The Stereochemistry of the Oxidation of Oximes to Nitrocycloalkanes with Peroxytrifluoroacetic Acid. Protonation of Nitronic Acid Derivatives in Cyclohexane Systems[1a]

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A series of 2-substituted cyclohexanone oximes has been shown to give predominantly *cis*-2-substituted nitrocyclohexanes upon peroxytrifluoroacetic acid oxidation. Analysis, by nmr spectroscopy, of 2-phenylnitrocyclohexane and methyl 2-nitrocyclohexaneacetate obtained from the appropriate oximes showed that the *cis* product predominated in both reactions. The extent of *cis* isomer was >95% in the former case and about 77% in the latter. Gas chromatographic and nmr analyses have shown that oxidation of 2-methylcyclohexanone oxime gives a mixture of *cis*- and *trans*-2-methylnitrocyclohexanes containing 80% *cis* isomer. The isomeric mixture of *cis*- and *trans*-ethyl 2-nitrocyclohexanepropionates from the appropriate oxime was shown to consist of about 85% *cis* isomer by converting the nitro ester mixture into a mixture of *cis*- and *trans*-decahydroquinolines which could be analyzed by glpc. Oxidation of norcamphor oxime gave mainly *endo*-2-nitronorbornane. The results are discussed in terms of the stereochemistry of protonation of nitronic acids and nitronate anions.

The oxidation of oximes with peroxytrifluoroacetic acid[2] is one of the general methods for synthesis of nitroalkanes.[3] We were interested in the stereochemistry of this reaction in connection with the synthesis of functionally substituted nitroalkanes. The steric outcome of the reaction is also of interest in connection with stereoselective synthesis of amines since it is possible to reduce nitroalkanes to amines with retention of configuration.[4] While little is known about the stereochemistry of per-acid oxidation of oximes to nitro compounds, some information is available for two other general procedures for converting oximes into nitroalkanes as the result of syntheses of nitro steroids. The Iffland procedure[5] involving bromination of the oxime, oxidation, and sodium borohydride reduction of the resulting α-bromonitroalkane gives 17β-nitro[6] and 3β-nitro steroids[7] from the appropriate oximino steroids. Nitric acid oxidation of steroidal oximes to *gem*-dinitro derivatives followed by catalytic reduction gives 4β-, 6β-, 7α-, and 17β-mononitro steroids. In each case the less hindered nitro group is selectively removed. Mixtures of 3α-nitro- and 3β-nitro-5α-cholestanes were obtained when this procedure was applied to 3-oximinocholestane.[8]

Results

We have investigated the stereochemistry of the oxidation of the 2-substituted cyclohexanone oximes **1a–d** and norcamphor oxime (**8**) to the corresponding nitro compounds. For nitro compounds **2a–c** and **3a–c** it was possible to determine the relative amounts of the isomers by nmr analysis. The crude reaction mixtures were purified by absorption chromatography on silicic acid and then were analyzed directly. Control experiments with *cis*- and *trans*-1-methyl-2-nitrocyclohexanes showed that the isomer ratio was unchanged by silicic acid chromatography.

1a, R = C_6H_5
b, R = CH_3
c, R = $CH_2CO_2CH_3$
d, R = $CH_2CH_2CO_2C_2H_5$

cis **2a–d** *trans* **3a–d**

cis- and *trans*-1-nitro-2-phenylcyclohexanes (**2a** and **3a**) have been well characterized,[9] and authentic samples were prepared. Comparison of the nmr spectrum of the mixture of **2a** and **3a** obtained by oxidation of the oxime **1a** showed that the product was at least 95% *cis* isomer **2a**. The triplet of doublets at 4.68 ppm characteristic of the axial C-1 proton in **3a** was not detectable.

The isomeric 2-methylnitrocyclohexanes (**2b** and **3b**) from oxidation of 2-methylcyclohexanone oxime were separated by preparative gas chromatography. The nmr spectrum of the major isomer shows a quintet assigned to the proton on C-1 at 4.52 ppm ($W_{1/2}$ = 15 Hz). The minor isomer shows a broader signal at 4.06 ppm. The major isomer was assigned the *cis* structure **2b** on the basis of the downfield position and narrower band width of the proton adjacent to the nitro group, relative to the corresponding signal in the minor isomer.[10,11] This assignment was confirmed by using sodium bicarbonate to isomerize[9,12] a sample of the major isomer **2b** to a mixture containing 92% the thermodynamically more stable isomer **3b** and 8% **2b** (glpc analysis). Analysis of the product obtained by oxidation of **1b** gave average values of 81 ± 4% **2b** by nmr analysis and 83 ± 1% **2b** by glpc analysis.

