no NH absorption in the infrared. A mixture melting point of the two fractions occurred at 115–118°.

Anal. Calcd. for $C_{27}H_{47}NO$: C, 80.73; H, 11.79; N, 3.49. Found for fraction I: C, 80.70; H, 11.93; N, 3.45. Found for fraction II: C, 80.47; H, 11.66, N, 3.64.

Fraction I was subsequently shown to be VIII and fraction II was shown to be VII. It was noted that, if the reaction time in the N-methylation were 1 hr., only one N-methyl derivative was recovered. It was identical with fraction I and accounted for approximately 30% of the starting material. The remainder of the material recovered was unsubstituted lactam, m.p. 217–219°, $[\alpha]^{25}D$ +54° (*c* 1.0, chloroform). The recovered unsubstituted lactam was treated with phosphorus pentachloride as described earlier in this paper (see IV and V). Two fractions were obtained but the ratio of IV to V was 4:1. These dichlorolactams accounted on a weight basis for 45% of the starting material used in the preparation of the N-methyl lactam under mild conditions. These results established that the N-methyl lactam (fraction I) formed under mild conditions was VIII. Fraction II was therefore VII.

N-Nitroso-2-aza-5α-cholestan-3-one and N-Nitroso-3-aza-5α-cholestan-2-one (IX′).—Two grams (0.0051 mole) of III was dissolved in a mixture of 50 ml. of glacial acetic acid and 80 ml. of acetic anhydride. The solution was cooled in an ice bath and 4 g. (10% excess) of sodium nitrite was added in small quantities with stirring.[21] A yellow precipitate began to separate immediately. After 24 hr. the yellow mixture was diluted with water and extracted with chloroform. The solvents were removed after drying over sodium sulfate. The residue was crystallized from acetone to yield 1.8 g. (85%) of IX as yellow platelets: m.p. 148–150°; $[\alpha]^{25}D$ +62° (*c* 1.0, chloroform); λ_{max}^{KBr} 5.82, 6.55, and 6.80 μ. Attempts to separate the isomers were unsuccessful.

Anal. Calcd. for $C_{26}H_{44}N_2O_2$: C, 74.95; H, 10.65; N, 6.72. Found: C, 75.14; H, 10.66; N, 6.11.

2-Aza-5α-cholestane and 3-Aza-5α-cholestane (X).—One gram (0.0026 mole) of III was dissolved in 200 ml. of freshly distilled dioxane. Lithium aluminum hydride (4.0 g.) was added in small portions to the resultant solution. The mixture was refluxed 8 hr. and cooled and the excess hydride was carefully decomposed with water. The inorganic salts were filtered and washed with 400 ml. of ether. The filtrate and washings were combined, dried over sodium sulfate, and filtered, and the solvent was removed *in vacuo*. Crystallization from acetone gave 0.2 g. of a product that melted over a wide range, 80–110°. An infrared spectrum of the product showed complete reduction of the lactam carbonyl. Attempts to purify this product or to separate the isomers were unsuccessful.

Hydrobromide Salt.—The product was dissolved in dry ether and treated with HBr. The precipitate was washed with dry ether after filtration and crystallized from ethanol–acetone to yield 1.0 g. (85%) of the hydrobromide of X as white crystals: m.p. 235–245°; $[\alpha]^{25}D$ +42° (*c* 1.0, chloroform).

Anal. Calcd. for $C_{26}H_{48}BrN$: C, 68.69; H, 10.64; Br, 17.58. Found: C, 68.39; H, 10.72; Br, 17.50.

(21) W. Hartman and L. Roll, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 460.

