Reductive Opening of Conjugated Cyclopropyl Ketones with Lithium in Liquid Ammonia[1]

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The reductive opening with lithium in liquid ammonia of a cyclopropane ring of a conjugated cyclopropyl ketone which is part of a bicyclo[3.1.0]hexane or bicyclo[4.1.0]heptane system is shown to proceed in a highly stereospecific manner. The cyclopropane bond which is cleaved is the one possessing the maximum overlap with the π-orbital system of the carbonyl group. The reaction offers a new method for the stereospecific introduction of angular methyl groups. In highly strained systems, the reductive opening does not always follow the foregoing simple generalization.

In recent years there has been much discussion pertaining to the conjugative properties of a cyclopropane ring with an adjacent unsaturated center.[2-4] The primary concern has been centered about the geometrical requirement for such a conjugative interaction and this requirement has principally been measured by effects on the electronic spectrum of the unsaturated center. It, therefore, was of interest to evaluate this same geometrical problem in a ground-state chemical reaction.

In 1949, Boord and co-workers[5] reported that methyl cyclopropyl ketone was reduced to a mixture of 2-pentanone and 2-pentanol with sodium in liquid ammonia in the presence of ammonium sulfate. In 1963, Norin[6] in his studies related to the determination of the structure of thujopsene noted that the simple, completely rigid cyclopropyl ketone system in **1** was transformed by lithium in liquid ammonia in almost quantitative yield to the related methyl derivative **2**. Later,

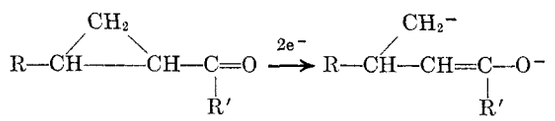
1 **2**

Burns, Davies, and Petrow[7] in synthesizing some 3-keto-4-ene 19-norsteroids *via* a Birch reduction reported that the 16α,17α-methano ring of a 20-keto steroid was transformed to a 16α-methyl group. Whether such a specificity was a general reaction for the cyclopropyl conjugated system was open to question since in the reduction of a related extended cyclopropyl-ene-one chromophoric system in **3**[8,9] with lithium in liquid ammonia only the double bond was reduced to give **4**.

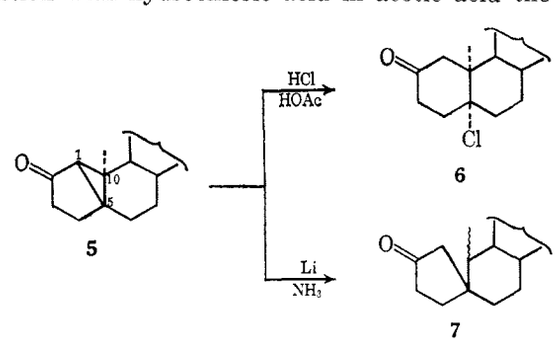
3 **4**

The scope of this reductive method for opening of a cyclopropane conjugated system has now been investigated and the specificity of the reaction has been evaluated. Attention has been directed only toward the cyclopropyl-one system. It has been found that the course of the reaction is controlled by the steric configuration of the molecule and that bond of the cyclopropane ring which better overlaps the π-bond system of the adjacent unsaturated center is the bond which is reductively cleaved. A similar generalization recently was published by Norin[10] and the present work extends the generality of the reaction.

The reaction of a conjugated cyclopropyl ketone with lithium in liquid ammonia can be viewed as an over-all two-electron reduction to yield the equivalent of a carbanion and an enolate ion. If such a process were controlled by thermodynamic considerations, the reduction should break that cyclopropane bond leading to the more stable carbanion (least substituted carbon) and in the earlier mentioned examples such was the case. However, examination of a model of ketone **1** indicated that the cyclopropane bond which was broken not only led to a primary carbanion but was also that bond which better overlapped the π system of the adjacent carbonyl group. The steric *vs.* thermodynamic control of the reaction was evaluated in the following manner.



Lumicholestenone (**5**), a photoproduct of cholestenone,[11] upon reaction could break either the C_1–C_5 or the C_1–C_{10} bond and in either case a tertiary center would be formed. It has been reported[11] that upon reaction with hydrochloric acid in acetic acid the 1,5



5 **6** **7**

(1) This work was supported in part by Public Health Service Grant No. CY-04284, National Cancer Institute, U. S. Public Health Service.

(2) N. H. Cromwell and G. V. Hudson, *J. Am. Chem. Soc.*, **75**, 872 (1953).

(3) E. M. Kosower and M. Ito, *Proc. Chem. Soc.*, 25 (1962).

(4) A. L. Goodman and R. E. Eastman, *J. Am. Chem. Soc.*, **86**, 908 (1964).