Oxidation of methyl 2-hydroxyiminocyclohexane acetate (**1c**) gave a 39% yield of a mixture of the nitro

(1) (a) This work was supported in part by funds from an Institutional Grant to the University of Virginia by the National Science Foundation. (b) NDEA Fellow, 1965–1968.

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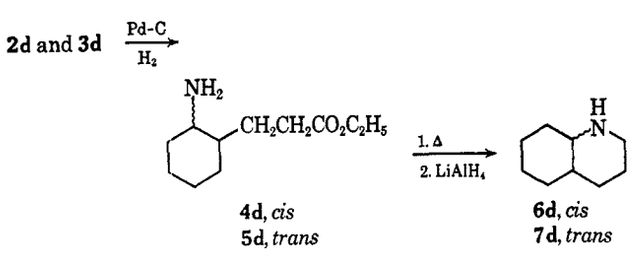
esters **2c** and **3c** after separation, by absorption chromatography, from the methyl 2-oxocyclohexaneacetate formed as a by-product. Two multiplets were visible in the nmr spectrum in the region expected for protons geminal to a nitro group. On amplification of the spectrum the higher field multiplet revealed the sextet structure expected for an axial proton. The shape of the lower field multiplet was typical of those found for compounds in the *cis* series and accounted for 76–78% of the area under the two signals. Epimerization with sodium bicarbonate reversed the relative intensity of the two signals. In the isomerized sample 82% of the area was under the higher field multiplet. Thus, the oxidation product consisted mostly (about 77%) of the thermodynamically less stable *cis* isomer **2c**.

A 49% yield of **2d** and **3d** was obtained by oxidation of **1d**. A multiplet having the characteristics of the equatorial proton of the *cis* series appears at 4.6 ppm, but precise nmr analysis of the mixture was precluded by the fact that the higher field multiplet of the *trans* isomer was partially obscured by the methylene quartet of the ethoxy group. The low-field multiplet corresponded to about 70% of the area expected for the pure *cis* isomer suggesting that **2d** must be the major component of the mixture. Confirmation of this conclusion was obtained by catalytically reducing the mixture to **4d** and **5d** under conditions expected to maintain the stereochemistry of the C–N bond.[4] Lactamization of the **4d–5d** mixture, followed by lithium aluminum hydride reduction, gave an over-all 61% yield of a mixture of *cis*- and *trans*-decahydroquinolines (**6d** and **7d**). Compounds **6d** and **7d** were isolated by preparative glpc. The mixture **6d–7d** was 85 ± 4% *cis* isomer (glpc analysis) supporting the conclusion that **2d** is the major component of the original nitro ester mixture. Isomerization of the **2d–3d** mixture, obtained by oxidation, with ethanolic sodium bicarbonate gave a sample containing about 75% **3d**.



Oxidation of norbornanone oxime provided a sample of 2-nitronorbornane (**9**, 31% yield) which showed melting point behavior similar to that of a previously described[13] sample of *endo*-2-nitro-3-^{14}C-norbornane. The nmr spectrum corresponded closely to that reported by Fraser[14] showing, in particular, a quintet at 4.84 ppm (lit.[14] 4.73 ppm) assigned[14] to an *exo* proton at C-2. Amplification of the signal reveals a multiplet at 4.39 ppm which becomes the major signal in the 4.0–5.0-ppm region after isomerization[13] of the sample to predominantly *exo*-2-nitronorbornane. Integration of the H-2 signals in three spectra by planimetry gave a value of 86 ± 4% for the percentage of *endo* isomer in the oxidation product. The stereochemical data and the pertinent nmr data are recorded in Tables I and II, respectively. Literature data on the oxidation of 4-*t*-butylcyclohexanone oxime[15] (**10**) is also included.