6α-Azido-3α,5α-cyclocholestane

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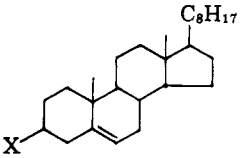
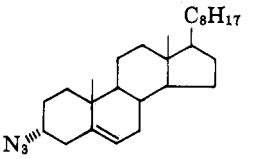
The need for preparative methods for syntheses of steroid amines prompted an investigation of recently reported reactions leading to steroid azides.[1,2] Alkyl azides can readily be reduced to amines with retention of configuration of the carbon–nitrogen bond.[3]

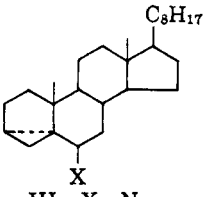
This investigation has resulted in the observation that cholesteryl 3β-*p*-toluenesulfonate (Ia) reacts with the strongly nucleophilic azide ion in various solvents to give, not only the known 3β-azidocholest-5-ene (Ib) and 6β-azido-3α,5α-cyclocholestane (IIIa), but also the undescribed 6α-azido-3α,5α-cyclocholestane (IVa). Depending on the solvent used, 3α-azido-cholest-5-ene (II) was also obtained. The yields of isomeric azides were determined in each of the solvents methanol, dimethyl sulfoxide (DMSO), and N-methylacetamide (NMA), and represent kinetically controlled product distributions, because the most labile epimer IIIa did not rearrange when subjected to the reaction conditions. The four azides were readily separated over Florisil columns by elution with *n*-pentane and *n*-pentane–benzene mixtures. They showed no tendency to rearrange during chromatography.[4]



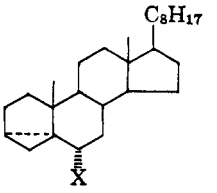
Ia, X = OTs
b, X = N_3



II



IIIa, X = N_3
b, X = OCH_3



IVa, X = N_3
b, X = $NHCOCH_3$

The structures of the steroid azides Ib, II, and IIIa were determined earlier by Jones,[5] who converted them to the known amines. Infrared and n.m.r. spectra of the azides fully confirmed these structural assignments.

The structure of IVa was determined from the following data. The presence of a cyclopropane ring was indicated by both the n.m.r. spectrum,[6] which showed a complex pattern between 0.6 and 0.0 p.p.m. and the infrared spectrum, which showed absorptions at 3069, 3028, and 3002 cm.$^{-1}$.[7] The n.m.r. spectrum showed no vinyl hydrogen. The presence of an azide group was indicated by the nitrogen analysis and by an intense asymmetric azide stretching band at 2100 cm.$^{-1}$.[8] A single-proton resonance occurred at 3.72 p.p.m. as a quartet with J_{ae} = 4.6 c.p.s. and J_{aa} = 12.0 c.p.s. An identical spin–spin coupling pattern was obtained by Tadanier and Cole[9] for the C-6 proton of 6α-substituted

(1) D. H. R. Barton and L. R. Morgan, *J. Chem. Soc.*, 622 (1962).

(2) R. Goutarel, A. Cavé, L. Tan, and M. Leboeuf, *Bull. soc. chim. France*, 646 (1962).

(3) J. H. Boyer and F. C. Canter, *Chem. Rev.*, **54**, 1 (1954), and references cited therein.

(4) The rearrangement of IIIa was observed by D. N. Jones during chromatography on an alumina column. See ref. 5.

(5) D. N. Jones, *Chem. Ind.* (London), 179 (1962).

(6) The n.m.r. spectra were determined at 60 Mc./sec. in deuteriochloroform using tetramethylsilane as an internal reference. Chemical shifts are reported in parts per million measured from tetramethylsilane (0.0 p.p.m.) in the direction of decreasing field.

(7) M. Hórak, J. Smejkal, and J. Farkas, *Collection Czech. Chem. Commun.*, **28**, 2280 (1963).

(8) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 263.

(9) J. Tadanier and W. Cole, *J. Org. Chem.*, **27**, 4610 (1962).