(5) R. V. Volkenberg, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *ibid.*, **71**, 3595 (1949).

(6) T. Norin, *Acta Chem. Scand.*, **17**, 738 (1963).

(7) D. Burns, M. T. Davies, and V. Petrow, *Steroids*, **3**, 583 (1964).

(8) R. B. Bates, G. Büchi, T. Matsuura, and R. R. Schaffer, *J. Am. Chem. Soc.*, **82**, 2327 (1960).

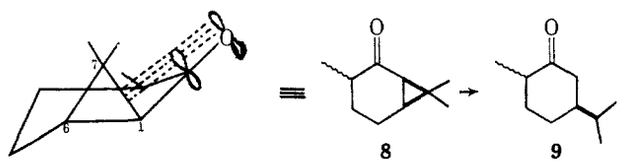
(9) See also R. E. Corbett and R. N. Speden, *J. Chem. Soc.*, 3710 (1958).

(10) T. Norin, *Acta Chem. Scand.*, **19**, 1289 (1965).

(11) B. A. Shoulders, W. W. Kwie, W. Klyne, and P. D. Gardner, *Tetrahedron*, **21**, 2973 (1965).

bond breaks to yield the chloride **6**. Sterically, the 1,10 bond better overlaps the π system of the carbonyl group and when **5** was allowed to react with lithium in liquid ammonia the spiro ketone **7**, 1(10→5α)-abeocholestane-2-one, was formed in high yield and no other product could be detected. Thus, **5** opened singularly in the direction of maximum overlap and no competition between the two tertiary centers was found. The stereochemistry of C_{10} in **7** was not established.

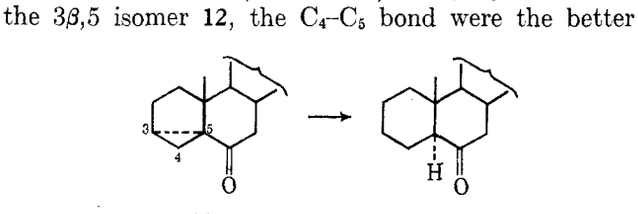
To further corroborate the steric overlap control of this reduction reaction, competition between various potential carbanions was evaluated. The first case studied was (+)-carone (**8**), an example in the bicyclo[4.1.0]heptane ring system. Owing to the geom-



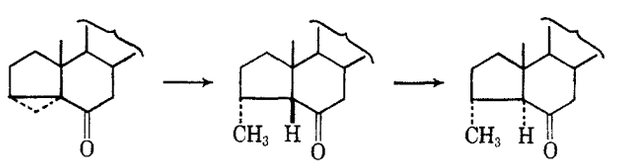
8 **9**

etry of the ring system, the internal C_1–C_6 bond does not overlap to any great extent with the π system of the carbonyl group, whereas the external C_1–C_7 bond is so placed to permit excellent overlap. Breaking the internal, nonoverlapping C_1–C_6 bond would lead to the more stable secondary carbanion, whereas cleavage of the external, overlapping C_1–C_7 bond would yield the less stable tertiary carbanion. It was found that upon reaction of a mixture of *cis* and *trans* carones (isomeric methyl groups) with lithium in liquid ammonia only cleavage of the external overlapping bond of the cyclopropane ring occurred to yield the known (−)-carvomenthone **9** and (−)-isocarvomenthanone. A similar result has been obtained by Norin.[10]

The next cases studied were the isomeric 3α,5- and 3β,5-cyclocholestan-6-ones, examples of a spiro[5.2]-octane ring system. Examination of models clearly showed that in the 3α,5 isomer **10**, the C_3–C_5 bond and in the 3β,5 isomer **12**, the C_4–C_5 bond were the better

