been reported in a recent communication by Carl Djerassi, Marvin Gorman, A. L. Naussbaum and J. Reynoso, THIS JOURNAL, **75**, 5446 (1953).

[4] M. W. Klohs, M. D. Draper, F. Keller and F. J. Petracek, *ibid.*, **75**, 4867 (1953).

[5] M. W. Klohs, M. D. Draper, F. Keller, W. Malesh and F. J. Petracek, *ibid.*, **76**, 1332 (1954).

[6] A. Chatterjee (née Mookerjee), *J. Indian Chem. Soc.*, **18**, 33 (1941).

[7] J. N. Mukherjee, *Science and Culture*, **18**, 338 (1953).

[8] The plant material in this investigation was kindly identified by Dr. H. W. Youngken, Mass. College of Pharmacy, Boston, Mass.

[9] The empirical formula $C_{35}H_{44}O_{10}N_2$ originally proposed by us for reserpine has now been revised to $C_{33}H_{40}O_9N_2$ which is in agreement with that suggested by other investigators.[3,10,11] Although the elementary analyses of reserpine and its derivatives reported by us fit both empirical formulas the results of more accurate equivalent weight determinations were incompatible with the original formula. The empirical formula for reserpinolic acid has likewise been changed to $C_{22}H_{28}O_5N_2$.

[10] A. Furlenmier, R. Lucas, H. B. MacPhillamy, J. M. Müller and E. Schlittler, *Experientia*, **9**, 331 (1953).

[11] N. Neuss, H. E. Boaz and J. W. Forbes, THIS JOURNAL, **75**, 4870 (1953).

[12] Potentiometric titration in glacial acetic acid with 0.01 N perchloric acid in dioxane.

[13] Potentiometric titration in 75% dimethylformamide-water with 0.01 N HCl.

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1,1,1-Trichloro-2-methylpropyl-2-phosphoric Acid from 1,1,1-Trichloro-2-methyl-2-propanol

BY DONALD G. KUNDIGER AND THEODORE J. COLLIER

RECEIVED NOVEMBER 6, 1953

We have found that 1,1,1-trichloro-2-methyl-2-propanol (I) is converted to the intermediate $Cl_3C-C(CH_3)_2-O-PBr_4$ (III) by the action of phosphorus pentabromide upon I under anhydrous conditions. III can be hydrolyzed to 1,1,1-trichloro-2-methylpropyl-2-phosphoric acid (IV),[1] which can be obtained in 26% yield from (I).

The structure of IV was established by ultimate analyses, by neutralization equivalent and by cleavage with aqueous potassium hydroxide to potassium phosphate and the known cleavage products, *viz.*, carbon monoxide and acetone,[2] of I.

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[1] *Cf.* the report by C. Willgerodt and F. Durr, *Ber.*, **20**, 539 (1887), wherein only replacement of the hydroxyl in I to give 1,1,1-trichloro-2-methyl-2-bromopropane (II) was indicated as the product of the reaction of phosphorus pentabromide upon I; no other product was indicated. This is the only previous report of this reaction.

[2] Bressanin and Segre, *Gazz. chim. ital.*, **41**, [I] 673 (1911).