3α,5α cyclo steroids. The optical rotation of IVa was more positive than that of IIIa as demonstrated for other C-6 epimeric 3α,5α cyclo steroids.[9,10] Finally, IVa was reduced with lithium aluminum hydride[11] and the crude product was acetylated with acetic anhydride. The product had the melting point and optical rotation of 6α-acetamido-3α,5α-cyclocholestane (IVb) prepared earlier by Evans and Summers.[12] The n.m.r. spectrum was entirely consistent with that expected for IVb.[9]

The results presented in Table I differ considerably from recent reports in the literature. First, Barton and Morgan[1] reported that reaction of Ia with lithium azide in refluxing methanol gave Ib in 57% yield. Second, reaction of the *p*-toluenesulfonate of 3β-hydroxypregn-5-en-20-one with sodium azide in DMSO was reported by Goutarel, Cavé, Tan, and Leboeuf[2] to give 3α-azidopregn-5-en-20-one as the only product, although in unspecified yield. The azide was isolated after crystallization and the mother liquors apparently were not examined.[13]

TABLE I

REACTION OF CHOLESTERYL 3β-*p*-TOLUENESULFONATE WITH AZIDE ION IN VARIOUS SOLVENTS

	%[a]		
Product	CH_3OH[b]	DMSO[c]	NMA[c]
3α-Azido-cholest-5-ene	...	31	12
3β-Azido-cholest-5-ene	8	13	19
6β-Azido-3α,5α-cyclocholestane	35	16	31
6α-Azido-3α,5α-cyclocholestane	*ca.* 1	6	10

[a] The yields are expressed as per cent of theoretical based on Ia calculated from weights of chromatographic fractions. [b] At reflux temperature, 0.92 *M* in lithium azide. [c] At 85–90°, *ca.* 1.5 *M* in sodium azide.

Other examples[5,14] of reaction of steroid Δ5-3β-*p*-toluenesulfonates with sodium azide in DMSO gave mixtures, which indicated competition between SN2 and SN1 mechanisms. The results reported in Table I for NMA parallel those in DMSO, although increased contribution of SN1 reaction was noted. This, together with the results of Knecht and Kolthoff[15] and also of Parker,[16] indicates that N-methyl-substituted amides are poor hydrogen bond donating solvents compared with water or alcohols and thus resemble dipolar aprotic solvents.

Although the solvolyses of steroid Δ5-3β-sulfonates have been studied for many years, the present work reports the first example of isolation of a 6α-substituted product, 6α-azido-3α,5α-cyclocholestane.[17] Solvolysis reactions of steroid Δ5-3β-sulfonates give 6β-substituted 3α,5α cyclo steroids as products of kinetic control.[18] The isolation of IVa may not be the consequence of the greater nucleophilicity of the azide ion, compared with other nucleophiles, resulting in less selective attack on the homoallylic cation. The solvent effect on increasing nucleophilicity of azide ion, being presumably greater in poor hydrogen bond donating solvents, should be DMSO ≫ NMA > methanol.[16,19] The 6β:6α ratios in Table II, however, do not follow the order anticipated on this basis. An interpretation of the 6β:6α ratios in terms of changes in electron distribution of a symmetrical or an unsymmetrical homoallylic cation[20] induced by solvent does not seem reasonable. Clearly, the 6β:6α ratio as a function of dielectric constant of the solvent does not reflect such a change. Therefore, neither the nucleophilicity of the azide ion nor the dielectric constant of the solvents suffice to explain the low 6β:6α ratio found in NMA and DMSO in contrast to the high 6β:6α ratio found in methanol and indicate the operation of another effect.

TABLE II

COMPARISON OF PRODUCT RATIOS WITH DIELECTRIC CONSTANT OF THE SOLVENT

Solvent	Dielectric constant, ε	6β:6α product ratio
CH_3OH	*ca.* 30 (25°)[a]	*ca.* 35
DMSO	47 (40°)[b]	2.7
NMA	179 (30°)[c]	3.1

[a] "International Critical Tables," Vol. 6, E. Washburn Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1929, p. 83. [b] H. L. Schlafer and W. Schaffernicht, *Angew. Chem.*, **72**, 618 (1960). [c] R.-y. Lin and W. Dannhouser, *J. Phys. Chem.*, **67**, 1805 (1963).