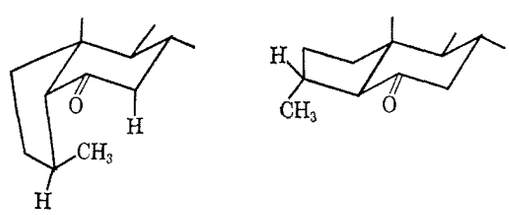


10 **11**



12 **13** **14**

overlapping bonds. A similar carbanion stability competition as in carone can be seen in these compounds. Lithium in liquid ammonia treatment of **10** produced only the known cholestan-6-one **11**; no trace of the other bond cleavage product or of the lesser stable C_5 epimer, coprostan-6-one could be detected before or after column chromatography.[12] Reduction of the 3β,5 isomer **12** yielded a ketonic product which possessed a single carbonyl absorption at 1695 cm^{-1}, due to **13**. When this material was chromatographed on alumina, however, the early eluates yielded the isomeric ketone **14** which displayed an absorption at 1718 cm^{-1}. Subsequent fractions possessed two absorptions bands at 1718 and 1695 cm^{-1}, and finally ketone **13** was eluted as a single material. The nmr spectrum of each pure compound displayed an additional methyl doublet (τ 9.00 and 9.03, respectively) not present in the spectrum of the starting material. These spectral data show that the two materials are isomeric 3α-methyl-A-norcholestan-6-ones. The specific stereochemistry of the A/B ring juncture follows from an evaluation of the ORD spectra. Ketone **13** possesses a specific rotation at its trough (322 mμ, α −1070°) just twice that of ketone **14** (doublet, 317 mμ, α −535°; 307 mμ, α −412°). A similar intensity relationship has been reported for coprostan-6-one and its A/B *trans* isomer.[13] Moreover, both *trans* isomers **11** and **14** are characterized by a doublet in their trough, whereas **13** possesses a single trough. Since it is well established[14] that the size of the ring not containing the carbonyl group causes only a change in amplitude and not in the sign of the Cotton effect, these amplitudes and multiplicity patterns clearly establish **13** as A/B-*cis* and **14** as the *trans* isomer. Thus, with the 3α,5-cyclo isomer **10** in which a decalin ring containing a 10β-methyl group is formed, both kinetic and thermodynamic controlled protonation work in the same direction to yield the stable 5α-*trans* isomer **11**. With the 3β,5-cyclo isomer **12** in which a dimethylhydrindane ring system is formed, apparently the kinetic controlled protonation during work-up gives rise to the 5β-*cis* isomer **13** which is not the thermodynamically stable isomer. When a 1:1 mixture of **13** and **14** was allowed to stand in ethanolic potassium hydroxide, the product obtained in 92% yield was pure *trans* **14**. Such as result is of interest since in the previously reported 6-keto[15] and 3-keto A-nor-steroids[16] the *cis* isomer was the more stable material. The greater stability of the *trans* **14** must be ascribed to the unfavorable interaction of the 3α-methyl group in the *cis* isomer **13**. This placement of the 3α-methyl group also must be responsible for the abnormally low carbonyl frequency in **13** since such shifts are known to occur when a carbonyl group is in a highly alkylated environment.



13 **14**

In the foregoing three examples it is seen that the lithium in liquid ammonia reduction reaction cleaved that bond of the cyclopropane ring possessing the maximum of orbital overlap with the π system of the carbonyl group, regardless of the relative stability of the

(12) D. N. Jones, J. R. Lewis, C. W. Shoppee, and G. H. R. Summers, *J. Chem. Soc.*, 2876 (1955).

(13) C. Djerassi, *Bull. Soc. Chim. France*, 741 (1957).

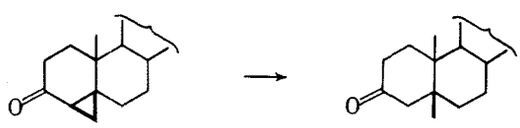
(14) C. Djerassi and J. E. Gurst, *J. Am. Chem. Soc.*, **86**, 1755 (1964).

(15) W. G. Dauben and G. A. Boswell, *ibid.*, **83**, 5003 (1961).

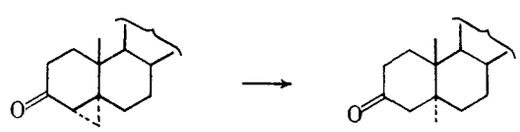
(16) J. Fried, French Patent 1,366,305 (1965); *Chem. Abstr.*, **62**, 2810 (1965).

various potential saturated carbanions which could have been formed. This generalization cannot, as yet, be applied to carbanions of highly different stabilities, say competition between an alkyl and an allyl, and this problem is now under investigation.

Next, it was of interest to investigate the general preparative synthetic aspects of this highly stereospecific reaction since all the compounds studied above afforded a single product in nearly quantitative yield. The isomeric 4,5-methano steroids **15** and **17** were studied and the same arguments for the direction of cleavage as mentioned for carone can be applied here. Both materials upon reaction with lithium in liquid

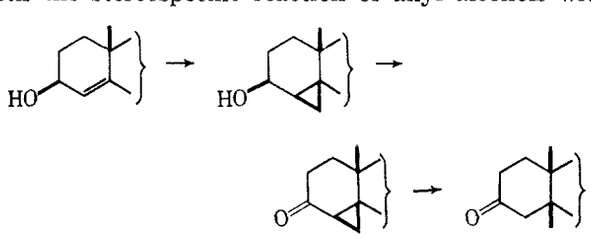


15 **16**



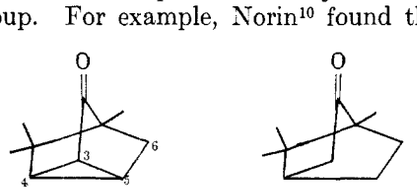
17 **18**

ammonia gave in high yield a single product, **16** and **18**, respectively. The structures of the products were confirmed by their comparison with authentic samples. Thus, again the conjugative overlap prediction was proven valid. This reduction reaction, when coupled with the stereospecific reaction of allyl alcohols with