TABLE I

STEREOCHEMISTRY OF OXIDATION

Compound	% yield	% *cis* (*endo*)[a]	% *trans* (*exo*)[a]	Analysis[b]
1a	38	>95	<5	Nmr
1b	24	81 ± 4	19 ± 4	Nmr
		83 ± 1	17 ± 1	Glpc
1c	39	77 ± 1	23 ± 1	Nmr
1d	49	>70	<30	Nmr
		85 ± 4	15 ± 4	*c*
8	31	86 ± 4	14 ± 4	Nmr
10	33[d]	31[d]	69[d]	Glpc[d]

[a] Except for **1a** the values quoted are the average values for two or three runs. [b] The estimated maximum relative error in determination of the per cent of the major isomer by nmr is ±5%. [c] Chemical transformation to **6d–7d** followed by glpc analysis. [d] Reference 15.

TABLE II

NMR DATA FOR $HCNO_2$

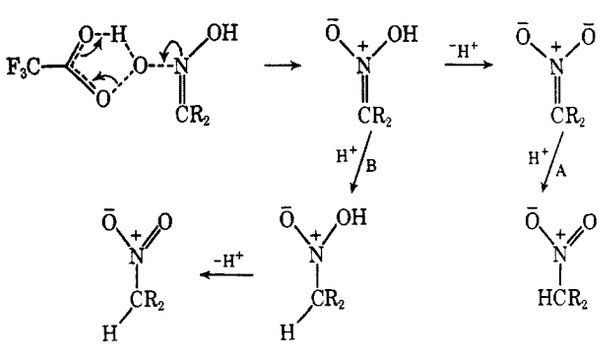
Compound	Chemical shift, ppm	$W_{1/2}$, Hz	J_{ee}, Hz	J_{aa}, Hz	J_{ae}, Hz	J_{ea}, Hz
2a	4.90	9.0		*a*	*a*	
3a	4.68	28.0		10.7	3.8	
2b	4.52	15.0		*a*	*a*	
3b	4.06	*b*		11.2	4.0	
2c	4.71	11.5	2.1			4.5
3c	4.36	22.5		11.0	4.0	
2d	4.6	12.5		*a*	*a*	
3d	4.2	*c*		*c*	4.5	

[a] Resolution is insufficient for first-order analysis. [b] The signal has the triplet of doublets structure characteristic of the *trans* series. The splitting between the outer doublets is about 22 Hz. [c] Obscured by O–CH_2CH_3.

Attempts to oxidize camphor oxime to 2-nitrobornane gave insufficient amounts of the desired nitro compound for adequate characterization. The peroxytrifluoroacetic oxidation of oximes is known to fail in highly hindered systems.[2]

Discussion

Emmons[2] represented the oxidation of oximes as occurring *via* the nitronic acid tautomer. Two slightly different sequences can be considered for subsequent proton transfers. The nitronate anion might be formed and undergo C protonation (process A) or the final step might involve C protonation on a nitronic acid intermediate (process B). The generation of



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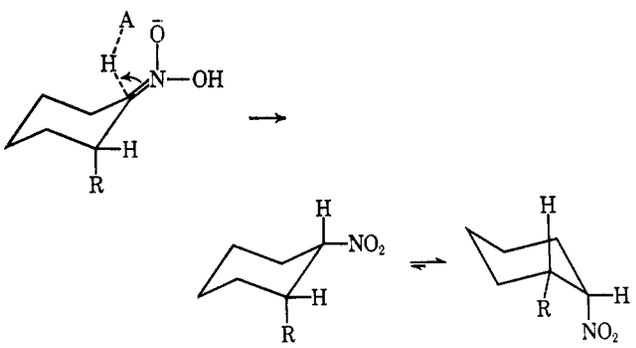
ketones as important by-products during the Emmons–Pagano oxidation seems to be quite general.[2,15] This observation implicates nitronate anions or nitronic acids as intermediates since they could give rise to the observed ketones *via* Nef reactions.[16] In either protonation process the stereochemistry of the reaction is determined by a proton transfer to an sp^2 carbon atom. The data of Huitric[15] concerning the oxidation of 4-*t*-butylcyclohexanone oxime shows that, in the absence of a substituent on C-2, there is a slight preference (3:1) for axial protonation giving the more stable *trans*-4-*t*-butylnitrocyclohexane. In the 2-substituted compounds **1a–d** there is, in contrast, a preference, ranging from ~4:1 to >19:1, for introduction of the proton such that its final conformation is equatorial, generating *cis* products. Our data clearly show that the oxidation products are the result of kinetic and not thermodynamic control. The discussions of Johnson and Malhotra[17] and of Bordwell and Vestling[18] on the C protonation of nitronates and nitronic acids are of direct interest. Malhotra and Johnson[17] conclude that the stable conformations of nitronic acids and nitronate anions in the cyclohexane system will have 2 substituents in the axial position if the substituent is large enough to give rise to nonbonded interaction with the nitronate group. They then anticipate protonation of the nitronate from the least hindered side of the molecule, *trans* to the 2 substituent, generating the *cis* product. Their theory explains our data satisfactorily.