A mechanism in which an aprotic solvent participates to increase the yield of 6α-azide may be the following. The reaction of the tosylate Ia in DMSO in the presence of the less nucleophilic acetate ion was shown to give 3α,5α-cyclocholestan-6-one (V) in 51% yield.[21] The formation of V was believed to proceed by reaction of the homoallylic ion VI with DMSO to form an intermediate VIIb, followed by base attack on the C-6 proton, eliminating dimethyl sulfide. There is ample evidence for the existence of intermediates such as VIIb.[22] If similar intermediates were reversibly formed in DMSO (VIIb) or NMA (VIIc) in the presence of azide ion, which is not unreasonable in view of the competition observed between azide ion and methanol (see Experimental), subsequent nucleophilic displacement at C-6 with inversion would give the 6α-azide IVa. Alkyl amidate salts are known to give nucleophilic substitution products with inversion at the O-alkyl bond.[23] That an aprotic solvent can influence the stereochemical result of nucleophilic substitution reactions by a similar mechanism involving reactive intermediates has been shown by Weiner and Sneen and others.[24] Because of rapid loss of a proton from VIIa, to form the 6β-methoxy derivative, this intermediate is an ineffective precursor of IVa.

(10) (a) E. M. Kosower and S. Winstein, *J. Am. Chem. Soc.*, **78**, 4347 (1956); (b) *ibid.*, **78**, 4354 (1956).

(11) J. H. Boyer, *ibid.*, **73**, 5865 (1951).

(12) D. E. Evans and G. H. R. Summers, *J. Chem. Soc.*, 906 (1957).

(13) F.-X. Jarreau, C. Monneret, Q. Khuong-Huu, and R. Goutarel, *Bull. soc. chim. France*, 2155 (1964).

(14) L. Labler, J. Hora, and V. Černy, *Collection Czech. Chem. Commun.*, **28**, 2015 (1963).

(15) L. A. Knecht and I. M. Kolthoff, *Inorg. Chem.*, **1**, 195 (1962).

(16) A. J. Parker, *J. Chem. Soc.*, 1328 (1961).

(17) The 6α-azide IVa (equatorial) was eluted from Florisil columns more rapidly than the 6β-azide IIIa (axial). This anomalous behavior facilitated separation of small amounts of 6α isomer.

(18) N. L. Wendler, "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p. 1077.

(19) A. J. Parker and R. Forster, *Quart. Rev.* (London), **16**, 163 (1962).

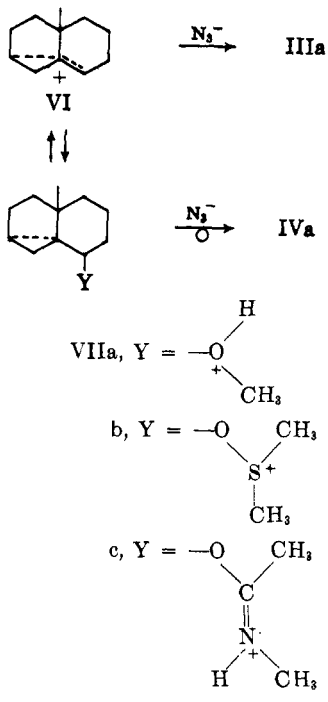
(20) (a) S. Winstein and E. M. Kosower, *J. Am. Chem. Soc.*, **81**, 4399 (1959); (b) G. H. Whitham and J. A. F. Wickramasinghe, *J. Chem. Soc.*, 1655 (1964).

(21) F.-X. Jarreau, B. Tchoubar, and R. Goutarel, *Bull. soc. chim. France*, 887 (1962).

(22) S. G. Smith and S. Winstein, *Tetrahedron*, **3**, 317 (1958).

(23) (a) C. L. Stevens, D. Morrow, and J. Lawson, *J. Am. Chem. Soc.* **77**, 2341 (1955); (b) F. Cramer and H.-J. Baldauf, *Chem. Ber.*, **92**, 370 (1959).

