ether in *n*-hexane afforded 1.1 g of **15**. The estimated yield of **15** from **13** was 67%: ir (neat) 2970, 2930, 1640, 1440, 1375, 1300, 1260, 840, 710 cm^{-1}; uv max (95% EtOH) 260 mμ (ϵ 18,900) and 267 (19,100) [lit.[17] uv max (95% EtOH) 259 mμ (ϵ 17,200) and 266 (17,200)]; nmr (CCl$_4$) δ 1.65 and 1.71 [2 s, 6, =C(CH$_3$)$_2$], 1.93 (s, 9, 3 CH$_3$), 3.10 (d, 2, J = 7.5 Hz, CH$_2$), 4.89 (t, 1, J = 7.5 Hz, CH=).

Anal. Calcd for $C_{14}H_{18}O$: C, 77.03; H, 8.31. Found: C, 76.83; H, 8.51.

6-Bromo-2,3-dimethoxy-5-methylbenzoquinone (**16**).—To a stirred solution of 10.6 g (0.058 mol) of **2**[18] in 120 ml of carbon tetrachloride was added dropwise 10.5 g (0.068 mol) of bromine at room temperature. The reaction mixture was stirred for 2 hr, treated with water, dried with magnesium sulfate, and evaporated. The dark residue was washed with a very small quantity of ethanol until the color of crystals turned to red and recrystallized from petroleum ether to afford 11.2 g (74%) of **16**: mp 73–74°; ir (KBr) 2850, 1650, 1600, 1280 cm^{-1}.

Anal. Calcd for $C_9H_9O_4Br$: C, 41.41; H, 3.47. Found: C, 41.26; H, 3.62.

6-Bromo-2,3-dimethoxy-5-methylhydroquinone (**17**).—The quinone **16** (5.0 g) was dissolved in warm methanol and to this solution was added warm aqueous sodium hydrosulfite until the red color of the solution disappeared. Removal of methanol under reduced pressure in a stream of nitrogen afforded 4.3 g (83%) of **17**: mp 73–74°; ir (KBr) 3300, 2880, 1450, 1420, 1280, 1105, 1070, 1000, 910 cm^{-1}; nmr (CCl$_4$) δ 2.21 (s, 3, CH$_3$), 3.84 and 3.88 (2 s, 6, 2 OCH$_3$), 5.14 and 5.27 (2 s, 2, 2 OH).

Anal. Calcd for $C_9H_{11}O_4Br$: C, 41.09; H, 4.21. Found: C, 40.81; H, 4.43.

6-Bromo-2,3-dimethoxy-5-methylhydroquinone Bis(methoxymethyl) Ether (**18**).—To a stirred solution of 6.0 g (0.023 mol) of **17** in 150 ml of absolute ethanol was added dropwise 0.6 g (0.025 mol) of sodium in 13 ml of absolute ethanol and then 2.0 g (0.025 mol) of chloromethyl methyl ether at −10 to 0° under a stream of nitrogen, and then 1.8 g of sodium in 39 ml of absolute ethanol and 6.0 g of chloromethyl methyl ether were added by the same method described in the preparation of **13**. The reaction mixture was stirred for 3 hr at −10 to 0°, filtered, and concentrated under reduced pressure in a stream of nitrogen. The concentrated solution was washed with dilute aqueous potassium hydroxide and water and extracted with ether. The extract was dried with magnesium sulfate, freed of solvent, and chromatographed on silica gel. Elution with 30% isopropyl ether in *n*-hexane afforded 6.7 g (83.2%) of **18**: $n^{20}\text{D}$ 1.5282; ir (neat) 2800, 1460, 1405, 1380, 1160, 1000, 965 cm^{-1}; nmr (CCl$_4$) δ 2.29 (s, 3, CH$_3$), 3.48 and 3.56 (2 s, 6, 2 OCH$_2$OCH$_3$), 3.79 (s, 6, 2 OCH$_3$), 4.93 and 4.98 (2 s, 4, 2 OCH$_2$O).

Anal. Calcd for $C_{13}H_{19}O_6Br$: C, 44.33; H, 5.72. Found: C, 44.52; H, 5.53.