Bordwell and Vestling[18] discuss this problem further in connection with their observation that *cis*-*p*-chlorophenylnitrocyclohexane undergoes proton loss about 200 times faster than the *trans* isomer. They attribute the rate retardation in the *trans* isomer to deformation of the cyclohexane ring resulting from the aryl and nitro groups bending away from one another. They suggest that in this deformed conformation the equatorial aryl group shields the axial proton more effectively from the abstracting base. They conclude, in agreement with Malhotra and Johnson,[17] that the 2-aryl substituent is in an axial position in the transition state for protonation. We suggest that, if the conclusion of Malhotra and Johnson[17] about the conformation of the nitronate anion of 2-phenylnitrocyclohexane is correct, then $A^{(1,3)}$ strain will result in resistance to proton abstraction from 2-arylnitrocyclohexanes having equatorial aryl groups. Proton abstraction from 2-arylnitrocyclohexanes may take place instead from conformations in which the aryl group occupies an axial or nearly axial position. The attainment of such a conformation would be more difficult in the *trans* system than in the *cis* since there would be two axial or nearly axial substituents in the *trans* case. This conformational effect offers an alternative explanation of the low rate of proton abstraction in the *trans* series. Malhotra and Johnson[17] have advanced an analogous explanation for the resistance of *trans*-2-phenylcyclohexyl phenyl ketone toward bromination.

The formation of *endo*-2-nitronorbornane from norbornanone oxime is also readily explained as a steric preference for proton delivery to the least hindered side of the nitronic acid or nitronate anion intermediate.

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Experimental Section

Except for compound **9** the nmr analyses of the products were carried out on a Varian HA-100 instrument using dilute deuteriochloroform solutions containing about 5% tetramethylsilane. A Varian A-60 instrument was used in the case of compound **9**. Glpc analyses were carried out on an Aerograph A90-P3 instrument. Absorption chromatography was carried out using 100 mesh silicic acid, redistilled hexane, reagent grade chloroform, and anhydrous reagent grade ether. Melting points were obtained on a calibrated Fisher-Johns apparatus. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

General Oxidation Procedure.—A mixture of 10 mmol of oxime, 0.2 g (3 mmol) of urea, 7.8 g (54 mmol) of disodium hydrogen phosphate,[19] and 20–25 ml of acetonitrile was stirred mechanically and heated to gentle reflux. A solution of peroxytrifluoroacetic acid was prepared by adding, dropwise during 10 min, trifluoroacetic anhydride (3.4 ml, 24 mmol) to a solution of 90% hydrogen peroxide (0.55 ml, 20 mmol) and acetonitrile (6 ml) chilled in an ice bath. *Extreme caution should be used in handling 90% hydrogen peroxide and the oxidizing solution.* The peroxytrifluoroacetic acid solution was then added dropwise over 1 hr to the stirred, heated oxime mixture. In most cases, the mixture turned blue or green as the oxidizing solution was added but became yellow by the time addition was complete. The reaction mixture was stirred at reflux for 1 hr after addition of peroxytrifluoroacetic acid was complete. The mixture was then centrifuged, and the yellow supernatant liquid was decanted and concentrated *in vacuo*. The residue was treated with water (15 ml) and then extracted with 3 portions (15 ml each) of methylene chloride. The combined organic extracts were washed with 5% aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated.

