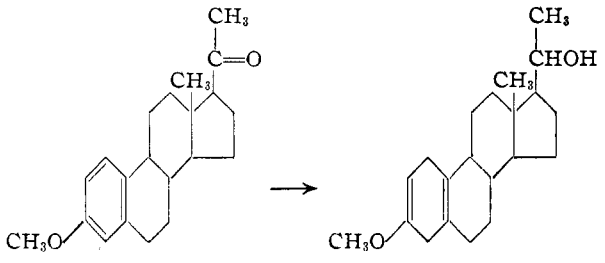
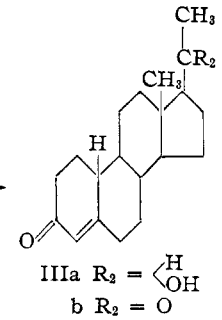
probably representing a mixture of 20-epimers; m.p. 174–177°, $[\alpha]^{20}D$ +42°, λ_{max}^{alc} 240 mμ (4.35), infrared bands (CS_2) at 3617 cm.$^{-1}$ (hydroxyl) and 1678 cm.$^{-1}$ (Δ^4-3-ketone). Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.45; H, 10.24. Chromium trioxide oxidation of IIIa in acetic acid solution afforded in 55% over-all yield (based on I) pure 19-norprogesterone (IIIb), m.p. 144–145°, $[\alpha]^{20}D$ +147°, λ_{max}^{alc} 240 mμ (4.36), infrared bands (CS_2) at 1706 cm.$^{-1}$ (20-ketone) and 1674 cm.$^{-1}$ (Δ^4-3-ketone). Calcd. for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 80.07; H, 9.28. The reddish-orange 3,20-bis-2,4-dinitrophenylhydrazone possessed m.p. 278–279°, $\lambda_{max}^{CHCl_3}$ 380 mμ (4.78).[8] Calcd. for $C_{32}H_{36}O_8N_8$: C, 58.17; H, 5.49; N, 16.95. Found: C, 58.28; H, 5.37; N, 16.57.





19-Norprogesterone (IIIb) exhibits approximately the same activity as natural progesterone in rabbits. Since the mode of synthesis automatically establishes the "natural" configuration for all asymmetric centers with the possible exception of C-10,[9] the replacement of the angular methyl group at C-10 by hydrogen in progesterone does not reduce biological activity.[10] This observation is of considerable importance since if it should also apply to the cortical hormones, notably cortisone, it would considerably simplify the total synthesis of anti-arthritic substances. In fact, the present preparation of 19-norprogesterone (IIIb) constitutes the first total synthesis of a potent progestational hormone, since the starting methyl ether I[7] has been obtained[11] from estrone which has already been synthesized totally.[12]

Further work on 19-norsteroids, particularly of the cortical hormone series, is in progress.

JOINT CONTRIBUTION FROM THE
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RECEIVED MAY 21, 1951

(8) Progesterone bis-dinitrophenylhydrazone shows $\lambda_{max}^{CHCl_3}$ 383 mμ (4.72) (C. Djerassi, *Anal. Chem.*, **20**, 880 (1948)).

(9) The hydrogen atom at C-10 most likely assumed the more stable "natural" β-configuration during the acid hydrolysis of II.

(10) The reason for the high biological activity of Ehrenstein's (ref. 1) mixture of 19-norprogesterones is still obscure since the presently described isomer IIIb could have been at best only a minor constituent of that mixture.

(11) L. Velluz and G. Muller, *Bull. Soc. Chim. France*, 166 (1950).

(12) G. Anner and K. Miescher, *Helv. Chim. Acta*, **31**, 2173 (1948); W. S. Johnson, D. K. Banerjee, W. P. Schneider and C. D. Gutsche, THIS JOURNAL, **72**, 1426 (1950).

CRYSTALLINE ALLETHRIN ISOMER

Sir:

The insecticide known as allethrin, now being produced commercially, is obtained by acylation of *dl*-2-allyl-4-hydroxy-3-methyl-2-cyclopenten-1-one[1] (*dl*-allethrolone) with a mixture of *dl-cis*- and *dl-trans*-chrysanthemum monocarboxylic acid chlorides.

Allethrin may be considered a mixture of four racemic forms (or eight individual optical and geometric isomers). Two racemic forms are esters of the *cis* acid and two of the *trans* acid.

When a sample of molecularly distilled allethrin was cooled to a low temperature, it crystallized in part, as likewise did samples of commercial allethrin kept at about 4°. Cold filtration and recrystallization from isooctane or pentane gave colorless crystals, m.p. 50.5–51°.