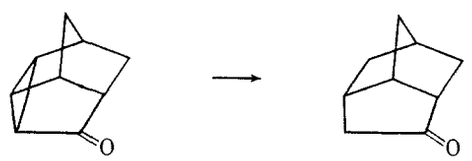
the Simmons Smith reagent,[17,18] is a new stereospecific reaction for the introduction of angular methyl groups (or methyl groups, in general) and it appears to be generally superior to methods previously employed for such additions to an α,β-unsaturated carbonyl system.[19,20]

When the cyclopropyl carbonyl system is incorporated into a highly bridged system, it often is difficult to predict which bond of the cyclopropane system possesses maximum overlap with the π system of the carbonyl group. For example, Norin[10] found that (+)-



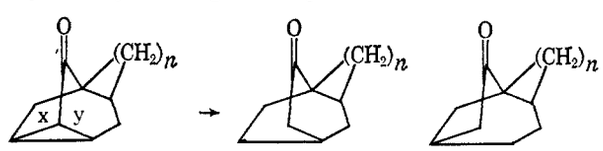
19 **20**

pericyclocamphanone **19** yielded only (+)-camphor **20** on reduction. From a study of models, it appears that both the C_3–C_4 and the C_3–C_5 bond overlap the carbonyl group equally. To rationalize the high specificity of the reaction, he postulated that a steric interaction between one geminal methyl group and a C_6 hydrogen atom causes a slight distortion of the ring system so as to make the C_3–C_5 bond overlap better. Recently, the lithium in liquid ammonia reduction of the tetracyclic ketone **21** was reported to yield only tricyclic ketone **22**,[21] the product predicted from the maximum overlap consideration. On the other hand, House[22]



21 **22**

has reported that reduction of the simple tricyclic ketone **23a** gave approximately equal amounts of **24a** and **25a**, by cleavage of both bonds x and y, while reduction of the related tetracyclic ketone **23b** yielded only **24b** by cleavage of only bond x. In both of these



23a, $(CH_2)_n$ = H, H; **b**, n = 3 **24a**, $(CH_2)_n$ = H, H; **b**, n = 3 **25a**, $(CH_2)_n$ = H, H; **b**, n = 3

cases, models indicate the y bond overlaps better with the carbonyl group and also no great change in geometry is noted by the addition of the extra ring in **23b**. Whether the small but unpredictable conformational effects of the type discussed by Norin are playing a decisive role in these last two examples awaits further study.

Experimental Section

Unless otherwise noted, the following general conditions were used in all reactions. Infrared spectra were recorded in carbon tetrachloride using either a Perkin-Elmer 137 Infracord or a 237 grating spectrophotometer. Nmr spectra were obtained with a Varian A-60 spectrometer using carbon tetrachloride as the solvent and tetramethylsilane as an external reference. Optical rotations were taken in chloroform. Optical rotatory dispersion measurements were obtained on a Cary 60 spectropolarimeter using a 1-cm cell and dioxane solutions. Mass spectral analyses were performed by the Mass Spectra Laboratory and elementry analyses and molecular weight determinations were obtained from the Microanalytical Laboratory, both of the College of Chemistry, University of California, Berkeley, Calif.

All column chromatographies were performed with neutral Woelm alumina of stated activity and all thin layer chromatography used Merck, Darmstadt, silica gel G. Gas–liquid partition chromatography analyses were carried out using either a Wilkens Aerograph A-90-P apparatus or a 600 C Hy-Fy apparatus with a $\frac{1}{8}$ in. × 5 ft, 1% SE-30 on 60–80 Chromosorb W column.

General Reduction Procedure.—The apparatus used for the reduction consisted of two units. The reaction was carried out in a 100-ml, three-necked, pear-shaped flask fitted with a dropping funnel, a sealed mechanical stirrer with a glass propeller, and a Dry Ice–isopropyl alcohol condenser having a side arm with a stopcock and a ball joint. For the drying and the distillation of the commercial liquid ammonia, a 500-ml, two-necked, round-bottomed flask was fitted on one neck with a Dry Ice–isopropyl alcohol condenser and the second neck was connected to the side