1-Nitro-2-phenylcyclohexanes (2a and 3a).—The crude product obtained by the standard oxidation procedure was a yellow-green oil (1.61 g). A portion of the oil (0.75 g) in chloroform (8 ml) was placed on a silicic acid column (1.3 × 52 cm, 25 g) packed using 10% chloroform in hexane. The column was eluted with hexane solutions containing increasing amounts of chloroform ranging from 10 to 25% (total 2 l.), and then with methanol. Fractions of 20-ml were collected. Like fractions were combined on the basis of tlc comparison. Evaporation of fractions 36–92 gave **2a–3a** (0.36 g, 38%): ir (KBr) 1725 (C=O, weak) and 1550 cm^{-1} (NO_2); nmr δ 4.89. At maximum spectrum amplitude there was no signal detectable at δ 4.68 (authentic **3a**, nmr δ 4.68). Fractions 99–103 afforded 0.11 g (13%) of oily solid shown to be 2-phenylcyclohexanone. No other fractions showed nitro absorptions in the ir spectrum. Total recovery from the column was 95%).

1-Methyl-2-nitrocyclohexanes (2b and 3b).—The yellow oil (0.99 g) obtained by the general oxidation procedure was subjected to absorption chromatography on a 1.3 × 53 cm silicic acid (25 g) column packed in 10% chloroform in hexane. Elution with 10% chloroform–hexane gave fractions 1–3 shown by tlc to contain nitro compounds **2b–3b** (24% yield). Glpc analysis

(19) The disodium hydrogen phosphate was prepared by grinding the heptahydrate with a mortar and pestle, drying overnight at 100°, and then grinding to a powder before use.

indicated 84% **2b** and 16% **3b**. Preparative glpc on a 5-ft acid-washed column of 5% Dow Corning 550 silicone oil on Chromosorb at 116° separated the material into two components. The material of shorter retention time was a clear liquid: ir ($CHCl_3$) 1545 cm^{-1} (NO_2); nmr δ 4.06 (sextet, 1 H, J = 11.2, 4.0 Hz, axial $-CHNO_2$). The material of longer retention time was a clear liquid: $n^{25}D$ 1.4627 (lit.[20] $n^{25}D$ 1.4608); ir ($CHCl_3$) 1542 cm^{-1} (NO_2); nmr δ 4.52 (quintet, 1 H, $W_{1/2}$ = 15.0 Hz, apparent J = 4.2 Hz, equatorial $-CH-NO_2$).

Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.98; H, 9.28; N, 9.84.

In a duplicate experiment, analysis of the crude product prior to chromatography showed the presence of 2-methylcyclohexanone (35% yield) and an unidentified component of high retention time as well as **2b** and **3b**. The total yield of **2b** and **3b** was 24% by glpc, and the ratio was 4.85:1 (83% *cis*). After silicic acid chromatography, nmr analysis indicated 85% *cis* isomer.

Isomerization of 2b to 3b.—A solution of 45 mg (0.3 mmol) of **2b** obtained by preparative gas chromatography in 95% ethanol (2 ml) was added to 5 ml of saturated sodium bicarbonate in 95% ethanol. The solution was refluxed for 21 hr, cooled, and concentrated. Water (5 ml) was added to the residue, and the mixture was extracted three times with 5-ml portions of ether. The dried extract was concentrated giving 13 mg (29%) of a liquid residue which was analyzed by glpc. The peak of shorter retention time (**3b**) accounted for 92% of the total area and that of longer retention time (**2b**) for 8%. No 2-methylcyclohexanone was present in the sample.

Methyl 2-Hydroxyiminocyclohexaneacetate (1c).—To a solution of methyl 2-oxocyclohexaneacetate[21] (10.2 g, 60 mmol) in methanol (200 ml) there was added a solution of hydroxylamine hydrochloride (11.1 g, 160 mmol) and anhydrous sodium acetate (22 g, 268 mmol) in water (45 ml). The resulting mixture was refluxed 1 hr, cooled, and concentrated, giving a pink slurry. Water (50 ml) was added, and the mixture was extracted with ether. The ether was washed with 5% sodium carbonate, dried, and evaporated, giving **1c** (4.95 g, 45%). Several recrystallizations from hexane gave white prisms, mp 82.5–84.5°.

Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.09; H, 8.23; N, 7.39.