(24) (a) H. Weiner and R. A. Sneen, *J. Am. Chem. Soc.*, **87**, 287 (1965); (b) R. Fuchs, G. E. McCrary, and J. J. Bloomfield, *ibid.*, **83**, 4281 (1961); (c) A. F. Diaz and S. Winstein, *ibid.*, **86**, 5010 (1964).



It is concluded that reaction of steroid Δ^5-3β-sulfonates with a strong nucleophile in a dipolar aprotic or poor hydrogen bond donating solvent may lead to 6α-substituted 3α,5α cyclo steroids as well as to the expected 6β-substituted 3α,5α cyclo steroids. Arbitrary assignment of the 6β-configuration to 3α,5α cyclo steroids, obtained under these conditions, no longer seems valid.

Experimental[25]

Reaction of Cholesteryl 3β-*p*-Toluenesulfonate (Ia) with Azide Ion in Various Solvents. A. Methanol.—A magnetically stirred suspension of cholesteryl 3β-*p*-toluenesulfonate (1.76 g., 3.26 mmoles) in 50 ml. of 0.92 *M* anhydrous methanolic lithium azide[26] was refluxed for 24 hr. Then, 25 ml. of methanol was distilled and 150 ml. of water was added. The product was extracted with ether, and the extract was washed with water and dried over magnesium sulfate. The ether was concentrated to dryness leaving 1.28 g. of oil, which crystallized on standing. A sample (0.704 g.) of the crude product in 10 ml. of *n*-pentane was chromatographed over 60 g. of Florisil.[27] The column was developed with *n*-pentane, and eluate fractions were cut at 60 ml. Fractions 1–4 were eluted with *n*-pentane, giving 10 mg. of an oil which showed negligible azide absorption at 2105 cm.$^{-1}$, and were discarded. Fraction 5 gave 7 mg. (1.0%) of an oil, identical by infrared spectrum with the 6α-azide IVa.

Fraction 6 gave 62 mg. of IIIa and had m.p. 66–68° with softening at 63°, $[\alpha]^{23}D$ +49.7° (*c* 0.60). The combined fractions 7–15 gave 196 mg. of IIIa, had m.p. 68–71° with softening at 65°, $[\alpha]^{23}D$ +46.6° (*c* 1.01), and brought the yield of the 6β-azide IIIa to 258 mg. (35.1%). The analytical sample was crystallized from methanol and had m.p. 68–70.5°; $[\alpha]^{23}D$ +49.3° (*c* 1.03) (lit.[5] m.p. 53–54°, $[\alpha]D$ +44°); ν_{max} 3060, 2998 (cyclopropyl), and 2091 cm.$^{-1}$ (N_3 asymmetric stretch); δ = 3.28 (H-6 triplet, J = 2.7 c.p.s.) and 0.70–0.30 (cyclopropyl) p.p.m.[13]

Anal. Calcd. for $C_{27}H_{45}N_3$: C, 78.75; H, 11.02; N, 10.21. Found: C, 78.70; H, 11.28; N, 10.41.

Fractions 16 and 17 eluted with *n*-pentane combined with fractions 18–21 eluted with 9:1 *n*-pentane–benzene provided 61 mg. (8.3%) of the 3β-azide Ib. The sample had m.p. 83–86° with softening at 80°, $[\alpha]^{23}D$ −18.7° (*c* 0.71). The analytical sample had m.p. 84–85°, $[\alpha]^{25}D$ −19.7° (*c* 1.04) (lit. m.p. 61–63°, $[\alpha]D$ −19°,[2] and m.p. 83–85°, $[\alpha]D$ −20°[5]), ν_{max} 2095 cm.$^{-1}$, δ = 5.41 (H-6) and 3.17 p.p.m. (H-3, half-band width 25 c.p.s.).

Anal. Calcd. for $C_{27}H_{45}N_3$: C, 78.75; H, 11.02; N, 10.21. Found: C, 78.85; H, 11.04; N, 10.05.