(17) W. G. Dauben and G. H. Berezin, *J. Am. Chem. Soc.*, **85**, 468 (1963).
(18) A. C. Cope, S. Moon, and C. H. Pork, *ibid.*, **84**, 4843 (1962).
(19) W. Nagata, H. Hirai, H. Itazaki, and K. Takeda, *J. Org. Chem.*, **26**, 2413 (1961); *Ann.*, **641**, 196 (1961).
(20) A. J. Birch and M. Smith, *Proc. Chem. Soc.*, 356 (1962).
(21) A. Nickon, H. Kwasnik, T. Swartz, R. O. Williams, and J. B. DiGiorgio, *J. Am. Chem. Soc.*, **87**, 1615 (1965).
(22) H. O. House, S. G. Boots, and V. K. Jones, *J. Org. Chem.*, **30**, 2519 (1965).

arm of the condenser on the reaction flask by means of glass tubing with a ball joint.

Approximately 300–400 ml of ammonia was placed into the distillation flask, the flask was attached to the reaction flask, and the stopcock was closed. A small piece of sodium was added, the flask was immersed in a water bath through which was circulated tap water, and the blue ammoniacal solution was allowed to reflux for 30 min.

The reaction flask was flushed with dry nitrogen, the stopcock was opened, the condenser on the distillation flask was removed, the neck was stoppered, and the ammonia was allowed to flush through the reaction apparatus prior to the addition of Dry Ice and isopropyl alcohol to its condenser. After 50 ml of pure, dry ammonia had been collected in the reaction flask, the distillation apparatus was disconnected, and a tube loosely packed with cotton was attached to the reaction condenser.

Small pieces of lithium wire, which had been washed with anhydrous pentane and weighed, were rapidly added to the vigorously stirred ammonia. A solution of the substrate in ether was added and the ammonia solution was allowed to reflux for the stated time. At the end of the reaction, a 100% excess of solid ammonium chloride was added to destroy the excess lithium, neutralize the lithium amide formed, and to hydrolyze the organolithium enolate. The ammonia was distilled, and 100 ml of distilled water and 100 ml of ether were added. The mixture was saturated with solid sodium chloride, the ethereal layer was separated, the water layer was extracted twice with 50-ml portions of ether, and the extracts were combined. The ethereal solution was washed with 50 ml of saturated sodium chloride solution and dried over anhydrous magnesium sulfate, and the solvent was evaporated.

Reduction of 1β,5-Cyclo-10α-cholestan-2-one (5).—A solution of 0.25 g (0.65 mmole) of **5** in 10 ml of anhydrous ether was reduced with 90 mg (0.013 g-atoms) of lithium in 50 ml of distilled ammonia. The reaction was allowed to proceed for 30 min. The crude product showed a single spot on tlc which was well separated from starting material and was a single peak on glpc. The material was chromatographed on alumina (activity III) and 176 mg of crystalline 1(10→5α)-abeocholestan-2-one was eluded with hexane and hexane–benzene (4:1). The material was recrystallized twice from absolute ethanol: mp 109–111°; $[\alpha]^{22}D$ +40° (*c* 1.04); ν_{max} 1745 cm^{-1}; nmr series of bands at τ 9.03 and 9.06 (C_{18}, C_{21}, C_{26}, C_{27}), 9.25 (singlet, C_{18}); in benzene, 9.36 (doublet, J = 4.4 cps, C_{19}), 9.43 (doublet, J = 5.4 cps, C_{21}, C_{26}, C_{27}), 9.69 (singlet, C_{18}); ord, peaks at 322 mμ (α: +784) and 311 mμ (α +696), trough at 276 mμ (α −368).

Anal. Calcd for $C_{27}H_{46}O$ (386.66): C, 83.87; H, 11.99. Found: C, 83.58; H, 11.71.

The properties of 5α,10α-cholestan-2-one,[11] the possible alternate structure, are mp 99–100°, $[\alpha]^{26}D$ +50°, ν_{max} 1712 cm^{-1}, negative Cotton curve.

Reduction of (+)-Carones (8).—A solution of 1.0 g of impure (+)-carones, $[\alpha]^{22}D$ +124°, which had been analyzed by glpc and shown to consist of 71% *trans*-(+)-carone, 11% *cis*-(+)-carone, 11% (−)-dihydrocarvone, and 7% carvenone, in 10 ml of anhydrous ether was reduced with 0.46 g of lithium in 75 ml of distilled ammonia; the reaction was allowed to proceed for 1 hr. Glpc analysis of the crude product at 170° on a 0.5 in. × 5 ft column containing 20% Carbowax 20 M on 60–80 Chromosorb P showed four peaks: 69% (16 min), 13% (18.5 min), 11% (20.5 min), and 7% (27 in). The first peak and the combined second and third peaks were collected by preparative glpc.