Methyl 2-Nitrocyclohexaneacetates (2c and 3c).—The oxidation of 10 mmol of **1c** by the general procedure gave 1.33 g of crude **2c–3c** containing methyl 2-oxocyclohexaneacetate as a significant contaminant (27% yield by glpc analysis). Chromatography on silicic acid using 5 and 10% ether in hexane as the eluting solvents gave fractions containing **2c–3c** (0.79 g, 39%). Short-path distillation (0.02 mm) gave a clear liquid: $n^{24}D$ 1.4708; ir (film) 1740 (C=O) and 1545 cm^{-1} (NO_2); nmr δ 4.71 (quintet, < 1 H, $W_{1/2}$ = 11.5 Hz, J = 2.1, 4.5 Hz, equatorial $-CHNO_2$), 4.35 (sextet, <<1 H, $W_{1/2}$ = 28 Hz, axial $-CHNO_2$), and 3.66 (s, 3 H, OCH_3). Integration of the signals at δ 4.71 and 4.35 indicated 78% **2c** and 22% **3c**.

Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.91; H, 7.72; N, 6.86.

Isomerization of 2c to 3c.—A solution of 0.40 g (2 mmol) of the **2c–3c** mixture described above in 41 ml of a saturated solution of sodium bicarbonate in 95% ethanol was refluxed for 21 hr, cooled, and concentrated. Water (15 ml) was added to the residue, and the mixture was extracted with ether. After drying and concentration the residue (0.34 g, 84%), was distilled (short path, 0.02 mm) giving a clear liquid: $n^{23}D$ 1.4666; ir (film) 1740 (C=O) and 1545 cm^{-1} (NO_2); nmr δ 4.7 (m, <<1 H, $W_{1/2}$ = 13 Hz, equatorial $-CHNO_2$), 4.36 (sextet, <1 H, $W_{1/2}$ = 22.5 Hz, J = 4.0, 11.0 Hz, axial $-CHNO_2$), and 3.62 (s, 3 H, OCH_3). From integration of the spectrum the sample is 82% **3c** and 18% **2c**.

Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.75; H, 7.68; N, 6.89.

Ethyl 2-Hydroxyiminocyclohexanepropionate (1d).—Ethyl 2-oxocyclohexanepropionate[22] was converted into **1d** using the procedure described for **1c**, except that ethanol was used in place of methanol as solvent. Distillation of the crude product gave **1d** as a viscous oil (67% yield): bp 135–138° (0.15 mm); $n^{23}D$ 1.4887.

Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98; N, 6.57. Found: C, 61.86; H, 8.93; N, 6.67.

Ethyl 2-Nitrocyclohexanepropionates (2d and 3d).—The oxidation of **1d** was carried out using the general procedure but on a 0.1-mol scale. The crude product (20.0 g) was obtained as a yellow oil containing about 20% ethyl 2-oxocyclohexanepropionate (glpc analysis). The oil was placed on a 4.5 × 52 cm column of silicic acid (400 g) packed in 10% ether in hexane. The column was eluted with 10% ether in hexane (650 ml) and with 15% ether–hexane (2.2 l.). Compounds **2d** and **3d** were detected in fractions 24–53 by glpc, and these fractions were combined, concentrated, and distilled in a short-path apparatus giving 11.3 g (49%) of a clear liquid: bp 124–126° (0.35 mm); ir (film) 1740 (C=O) and 1545 cm^{-1} (NO_2); nmr δ 4.6 (m, 0.7 H, $W_{1/2}$ = 12.5 Hz, equatorial $-CHNO_2$), 4.2 (m, <<1 H, axial $-CHNO_2$), 4.1 (q, 2 H, J = 7.0 Hz, OCH_2), 2.4 (t, 2 H, J = 7.5 Hz, $CH_2CO_2C_2H_5$), and 1.3 (t, 3 H, J = 7.0 Hz, OCH_2CH_3).

Anal. Calcd for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.78; H, 8.42; N, 6.11.

Isomerization of 2d to 3d.—The procedure described for **2c** was used, except that a 15 hr reflux period was used. Short-path distillation (0.02 mm) gave a 69% yield of a clear liquid: $n^{24}D$ 1.4675; ir (film) 1735 (C=O), 1538 cm^{-1} (NO_2); nmr δ 4.63 (m, <<1 H, equatorial $-CHNO_2$), 4.2 (sextet, <1 H, axial $-CHNO_2$), 4.1 (q, 2 H, OCH_2CH_3), 2.28 (m, $CH_2CO_2C_2H_5$), and 1.24 (t, 3 H, OCH_2CH_3). By integration of the nmr spectrum at 4.63 and 4.2 ppm the composition of the mixture was calculated to be 75% **3d** and 25% **2d**.