Continued elution with 9:1 *n*-pentane–benzene gave 174 mg. of the 6β-methoxy ether IIIb, which after crystallization from methanol had m.p. 79–80°, $[\alpha]^{25}D$ +53.5° (*c* 0.97) (lit.[28] m.p. 79°, $[\alpha]D$ +55°).

B. Dimethyl Sulfoxide.—A magnetically stirred solution of the tosylate Ia (2.00 g., 3.69 mmoles) and sodium azide (7.0 g.) in 87 ml. of anhydrous DMSO was maintained at 85° for 2 hr. The mixture was cooled, and 270 ml. of water was added. The product was isolated with ether, washed with water, and dried over magnesium sulfate. Evaporation of the ether gave 1.50 g. of an oily residue.

A sample of the crude product (518 mg.) in 10 ml. of *n*-pentane was chromatographed over 60 g. of Florisil. The column was developed with *n*-pentane, and fractions were cut at 60 ml. The combined fractions 1–4 gave 25 mg. of oil, which showed no azide absorption in the infrared.

The infrared spectrum of combined fractions 5–7 (30 mg., 5.7%) was identical with that of the 6α-azide IVa. The sample had $[\alpha]^{22}D$ +98.1° (*c* 0.51).

Fractions 8–11 gave 82 mg. (15.5%) of the 6β-azide IIIa and had m.p. 69–72° with softening at 65°. The mixture melting point with authentic IIIa was undepressed.

Continued elution with *n*-pentane gave 164 mg. (31.0%) of the 3α-azide II. The sample had m.p. 110–112° with softening at 108°. Crystallization from methanol gave 115 mg. of II, m.p. 114–115°, $[\alpha]^{22}D$ −4.8° (*c* 0.56) (lit.[5] m.p. 115–116°, $[\alpha]D$ −4°), ν_{max} 2085 and 2110 cm.$^{-1}$, δ = 5.43 (H-6) and 3.90 p.p.m. (H-3, half-band width 9.0 c.p.s.).

Anal. Calcd. for $C_{27}H_{45}N_3$: C, 78.75; H, 11.02; N, 10.21. Found: C, 78.67; H, 10.88; N, 10.10.

Further elution with *n*-pentane and 8:2 *n*-pentane–benzene gave 67 mg. (12.7%) of the 3β-azide Ib, m.p. 84–86° with softening at 80°. The mixture melting point with authentic Ib was undepressed.

C. N-Methylacetamide.—A mixture of the tosylate Ia (1.12 g., 2.7 mmoles) and 4.0 g. of sodium azide in 40 ml. of NMA was heated at 85–90° for 1.0 hr. with occasional swirling on a steam bath. The mixture was cooled and diluted with 200 ml. of water. The product was extracted with ether, washed with water, and dried over magnesium sulfate. The ether was evaporated, giving 0.823 g. of an oily residue.

A sample of this product (415 mg.) was chromatographed over Florisil as described above. The third and fourth fractions were combined and gave 43 mg. of an oil. Quantitative infrared analysis of the azide band at 2100 and the CH_2 stretching band[29] at 2865 cm.$^{-1}$ indicated this sample contained 34% or 15 mg. of the 6α-azide IVa. Fraction 5 gave 29 mg. of an oil, which had an infrared spectrum identical with IVa, $[\alpha]^{25}D$ +95.7° (*c* 0.51). The yield of IVa was 44 mg. (10.2%).

Continued elution with *n*-pentane (fractions 6–8) gave the 6β-azide IIIa (135 mg., 31.2%). The sample had m.p. 68–70° with softening at 66°, $[\alpha]^{25}D$ +48.2° (*c* 1.00).

Further elution with *n*-pentane gave II (51 mg., 11.8%), m.p. 104–111°. The mixture melting point with authentic II was 110–114°.

Finally, elution with *n*-pentane gave 80 mg. (18.6%) of the 3β-azide Ib (m.p. 84–86°). The melting point was undepressed on mixing with authentic Ib.