2,3-Dimethoxy-5-methyl-6-(3-methyl-2-butenyl)benzoquinone (Coenzyme Q_1) (**20**).—**9** was prepared from 4.5 g (0.03 mol) of **8** and 8.7 g (0.05 mol) of nickel carbonyl by the same method described above. To the solution of **9** in 36 ml of HMPA was added 5.4 g (0.015 mol) of **18** in 20 ml of HMPA at room temperature. The reaction mixture was warmed to 60° and stirred for 12 hr. The solution was treated with water containing a small quantity of ammonia and ammonium chloride, filtered, and extracted with petroleum ether. The extract was washed with water, dried with magnesium sulfate, and freed of solvent, affording a residual liquid (4.9 g) which consisted of **18** (43%) and **19** (57%) by nmr assay.[19] This liquid was chromatographed, but **19** could not be isolated. A 3-g portion of the liquid was dissolved in 50 ml of methanol containing a drop of hydrochloric acid. The solution was refluxed for 1 hr, cooled, neutralized with alcoholic potassium hydroxide, and freed of solvent. The residue was dissolved in 15 ml of ether, oxidized with aqueous ferric chloride, and extracted with ether. The extract was washed with water, dried with magnesium sulfate, and freed of solvent to afford a reddish oil, which was chromatographed on silica gel. Elution with 20% isopropyl ether in *n*-hexane afforded 0.89 g of **20**. The estimated yield of **20** from **18** was 40%: ir (neat) 2950, 1650, 1460, 1270, 1100, 1020 cm^{-1}; uv max (*n*-hexane) 270 mμ (ϵ 15,100); nmr (CCl$_4$) δ 1.65 and 1.73 [2 s, 6, =C(CH$_3$)$_2$], 1.94 (s, 3, CH$_3$), 3.08 (d, 2, J = 7.5 Hz, CH$_2$), 3.89 (s, 6, 2 OCH$_3$), 4.82 (t, 1, J = 7.5 Hz, CH=).

Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.28; H, 7.39.

Registry No.—**10,** 4489-84-3; **11,** 1200-09-5; **13,** 34417-76-0; **15,** 2134-78-3; **16,** 30685-17-7; **17,** 34417-79-3; **18,** 34407-31-3; **20,** 727-81-1.

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[19] As a result of comparison with the nmr spectrum of **18**, chemical shifts of protons in **19** are as follows: δ (CCl$_4$) 1.67 and 1.73 [2 s, =C-(CH$_3$)$_2$], 2.09 (s, CH$_3$), 3.28 (d, CH$_2$), 3.47 (s, 2 OCH$_2$OC**H**$_3$), 3.67 (s, 2 OCH$_3$), 4.90 (s, 2 OCH$_2$O), 5.09 (m, =CH).

Synthesis of Steroidal Aziridines

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Desmostanyl 3α-acetate (**5**) was synthesized from litocholic acid and converted into the aziridine **8**, the essential steps being addition of iodine isocyanate to **5** which was converted to the corresponding carbamate **7**. Treatment of **7** with alcoholic base formed the aziridine **8**. Analogous sequence of reactions led to the formation of aziridine **9** from stigmasteryl acetate.

It has been reported recently that the aziridine functional grouping shows favorable carcinostatic activity in a number of tumor systems.[1] Most of the compounds reported to date have had the nitrogen mustard group attached to certain positions on the nucleus of the steroid. In connection with our work on the utilization of natural sterols and their derivatives by insects,[2] it was of interest to synthesize some steroidal aziridines having the nitrogen function in the side chain of the steroid.[3]

In the present communication we report the synthesis of 5,6-dihydro-24,25-iminodesmostanyl acetate (**8**) and 22,23-iminostigmasteryl acetate (**9**). Desmostanyl 3α-acetate (**5**) was readily obtained by the photochemical Wolff rearrangement in a THF–methanol solution of diazo ketone **2**[4] to give the methyl ester **3**. Grignard reaction of **3** with methylmagnesium iodide and subsequent dehydration[5] yielded **5**. Addition of iodine isocyanate[6] to **5** gave the adduct **6**,[7]

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[1] S. A. Dyogtera, *Angew. Chem., Int. Ed. Engl.*, **1**, 600 (1962).