Anal. Calcd for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.91; H, 8.37; N, 6.31.

***cis*- and *trans*-Decahydroquinolines (6d and 7d).**—A solution of **2d–3d** (2.5 g, 11 mmol), obtained by chromatography of the crude oxidation product as described above in methanol (50 ml) and concentrated H_2SO_4 (1.3 ml), was hydrogenated over 10% palladium-on-charcoal catalyst (1.0 g) for 4 hr at an initial H_2 pressure of 45 psi; the mixture was filtered through a Celite pad into water (50 ml) and washed with methanol. The combined filtrates were concentrated, chilled in an ice bath, and brought to pH 9 with 5% aqueous sodium hydroxide. The mixture was extracted five times with 50-ml portions of ether and the extracts were dried over $MgSO_4$. Then the solution was refluxed for 22 hr. The solution was cooled and concentrated giving a mixture of *cis*- and *trans*-octahydrocarbostyrils.[23,24] The residue was dissolved in dry ether and added slowly to a stirred mixture of lithium aluminum hydride (1.04 g, 27.5 mmol) in dry ether (200 ml). After addition was complete the mixture was refluxed in a nitrogen atmosphere for 24 hr. The reaction mixture was cooled, and water was carefully added until aluminum salts precipitated as a granular mass. The mixture was filtered, and the precipitate was washed with hot tetrahydrofuran. After drying, the combined filtrates were concentrated to a clear oil, and the basic product was isolated by a standard extraction sequence, giving a clear oil (0.85 g, 61%). Preparative glpc was carried out on a 10-ft column of 10% Apiezon L, 5% KOH on Chromosorb G at 197°. The peak of low retention time was collected as white needles: mp 45.5–46.0° (lit. mp 48,[25,26] 45–47,[27] and 47.5–48.5°[28] for *trans*-decahydroquinoline[26]). The ir spectrum was superimposable with that of authentic[26] *trans*-decahydroquinoline. The peak of longer retention time was collected as a liquid and converted into a benzamide: mp 96.5–99.5° (lit. mp 96[26] and 99–100°[29] for *cis*-decahydroquinoline benzamide). The area of the two peaks was measured by planimetry and indicated that the decahydroquinoline mixture consisted of 86% *cis* isomer and 14% *trans* isomer.

(20) The literature[5] value is on a product of unspecified stereochemistry.

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(23) In one run this mixture was purified by chromatography. The ir spectrum of the purified octahydrocarbostyril mixture was compared with published spectra[24] of the pure *cis* and *trans* isomers. This comparison indicated that the product consisted of a mixture of the isomers.

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2-Nitronorbornane.—The general oxidation procedure performed on a 20-mmol scale gave a yellow-green liquid (1.95 g). Chromatography on silicic acid (60 g) using chloroform–hexane mixtures increasing from 10 to 30% chloroform was followed by tlc. Fractions 47–113 were combined and concentrated giving crude 2-nitronorbornane (0.86 g, 31%). Short-path distillation (0.08 mm) gave a solid: mp 64–68°, softening from 45° (lit.[13] mp 64–67° for >90% *endo*-2-nitronorbornane-3-^{14}C; nmr δ 4.84 (quintet, <1 H, J = 5.0 Hz, *exo* $-CHNO_2$) and 4.39 (m, <<1 H, *endo* $-CHNO_2$) (lit.[14] δ 4.73 for *exo* $-CHNO_2$). The nmr spectrum was integrated by planimetry and indicated 91% *endo*-2-nitronorbornane and 9% *exo*-2-nitronorbornane.

Isomerization of 2-Nitronorbornane.—The method of Roberts[13] gave after distillation a liquid: nmr δ 4.8 (m, <<1 H, *exo* $-CHNO_2$) and 4.39 (m, <1 H, *endo* $-CHNO_2$). Integration of the peaks at δ 4.8 and 4.39 ppm indicated that the product was at least 72% *exo* isomer. Roberts[13] estimated the composition as 70–80% *exo* by another method.

Attempted Oxidation of Camphor Oxime.—The general procedure was applied to *anti*-camphor oxime, but the yield of material showing nitro absorption was <5%. Camphor was recovered and identified.