The 69% product had the following properties: ν_{max} 1706 cm^{-1}; nmr, τ 8.99 (6 H, doublet, J = 6 cps, C_5–$CH(CH_3)_2$), 9.01 (3 H, doublet, J = 5.5 cps, C_2CH_3); $[\alpha]^{22}D$ −23.9° (*c*, 1.03). Based on the optical rotation the material is 65% (−)-carvomenthone and 35% (−)-isocarvomenthanone.[23] These percentages are based on the rotational values:[24] (−)-carvomenthone, $[\alpha]D$ −6°, and (−)-isocarvomenthone, $[\alpha]D$ −56°.

Anal. Calcd for $C_{10}H_{18}O$ (154.25): C, 77.87; H, 11.76. Found: C, 77.86; H, 11.57; mol wt, 154 (mass spectrum).

The semicarbazone of this mixture was recrystallized twice from methanol, mp 184–190°, $[\alpha]^{22}D$ −13° (*c* 0.79). The literature values[24] for (−)-carvomenthone semicarbazone are mp 192°, $[\alpha]D$ −13.3°.

The combined second and third peaks, $[\alpha]^{22}D$ +18.4° (*c* 2.30), was shown by infrared and nmr spectroscopy to be a mixture of (−)-dihydrocarvone and unreacted (+)-carones.

Reduction of 3α,5-Cyclocholestan-3-one (10).—A solution of 0.25 g (0.65 mmole) of **10**[25] in 10 ml of anhydrous ether was reduced with a total of 120 mg (0.017 g-atom) of lithium; this large excess of lithium was needed to keep the solution blue throughout the reaction. The crude product was found by tlc to contain mainly one new product and a trace of starting material. Hy-Fy glpc showed 10% starting material and 90% product. The material was chromatographed on alumina (activity III) and 152 mg of crystalline cholestan-6-one (**11**) was eluted with hexane–benzene (95:5). Further fractions obtained by increasing the polarity of the solvent to pure benzene eluted 43 mg of a mixture of cholestan-6-one and starting material. The main fraction was recrystallized twice from methanol mp 98.5–99.5°; $[\alpha]^{22}D$ −1.5°; ν_{max} 1712 cm^{-1}; nmr τ 9.06 (doublet, J = 5.5 cps, C_{21}, C_{26}, C_{27}), 9.22 (singlet, C_{18}), 9.25 (singlet, C_{19}); ORD negative Cotton effect, troughs at 317 mμ (α −755) and 307 mμ (α −450), peak at 275 mμ (α +970). The literature values for cholestan-6-one are mp 96°, $[\alpha]D$ −2°,[12] ORD negative Cotton effect, trough 308 mμ (α −780°), peak 270 mμ (α +1210).[13]

Reduction of 3β,5-Cyclocholestan-6-one (12).—A solution of 0.25 g (0.65 mmole) of **12**[26] in 25 ml of anhydrous ether was reduced with 120 mg (0.017 g-atom) of lithium. The crude product (ν_{max} 1695 cm^{-1}) showed on tlc a diffuse spot which ran slightly faster than starting material and displayed a single peak, different from starting material, on Hy-Fy glpc. The material was chromatographed on alumina (activity II) and 41 mg of crystalline 3α-methyl-A-norcholestan-6-one (**14**) (ν_{max} 1718 cm^{-1}) was eluted with hexane–benzene (19:1), 134 mg of a mixture of **13** and **14** (ν_{max} 1718 and 1695 cm^{-1}) with hexane–benzene (9:1 to 1:1), and 47 mg of crystalline 3α-methyl-A-norcoprostan-6-one (**13**) (ν_{max} 1695 cm^{-1}) with benzene.

The 3α-methyl-A-norcholestan-6-one was recrystallized from methanol: mp 92–96°; $[\alpha]^{22}D$ −31.5° (*c* 1.27); nmr, τ 9.00 (doublet, J = 5.7 cps, C_3-α-CH_3), 9.10 (doublet, J = 5.5 cps, C_{21}, C_{26}, C_{27}), 9.28 (singlet, C_{18}), 9.30 (singlet, C_{19}); ORD negative Cotton effect, troughs at 317 mμ (α −535°) and 307 mμ (α −412°), and peak at 275 mμ (α +261°).

Anal. Calcd for $C_{27}H_{46}O$ (386.67): C, 83.87; H, 11.99. Found: C, 83.56; H, 11.73.

The 3α-methyl-A-norcoprostan-6-one was recrystallized from methanol: mp 108–112°; $[\alpha]^{22}D$ −30° (*c* 0.22); nmr, τ 8.94 (singlet, C_{19}), 9.03 (doublet, J = 5.7 cps, C_3-α-CH_3], 9.08 (doublet, J = 5.5 cps, C_{21}, C_{26}, C_{27}), 9.27 (singlet, C_{18}); ORD negative Cotton effect, trough at 322 mμ (α −1070) and peak at 278 mμ (α +1310).