[2] R. Ikan, A. Markus, P. Klein, Z. Levinson, and E. D. Bergmann, *J. Insect Physiol.*, submitted for publication.

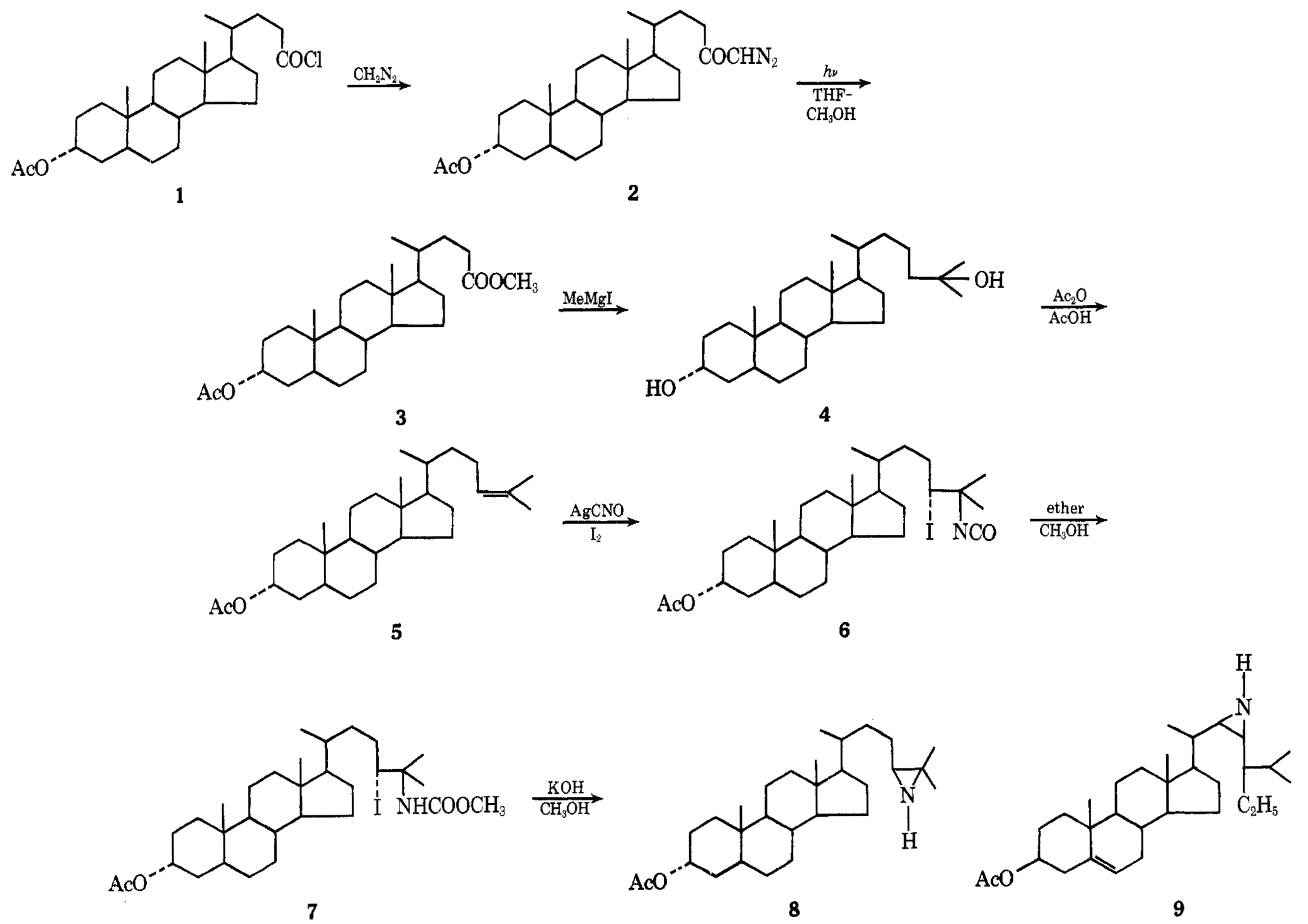
[3] Preliminary tests have indicated that the new aziridines caused total mortality of the larvae of *Dermestes maculatus*.