6α-Azido-3α,5α-cyclocholestane (IVa).—Cholesteryl 3β-*p*-toluenesulfonate (10.0 g., 0.018 mole) was converted to 7.4 g. of crude azide product by the DMSO procedure. Chromatography over Florisil afforded 300 mg. of pure IVa. The 6α-azide IVa had m.p. 39–42°; $[\alpha]^{25}D$ +106° (*c* 1.05); ν_{max} 3069, 3028, 3002 (cyclopropyl), and 2100 cm.$^{-1}$ (N_3 asymmetric stretch); δ = 3.72 (6-H quartet, J_{ae} = 4.6 c.p.s. and J_{aa} = 12.0 c.p.s.) and 0.0–0.60 (cyclopropyl) p.p.m.

Anal. Calcd. for $C_{27}H_{45}N_3$: C, 78.75; H, 11.02; N, 10.21. Found: C, 78.80; H, 11.13; N, 10.07.

6α-Acetamido-3α,5α-cyclocholestane (IVb).—To a solution of 93.4 mg. of IVa in 20 ml. of absolute ether was added 96 mg. of powdered lithium aluminum hydride. The mixture was stirred

(25) Melting points were taken with a Thomas–Hoover Unimelt and are corrected. Infrared spectra were determined in carbon tetrachloride solution or, as stated, on a Perkin-Elmer Model 421 spectrophotometer. Optical rotations were determined on a Hilger and Watts polarimeter in chloroform solutions. N.m.r. spectra were recorded with a Varian Associate Model A-60 spectrophotometer.

(26) R. Huisgen and I. Ugi, *Chem. Ber.*, **90**, 2914 (1957).

(27) Florisil, obtained from the Floridin Co., is the trade name for a chromatographic grade of magnesium silicate.

(28) W. Stoll, *Z. physiol. Chem.*, **207**, 147 (1932).

(29) Reference 8, p. 15.

at 25° for 1.5 hr., and excess lithium aluminum hydride was decomposed with wet ether. The mixture was filtered to remove insoluble salts and the filtrate was washed with 50 ml. of water. The ether was separated and dried over potassium hydroxide pellets. Evaporation of the ether gave 86 mg. of an oil which was acetylated by dissolving in a mixture of 6.2 ml. of pyridine and 4.9 ml. of acetic anhydride and allowing the solution to stand overnight at 25°. Excess acetic anhydride was decomposed by addition of ice, and the mixture was diluted with water. The product was extracted with ether, and the ether was washed successively with dilute hydrochloric acid, dilute sodium hydroxide, and water. The ether was dried over magnesium sulfate and evaporated to give 84 mg. of crude product. Crystallization from acetone afforded 61 mg. of IVb which had m.p. 217–220°; $[\alpha]^{24}D$ +81.6° (*c* 0.84) (lit.[12] m.p. 213°, $[\alpha]D$ +72°); $\nu_{max}^{CHCl_3}$ 3450 (N-H) and 1685 (amide C=O) cm.$^{-1}$; δ = 5.01 (N-H), 4.25 (6-H), and 0.50–0.0 (cyclopropyl) p.p.m.

Anal. Calcd. for $C_{29}H_{49}NO$: N, 3.28. Found: N, 3.49.

Attempted Isomerization of IIIa under the Reaction Conditions.—To a mixture of 4.0 g. of sodium azide and 320 mg. of *p*-toluenesulfonic acid (m.p. 103–107°) in 60 ml. of NMA was added 96.4 mg. of the 6β-azide IIIa. The mixture was heated with stirring at 87° for 4.5 hr. The mixture was cooled, diluted with 200 ml. of water, and extracted with ether. The ether was washed with water and was dried over magnesium sulfate. Evaporation of the ether gave 93.6 mg. of IIIa, m.p. 66–68° with softening at 63°, $[\alpha]^{25}D$ +43.1° (*c* 0.76).