Anal. Calcd for $C_{27}H_{46}O$ (386.67): C, 83.87; H, 11.99. Found: C, 83.58; H, 11.79.

Equilibration of a 1:1 Mixture of 3α-Methyl-A-norcoprostan-6-one (13) and 3α-Methyl-A-norcholestan-6-one (14).—A solution of a 1:1 mixture of **13** and **14** in 3 ml of absolute ethanol containing 20 mg of potassium hydroxide was allowed to stand under a nitrogen atmosphere for 24 hr. The solution was poured into 6 ml of distilled water, the mixture was extracted with three 5-ml portions of chloroform, and the organic extract was washed with water and dried. The solvent was removed under reduced pressure to yield 22 mg (92%) of crude, crystalline 3α-methyl-A-norcholestan-6-one, ν_{max} 1718 cm^{-1}.

Reduction of 4β,5-Methanocholestan-3-one (15).—A solution of 0.2 g (0.5 mmole) of **15**[27] in 10 ml of anhydrous ether was reduced with 40 mg (0.006 g-atom) of lithium for 1 hr. The crude reaction product (ν_{max} 1715 and 1692 cm^{-1}) on tlc showed one strong spot of a new material and one weak spot of starting material. The solid was filtered through 4 g of alumina (activity III) with benzene to yield 150 mg of crude 5β-methylcholestan-3-one which was recrystallized twice from methanol–ether: mp 86–88°; $[\alpha]^{22}D$ +36° (*c* 0.91); ν_{max} 1712 cm^{-1}; nmr, τ 7.11 (1 H, doublet, J = 14 cps, C_4-β-equatorial H), 9.10 (singlet, C_{19}), 9.13 (doublet, C_{21}, C_{26}, C_{27}), 9.14 (singlet, C_5-β-CH_3), 9.33 (singlet, C_{18}); ORD negative Cotton effect, trough at 315 mμ (α +27°). The material when mixed with an authentic

(23) The product obtained by Norin[10] possesses $[\alpha]D$ −18°. The literature values he quotes for the optical rotation of pure (−)-carvomenthone was listed incorrectly. Thus, his material also was a mixture of about 75% (−)-carvomenthone and 25% (−)-isocarvomenthone.

(24) R. G. Johnson and J. Read, *J. Chem. Soc.*, 1138 (1935).

(25) R. M. Dodson and R. R. Riegel, *J. Org. Chem.*, **13**, 424 (1950).

(26) W. G. Dauben and J. A. Ross, *J. Am. Chem. Soc.*, **81**, 6521 (1959), and unpublished results; G. H. Whitham and J. A. F. Wickramasinghe, *J. Chem. Soc.*, 1655 (1964).

(27) W. G. Dauben, P. Laug, and G. H. Berezin, *J. Org. Chem.*, in press.

sample[28] showed no melting point depression and coinjection in Hy-Fy glpc gave a single peak. The literature values[19] for 5β-methylcholestan-3-one are mp 88–89°, ν_{max} 1708 cm^{-1} ($CHCl_3$), $[\alpha]^{29}D$ +35°, ORD negative Cotton effect, trough ~300 mμ (α +32°).

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 83.64; H, 11.91; mol wt, 400 (mass spectrum).

Reduction of 4α,5-Methanocholestan-3-one (17).—A solution of 0.2 g (0.5 mmole) of 17[27] in 10 ml of anhydrous ammonia was reduced with 70 mg (0.01 g-atom) of lithium for 20 min. Tlc analysis of the crude product showed only a trace of starting material. The material was chromatographed on alumina (activity III) and 140 mg of 5α-methylcholestan-3-one was eluted with hexane–benzene (9:1). The product wasre crystallized from acetone: mp 162–163°; mixture melting point with authentic sample[28] showed no depression; ν_{max} 1704 cm^{-1}; nmr, τ 8.74 (singlet, C_{19}), 8.98 (singlet, C_5-α-CH_3), 9.03 (doublet, J = 5.5 cps, C_{21}, C_{26}, C_{27}), 9.23 (singlet, C_{18}); $[\alpha]^{22}D$ +47.5° (c 0.98); ORD positive Cotton effect, peak at 315 mμ (α +825) and trough at 270 mμ (α −628°). The literature values for 5α-methylcholestan-3-one are mp 168–169°, ν^{Nujol}_{max} 1724 cm^{-1}, $[\alpha]^{29}D$ +49°, ORD positive Cotton effect, peak at ~300 mμ (α +970°) and trough at ~252 mμ (α −615°).