[4] A. S. Kende and Z. Goldschmidt, *Org. Photochem. Syn.*, **1**, 92 (1971).

[5] G. Habermehl and G. Volkwein, *ibid.*, **742**, 145 (1970).

[6] A. Hassner, M. E. Lorber, and C. Heathcock, *J. Org. Chem.*, **32**, 540 (1967).

[7] Structure **6** was tentatively assigned on the basis of the previous studies of INCO addition to olefins.[6]



which was converted with methanol to the corresponding methyl iodocarbamate **7**. Treatment of **7** with ethanolic potassium hydroxide readily effected the ring closure to form the expected aziridine **8**. The parallel synthesis using stigmasteryl acetate and iodine isocyanate yielded the aziridine **9**.

Experimental Section[8]

Methyl Homolitocholate 3α-Acetate. (**3**).—To a solution of 10 g of litocholic acid 3α-acetate in 100 ml of dry benzene, 3.5 g of oxalyl chloride was added dropwise. The mixture was refluxed for 3 hr, benzene was removed under reduced pressure, and the residue was triturated with dry petroleum ether (bp 30–60°), leaving 9 g of solid residue of litocholyl chloride 3α-acetate (**1**), which was dissolved in 100 ml of benzene and added dropwise at 5° to a dry ethereal solution of diazomethane (prepared from 40 g of nitrosomethylurea). The mixture was left overnight at room temperature and the ether was evaporated, leaving the diazo ketone **2** as yellowish crystals (9 g): ν_{max} 2100 (–$COCHN_2$), 1725 cm^{-1} (–$COOCH_3$); λ_{max} 253 mμ (ε 20,000) and 310 (9000). Diazo ketone **2** (9 g) was dissolved in 160 ml of tetrahydrofuran and 40 ml of methanol, and the solution was irradiated in a Pyrex vessel, using a Hanovia Q-81 high-pressure burner immersion lamp until no nitrogen was evolved. The solution was concentrated *in vacuo*, and the residue was chromatographed on a Florisil (200 g) column. The products were eluted with 100 ml each of solutions of benzene in hexane with concentrations of 10, 20, 40, and 50% (v/v), followed by solutions of chloroform in benzene, 10, 20, 40, and 50% (v/v), and finally with chloroform. Fractions which contained the desired product (as detected by tlc) were pooled, concentrated, and recrystallized from methanol: mp 69–70°; yield 6.3 g (71%); $[\alpha]^{20}{}_{D}$ +46.9° (*c* 1.0); ν_{max} 1725 cm^{-1}.

Anal. Calcd for $C_{28}H_{46}O_4$: C, 75.3; H, 10.3. Found: C, 75.4; H, 10.4.

25-Hydroxycholestan-3α-ol (**4**).—To the Grignard reagent prepared from 3 g of magnesium and 19.2 g of methyl iodide in 50 ml of ether, 8 g of **3** in 50 ml of dry benzene was added dropwise and the mixture was refluxed for 1 hr. Ether was distilled off and then the mixture was refluxed for a further 4 hr and allowed to stand overnight at room temperature. Hydrochloric acid (5%) was added and the product was extracted with benzene. Distillation of benzene and recrystallization of the residue from methanol yielded 5.2 g (70%) of the product melting at 130–132°, ν_{max} 3350 cm^{-1} (–OH), $[\alpha]^{25}{}_{D}$ +30.2° (*c* 1.0).

Anal. Calcd for $C_{27}H_{48}O_2$: C, 80.6; H, 11.4. Found: C, 80.4; H, 11.5.