Anal.[2] Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.41; H, 8.67.

Upon saponification of the crystalline product, *dl-trans*-chrysanthemum monocarboxylic acid was obtained, which, after recrystallization from pentane or nitromethane, melted at 55–56° and gave no depression in a mixture melting-point determination with the authentic acid.[3]

dl-Allethrolone when acylated with *dl-cis*-chrysanthemum monocarboxylic acid chloride furnished an ester mixture, b.p. 146–149° (0.4 mm.), $n^{25}D$ 1.5070,[4] which, on being cooled and seeded with the above-mentioned crystalline compound, could not be induced to crystallize. Acylation of *dl*-allethrolone with *dl-trans*-chrysanthemum monocarboxylic acid chloride furnished an ester mixture, b.p. 147–150° (0.4 mm.), $n^{25}D$ 1.5047,[4] which crystallized in part on being cooled and seeded. When 8.4 g. of this ester mixture was dissolved in 12.6 ml. of isooctane, cooled, and filtered on a cold-jacketed filter kept at about −30°, about half was obtained as the crystalline form. Removal of solvent from the filtrate *in vacuo* left 4.4 g. of oil, $n^{25}D$ 1.5050. The crystalline portion, when recrystallized from isooctane, melted at 50.5–51° and did not depress the melting point of the crystalline compound obtained from allethrin. The crystalline isomer will be called the α-*dl-trans* isomer, and the other isomer found concentrated in the filtrate, the β-*dl-trans* isomer of allethrin. Based on the yield, the concentrate of β-*dl-trans* isomer contained about 5% of dissolved α-*dl-trans* isomer.

The crystalline α-*dl-trans* isomer must consist of one of the racemic ester pairs, *d-trans* acid with *d*-allethrolone plus *l-trans* acid with *l*-allethrolone,

(1) M. S. Schechter, N. Green, and F. B. LaForge, THIS JOURNAL, **71**, 1517 (1949); **71**, 3165 (1949); *Agr. Chemicals*, **4** (6), 57 (1949).

(2) J. S. Ard, Bureau of Agricultural and Industrial Chemistry, U. S. Department of Agriculture.

(3) I. G. M. Campbell and S. H. Harper, *J. Chem. Soc.*, 283 (1945).

(4) Compare, L. Crombie, A. J. B. Edgar, S. H. Harper, M. W. Lowe, and D. Thompson, *J. Chem. Soc.*, 3553 (1950).

or *d-trans* acid with *l*-allethrolone plus *l-trans* acid with *d*-allethrolone; the *β-dl-trans* isomer consists of the other pair.

Entomological tests[5] on house flies indicate the *α-dl-trans* isomer to be less effective and the *β-dl-trans* isomer to be more effective than allethrin.

The pure, crystalline *α-dl-trans* isomer of allethrin should serve as a useful reference standard in Peet-Grady, Campbell turntable, and other insecticide test methods, and for checking chemical analytical methods for substances of the pyrethrin or allethrin type.

(5) By W. A. Gersdorff, N. Mitlin, and J. H. Fales, Bureau of Entomology and Plant Quarantine.

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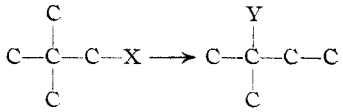
NON-REARRANGEMENT REACTIONS OF THE NEOPENTYL-OXYGEN BOND. NEW SYNTHESES OF NEOPENTYL HALIDES

Sir:

Anionoid substitution reactions of neopentyl compounds have long been known to proceed with rearrangement of the carbon skeleton.[1] Indeed,



these changes are often cited in textbooks as classical simple examples of the Wagner–Meerwein rearrangement.

In a recent elegant series of papers, however, I. Dostrovsky, E. D. Hughes and C. K. Ingold[2] have demonstrated rearrangement for neopentyl bromide in S_N1 reactions and non-rearrangement in S_N2 reactions. This suggested to us that similar non-rearrangement reactions of the neopentyl–oxygen bond might be isolated by appropriate structural variations in neopentyl alcohol (which did not disturb the neopentyl–oxygen configuration) or by reaction conditions unfavorable to reaction of the alcohol by an S_N1 mechanism.