(28) We are indebted to Dr. W. Nagata for the authentic sample.

The Chemistry of Sulfonyl Isocyanates. III.[1] Reactions with Triarylcarbinols[2]

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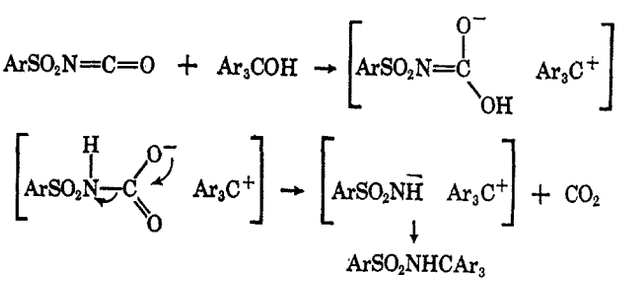
Phenylsulfonyl isocyanate (I) and *p*-toluenesulfonyl isocyanate (II) reacted with triphenylmethanol and with triphenylmethanols containing phenyl, methyl, methoxyl, and chloro ring substituents to afford N-(triarylmethyl)sulfonamides (III) and carbon dioxide. *p,p',p''*-Trinitrotriphenylmethanol (V) and II gave *p,p',p''*-trinitrotriphenylmethyl *p*-tolylsulfonylurethan (VI). Phenyl isocyanate (2 moles) combined with 1 mole of triphenylmethanol to give N,N'-diphenyl-N-(triphenylmethyl)urea (VIII). *p*-Tolyl isocyanate and triphenylmethanol gave *p*-tolyl(triphenylmethyl)amine (IX). Possible mechanisms for the reactions are discussed.

It has been shown that sulfonyl isocyanates react with hindered phenols and alcohols to give the normal urethan products.[4] Extending the reaction from alkyl tertiary carbinols to tertiary carbinols containing aryl groups adjacent to the carbinol function afforded in most cases products which were not the urethans.

Phenylsulfonyl isocyanate (I) and *p*-toluenesulfonyl isocyanate (II) reacted with triphenylmethanol and triarylcarbinols containing electron-donating groups at temperatures from 0 to 100° in toluene. The products were the N-(triarylmethyl)sulfonamides (III) and carbon dioxode. (Table I). One of the products, N-(triphenylmethyl)benzenesulfonamide (IIIa), was independently synthesized from sodium benzenesulfonamide and triphenylchloromethane. The inability to obtain urethan even at 0° is interesting in view of the fact that diphenylmethanol and I gave urethan in good yields.[4] The only other products obtained besides the sulfonamides were very small amounts of disulfonylureas.

The most obvious mechanism for the formation of the products would be the intermediate production of urethan which would lose carbon dioxide gas. The fact that no urethan could be isolated, however, even at low temperatures indicates the mechanism to be a doubtful one or that the urethan formed is extremely unstable. The solutions became colored during the reaction. Furthermore, solutions containing sulfonyl isocyanate and a triarylcarbinol absorbed in the 400–450-mμ range. Solutions containing triphenylcarbinol showed absorption at 420 mμ which built up slowly during the early stages of reaction and then fell off in intensity during the latter stages.

Since triphenylmethylcarbonium ion, prepared from triphenylmethanol and sulfuric acid, absorbs at about 420 mμ[5] it is believed that $(C_6H_5)C^+$ or an ion pair is being formed in solution. Whether this arises *via* urethan or by the alternate mechanism below cannot presently be stated.



It may be noted that all of the triarylcarbinols in Table I would be expected to give rather stable carbonium ions. Triarylcarbinols with strongly electron-withdrawing groups should give less stable carbonium ions and may follow a different mechanism in reacting with socyanates. *p,p',p''*-Trinitrotriphenylmethane (IV) was prepared by nitrating triphenylmethane. Compound IV was converted to *p,p',p''*-trinitrotriphenylmethanol (V) by chromic acid. Upon the reaction of V and II, no carbon dioxide was evolved and 64.6% of *p,p',p''*-trinitrotriphenylmethyl *p*-tolylsulfonylurethan was obtained. No absorption in the 400–450-mμ range was shown by the reaction solution. Such

(1) For paper II, see J. W. McFarland and W. A. Burkhardt, III, *J. Org. Chem.*, **31**, 1903 (1966).

(2) Taken in part from the M.S. Theses of D. E. L. (1963) and D. J. G. (1965), DePauw University, and presented at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965, Abstracts of Papers, p 2-S.

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(4) J. W. McFarland and J. B. Howard, *J. Org. Chem.*, **30**, 957 (1965).

(5) N. C. Deno, J. J. Jaruzelski, and A. Schriesheim, *J. Am. Chem. Soc.*, **77**, 3044 (1955).