5,6-Dihydrodesmostanyl 3α-Acetate (**5**).—25-Hydroxycholestan-3α-ol (5.7 g), 270 ml of acetic acid, and 27 ml of acetic anhydride were refluxed for 20 hr.[5] The cooled solution was concentrated *in vacuo* and the residue was treated with 500 ml of water. The oily product was extracted with benzene and chromatographed on a Florisil (100 g) column. The product was recrystallized from acetone: mp 93°; yield 4.1 g (70%); $[\alpha]^{25}{}_{D}$ +47.5°; ν_{max} 1720 cm^{-1}; nmr δ 2.0 (–$COOCH_3$ s), 5.2 (–HC=C<, m).

Anal. Calcd for $C_{29}H_{48}O_2$: C, 81.3; H, 11.2. Found, C, 81.6; H, 11.4.

24,25-Iminodesmostanyl Acetate (**8**).—5,6-Dihydrodesmostanyl 3α-acetate (1.5 g) was dissolved in 20 ml of anhydrous ether, and 1.8 g of silver cyanate was added.[9] The suspension was cooled in an ice–salt bath while being stirred magnetically. When the slurry had cooled to −15°, 1 g of solid iodine was added and the stirring was continued for 2 hr in the cold and then for 6 hr at room temperature. At the end of the reaction, the slurry had a bright canary yellow color. The ether solution was filtered through Celite to remove the yellow inorganic salts, then evaporated in the cold. There was obtained 1.7 g (80%) of light tan solid, mp 125°, ν_{max} 2260 (–N=C=O), 1720 cm^{-1}

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(8) Melting points were determined on a Thomas-Hoover apparatus. Optical rotations were measured in chloroform. Nmr spectra were recorded for deuteriochloroform solutions using a Varian HA-100 spectrometer. Infrared spectra were recorded on a Perkin-Elmer 137 spectrometer using Nujol oil, and ultraviolet spectra were recorded on a Unicam SP-800 spectrophotometer using ethanol.

(9) A. Hassner and C. Heathcock, *J. Org. Chem.*, **30**, 1748 (1965).

(-COOCH$_3$), which was dissolved in 50 ml of 1:1 ether–methanol and refluxed for 4 hr. The solvent was distilled off and the residue was recrystallized from methanol to give 1.5 g (80%) of **7**: mp 96–97°; ν_{max} 3430, 1740, 1725, 1520, 1225, 775, 648 cm^{-1}; λ_{max} 265 mμ (ϵ 480); nmr δ 4.8–5.2, 3.6 (-OCH$_3$).

A solution of 1.5 g of the carbamate **7** and 5 g of potassium hydroxide in 50 ml of ethanol and 5 ml of water was refluxed for 30 min.[10] The solution was cooled to room temperature and poured into water. The turbid solution was extracted with benzene, washed thoroughly with water, dried over magnesium sulfate, and filtered and the solvent was evaporated. The residue crystallized upon standing: mp 88–89°; yield 0.8 g (70%); $[\alpha]^{25}\text{D}$ +21°; ν_{max} 1730 cm^{-1}; molecular ion *m/e* 383 (calcd, 383).

Anal. Calcd for $C_{29}H_{49}NO_2$: N, 3.1. Found: N, 2.9.

22,23-Iminostigmasteryl Acetate (9).—The reactions were carried out analogously to the preparation of **8**. Thus addition of INCO to stigmasteryl acetate in dry THF gave a 79% yield of an adduct (ν_{max} 2260 and 1725 cm^{-1}). Treatment of the adduct with methanol gave a 90% yield of the iodo carbamate: mp 128°; ν_{max} 3430, 1740, 1725, 1520, 1227, 775, 648 cm^{-1}; λ_{max} 265 mμ (ϵ 450); nmr δ 5.6 (H , broad doublet), 5.0 (NH), 4.8 (CHI), multiplet), 4.2 (CHNHCOOCH$_3$, multiplet). The aziridine **9** was obtained in 90% yield: mp 88–89°; $[\alpha]^{25}\text{D}$ −24.5°; ν_{max} 3270 cm^{-1} (-NH); molecular ion *m/e* 409 (calcd, 409).

Anal. Calcd for $C_{31}H_{51}NO_2$: N, 3.2. Found: N, 3.1.

Registry No.—**3**, 34389-06-5; **4**, 34389-07-6; **5**, 34389-08-7; **6**, 34389-09-8; **7**, 34389-10-1; **8**, 34388-68-6; **9**, 34388-69-7.