In this communication we wish to report what we believe to be the first unequivocal examples of reactions of the neopentyl–oxygen bond proceeding without rearrangement.

$$Me_3CCH_2OSiEt_3 + PBr_3 \xrightarrow{C_9H_7N\cdot HX} Me_3CCH_2Br + Et_3SiBr$$

$$Me_3CCH_2OSiEt_3 + SOCl_2 \xrightarrow{C_9H_7\cdot HX} Me_3CCH_2Cl + Et_3SiCl$$

$$Me_3CCH_2OH + PBr_3 + C_9H_7N \longrightarrow Me_3CCH_2Br + C_9H_7N\cdot HBr$$

Triethylneopentoxysilane, b.p. 67° (10 mm.), $n^{20}D$ 1.4189 (calcd. for $C_{11}H_{26}OSi$: Si, 13.84. Found: Si, 13.78) was prepared by the method of R. O. Sauer[3] using neopentyl alcohol, triethylchlorosilane, and quinoline, in a benzene solvent. Pure neopentyl bromide, b. 104° (733 mm.), $n^{20}D$ 1.4371, d^{20} 1.200, lit.[1c] b.p. 105°, $n^{20}D$ 1.4370, d^{20} 1.199; anilide, m.p. and mixed m.p. 130°; less than 0.5% reaction with NaOEt in EtOH at reflux for four hours; (calcd. for $C_5H_{11}Br$: Br, 52.9. Found: Br, 52.9) was formed in 85% yield by heating 2 moles of triethylneopentoxysilane with four moles of phosphorus tribromide at 173° for 16 hours in the presence of 3 g. of quinoline hydrochloride.[4]

A similar reaction using thionyl chloride and carried out at 115° for 23 hours gave a 61% yield of pure neopentyl chloride, b.p. 83° (725 mm.), $n^{20}D$ 1.4043, d^{20} 0.8659, lit.[1c] b.p. 83.5° (740 mm.), $n^{22}D$ 1.4043, d^{20} 0.865; completely inert to NaOEt in EtOH; anilide, m.p. and mixed m.p. 130° (calcd. for $C_5H_{11}Cl$: Cl, 33.27. Found: Cl, 32.58).

Neopentyl bromide, b.p. 104.5° (728 mm.), $n^{20}D$ 1.4370, d^{20} 1.200, was also prepared in 47% yield by heating a mixture of neopentyl alcohol (2 moles), quinoline (2.43 moles) and bromobenzene (900 cc.) at 181° for 24 hours.

From the above data it is now clear that use of neopentyl as a critical group in experiments aimed at determining the mechanism of cleavage of a carbon–oxygen bond in a given reaction[5] (based on the postulate[1a] that neopentyl–oxygen fission invariably gives rearrangement) are of little absolute value in the elucidation of such mechanisms.

A further consequence of the present work is that neopentyl bromide is now as readily available as other aliphatic bromides from reaction of the alcohol with phosphorus tribromide and quinoline.

The mechanisms and possible extensions of the above reactions are under investigation.

(1) (a) F. C. Whitmore, THIS JOURNAL, **54**, 3274 (1932); (b) F. C. Whitmore and H. S. Rothrock, *ibid.*, **54**, 3431 (1932); (c) F. C. Whitmore, E. L. Wittle and B. R. Harriman, *ibid.*, **61**, 1586 (1939).

(2) Hughes and Ingold, *J. Chem. Soc.*, 157 (1946).

(3) Sauer, THIS JOURNAL, **66**, 1707 (1944).

(4) The latter is a necessary catalyst whose broad function probably involves action as a good source of halide ions and in addition includes a labilizing effect on the Si–O–C grouping *via* electrophilic attack by quinolinium ions; *cf.* W. Gerrard and A. French, *Nature*, **159**, 263 (1947).

(5) *Cf.* A. Scattergood, W. H. Miller and J. Gammon, THIS JOURNAL, **67**, 2150 (1945); N. C. Deno and M. S. Newman, *ibid.*, **72**, 3852 (1950).

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RECEIVED APRIL 11, 1951

THE NATURE OF THE INTERMEDIATE IN CARBONIUM ION-TYPE INTERCONVERSION REACTIONS OF CYCLOBUTYL, CYCLOPROPYLCARBINYL AND ALLYLCARBINYL DERIVATIVES[1]

Sir:

The striking ease of interconversion of cyclobutyl and cyclopropylcarbinyl derivatives in carbonium ion-type reactions[2] and the abnormally large solvolytic reactivities of cyclobutyl and cyclopropylcarbinyl halides[2] and sulfonate esters[3,4] have led to a

(1) Supported by the program of research of the U. S. Atomic Energy Commission.

(2) J. D. Roberts and R. H. Mazur, THIS JOURNAL, **73**, 2509 (1951).

(3) J. D. Roberts and V. C. Chambers, *ibid.*, **73**, 3176 (1951).

(4) C. G. Bergstrom and S. Siegel, Abstracts of the 119th Meeting of the American Chemical Society, Boston, Mass., April 4, 1951, p. 33M.