Registry No.—**1c**, 17448-49-6; **1d**, 17448-51-0; **2a**, 17448-50-9; **2b**, 17448-52-1; **2c**, 17448-53-2; **2d**, 17448-54-3; **3a**, 17448-55-4; **3b**, 17448-56-5; **3c**, 17448-57-6; **3d**, 17448-46-3; **6d**, 10343-99-4; **7d**, 767-92-0.

Cyclopropanes. XXV. Cleavage of Cyclopropane Rings by Solutions of Sodium in Liquid Ammonia[1]

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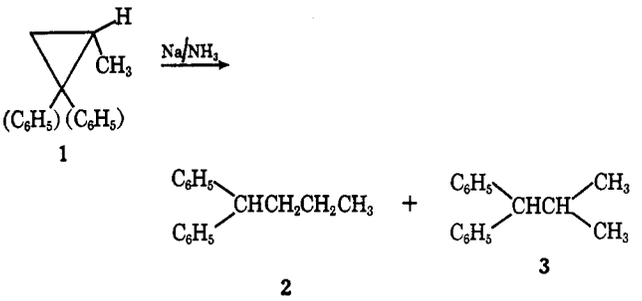
Reduction of 1-methyl-2,2-diphenylcyclopropane (**1**) in sodium and liquid ammonia led to ring cleavage with the formation of 1,1-diphenylbutane (**2**) and 1,1-diphenyl-2-methylpropane (**3**). Under similar conditions (−)-(*R*)-1-*n*-pentyl-1-methyl-2,2-diphenylcyclopropane and (+)-(*R*)-1-methyl-2,2-diphenylcyclopropanecarboxylic acid yielded racemic 1,1-diphenyl-3-methyloctane and 4,4-diphenyl-2-methylbutanoic acid, respectively. A mechanism for this reductive cleavage, involving ion-radical intermediates, is presented.

It has been known for some time that alkali metals in liquid ammonia solutions in the presence of a suitable acid (*i.e.*, NH_4X^-) causes cleavage of the cyclopropane ring in α-cyclopropyl ketones. Thus Van Volkenburg and coworkers[2] have found that the ring in cyclopropyl methyl ketone is opened to give a mixture of methyl propyl ketone and 2-pentanol by reaction with sodium and liquid ammonia in the presence of ammonium sulfate. Similarly, in some recent studies, Norin[3] and Dauben[4] have observed that solutions of lithium in liquid ammonia bring about a stereospecific opening of the cyclopropane ring in such a manner that the bond cleaved is the one possessing the maximum overlap with the π orbital of the carbonyl group. It has also been demonstrated that cyclopropyl esters[5] (but not acids) will undergo an analogous cleavage. On the other hand it has been shown that the cyclopropane ring in 2-cyclopropylpent-1-ene is not opened by sodium in liquid ammonia alone nor in the presence of ammonium bromide.[6] In the presence of methanol the double bond is reduced but the ring remains intact. Nefedov[7] has reported that the sodium–liquid ammonium reduction of 1,1-dichloro-2-phenylcyclopropane produced, besides the expected phenylcyclopropane, a 17% yield of propylbenzene.

During our studies on the reduction of optically active 1-bromo-1-methyl-2,2-diphenylcyclopropane with solutions of sodium in liquid ammonia[8] we found that the primary reduction product, 1-methyl-2,2-diphenylcyclopropane (**1**), was further reduced under the reaction conditions to give a mixture of 1,1-diphenylbutane (**2**) and 1,1-diphenyl-2-methylpropane (**3**). This observation has led us to study the cleavage of such compounds by sodium in liquid ammonia in more detail, and we now wish to report our results.



The yields of **2** and **3** produced by reduction of **1** have been found to vary with the concentration of the sodium in liquid ammonia solution used as reducing agent. In particular, when solutions of sodium in liquid ammonia of above 8% are used no reaction occurs over a 2-hr period; at concentrations of from 1 to 8% a mixture of **2**, **3**, and recovered **1** is produced; and at concentrations of less than 1% only **2** and **3** are formed. The yields of the two products and of recovered starting material are shown in Table I as a function of the concentration of the sodium in liquid ammonia reducing solutions. The yields shown represent the relative yields of each product as determined by gas chromatography of the reaction mixture. The total yield of these products was always greater than 90%. It will be noted that the ratio of the yields of **2** and **3**, when they are produced, remains fairly constant over

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