Acknowledgment.—The author wishes to thank the following members of the staff of Abbott Laboratories for their contributions to this work: Mr. O. Kolsto and co-workers for microanalyses, Dr. R. W. Mattoon and Mr. R. Kriese for n.m.r. spectra, and Mr. W. Washburn and Mrs. A. Ward for infrared spectra. The author is also indebted to Dr. John Tadanier for helpful discussions.

The Bromine and N-Bromosuccinimide Oxidation of the Saturated Hydrocarbon, Friedelane[1,2]

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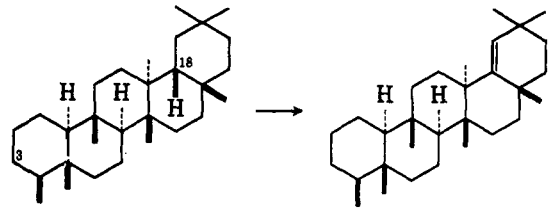
The mechanism of allylic and benzylic bromination by N-bromosuccinimide (NBS) first proposed 20 years ago postulated a free-radical chain mechanism involving the succinimide radical as the chain-carrying species[3,4] and the radical-chain character of the reaction was established by later mechanistic studies.[5] An alternative mechanism, proposed by Goldfinger,[6–8] indicated that the function of the NBS was to provide molecular bromine at very low concentration. In the case of *allylic* substitution, strong evidence in favor of this latter mechanism has been provided by Sixma[9] and by Tedder[10] and, in the case of *benzylic* bromination, by Martin[11] and Russell[12] and their colleagues. From this work, it appears that the bromine atom, rather than the succinimide radical, is the hydrogen-abstracting species. Furthermore, Skell[13] has recently provided evidence that in the NBS bromination of alkyl bromides the intermediate alkyl radical does not react with NBS but presumably bromine to complete the bromination process.

We have reported[14,15] that the *saturated* hydrocarbon, friedelane (I), is oxidized by NBS to the olefin, friedel-18-ene (II). In view of the likelihood that the function



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of NBS in this reaction also is to provide molecular bromine (under our conditions an orange color appeared after 12-min. reflux of the reactants in carbon tetrachloride and faded rapidly), we sought to compare the action of bromine on I in carbon tetrachloride solution. The experimental conditions for this comparison are conveniently noncritical, since the special techniques (prevention of high local halogen concentration and efficient removal of hydrogen halide) usually necessary[10] in the reaction of bromine with an olefin to effect allylic bromination rather than halogen addition, are here unnecessary.

A solution of bromine in carbon tetrachloride added to friedelane was decolorized, and the reaction mixture, when worked up as previously described[15] in the NBS reaction, yielded friedel-18-ene in comparable yield. This demonstrates that in this highly selective oxidation, the intermediacy of the succinimide radical is unessential. The yield of friedel-18-ene from friedelane was shown to be 40% by peracid titration and isolation of the derived epoxide. No unchanged friedelane was recovered by chromatographic examination. There was isolated, in addition, however, an unstable bromofriedelane which readily yielded friedel-18-ene and is consequently considered to be an 18-bromofriedelane.

It now appears likely that the discrepancies and poor reproducibility reported[15] in the bromination of the 3-ketone, friedelin, particularly in the formation of di- and tribromo derivatives at C-2 and/or C-4, may be attributed to accompanying halogenation at C-18.

Experimental

Action of Bromine on Friedelane. A.—A solution of friedelane (50 mg., 0.121 mmole) in carbon tetrachloride (20 ml.) was heated under reflux by an infrared lamp, and bromine (17.5 mg., 0.0975 mmole) in carbon tetrachloride (2 ml.) was added dropwise until the color of bromine persisted. After heating for 30 min., the mixture was cooled, washed with water, sodium hydrogen car-

(1) This is regarded as Part VII in the series, Friedelin and Related Compounds. Part VI: R. Stevenson, *J. Org. Chem.*, **28**, 188 (1963).

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