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The Stereochemistry of Azetidine Deaminations. On the Nature of the Trimethylene Intermediate

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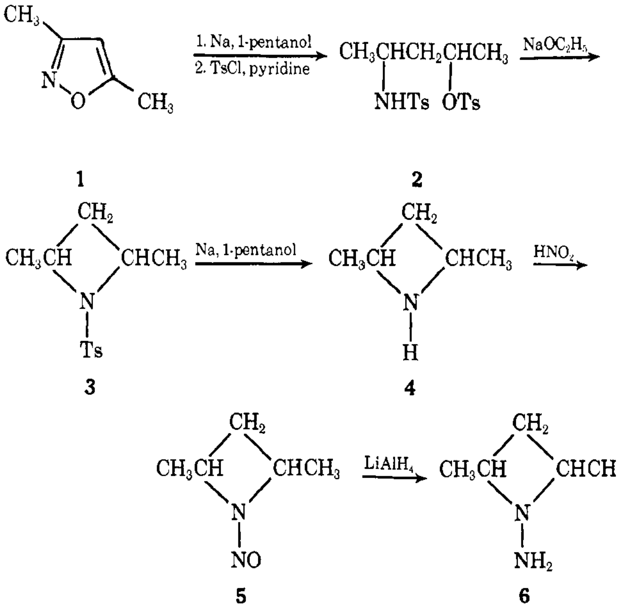
Pure stereoisomers of 2,4-dimethylazetidine (**4**), *N*-nitroso-2,4-dimethylazetidine (**5**), and *N*-amino-2,4-dimethylazetidine (**6**) were prepared. Reaction of *cis*-**4** with difluoramine, of *cis*-**5** with sodium dithionite, and of *cis*-**6** with mercuric oxide produced virtually identical mixtures of *cis*- and *trans*-1,2-dimethylcyclopropanes (**7**), in which *trans*-**7** predominated, thus indicating that these deaminations proceed through a common diazene intermediate. Analogous reactions of *trans*-**5** and *trans*-**6** yielded *cis*-**7** and *trans*-**7** in the ratio of 68:32. It is proposed that a mechanism involving a planar trimethylene intermediate could account for the stereochemical crossover and for the differences in the product distribution between azetidine deaminations and 1-pyrazoline pyrolyses, but that a superposition of "quasi-concerted" processes may offer a more attractive rationalization.

The trimethylene diradical has frequently been invoked[3] as an intermediate in the isomerization of cyclopropanes[3–6] and in the decomposition of 1-pyrazolines.[3,7,8] Since trimethylenediazene is known[12] to afford cyclopropane and nitrogen under very mild conditions and since the electronic structure of trimethylene is thought[10] to depend critically on the CCC angle, we considered it worthwhile to investigate the stereochemistry of azetidine deaminations.

The synthesis of the starting materials **4**, **5**, and **6** is outlined in Chart I. A crystalline diastereomer of mp 120–120.5° could be obtained from the oily mixture of ditosylates **2** by fractional recrystallizations from methanol. By implication, this must be *threo*-**2**, since it yields pure *cis*-**3** on treatment with sodium ethoxide in ethanol. The stereochemistry of *cis*-**3** is rigorously established by its nmr spectrum, which exhibits three complex groups of signals for the ring protons, centered at about δ 1.3 (1 H), 2.1 (1 H), and 3.65 (2 H). The stereochemical purity of *cis*-**3** follows from its conversion to *cis*-**4** and *cis*-**5**, the latter containing less than 0.3% *trans*-**5** as shown by vpc analysis.

The mother liquors of **2**, enriched in the erythro diastereomer, were subjected to an analogous reaction sequence and afforded a mixture consisting approxi-

CHART I



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[1] This work is based on a dissertation submitted by D. G. P. in partial fulfillment of the requirements for the Ph.D. degree at the University of Notre Dame.

[2] Alfred P. Sloan Research Fellow.

[3] For the extensive earlier literature on this problem and for the intriguing history of the ideas consult the bibliography in ref 4–11.

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