gave an additional 1.3 g of unreacted **2**. The yield of crude **5** is thus 73.5% of the reacted **2**, bp 60° (0.5 mm). It showed the expected azide and nitro absorption in the ir and was analyzed as the adduct to propiolic acid.

1-(2-Fluoro-2,2-dinitroethyl)-4- (or 5-) carboxy-1,2,3-triazole (6).—To 2.15 g of **4** in 10 ml of chloroform was added 0.9 g of propiolic acid, and the mixture was allowed to stand at room temperature for 3 days. The solid was filtered off and washed with a small amount of chloroform, and a second crop was obtained by chilling the filtrate. After recrystallization from acetonitrile–carbon tetrachloride (1:1), there was obtained 2.65 g (88.5%) of **6**: mp 160° with gassing (decarboxylation); nmr (acetone-d_6) δ 8.73 (s), 6.37 (d, J_{HF} = 16 cps), 4.64 (s, COOH); relative areas, 1:2:1.

Anal. Calcd for $C_5H_4FN_5O_6$: N, 28.11; F, 7.63; mol wt and neut equiv, 249.12. Found: N, 27.91; F, 7.80; mol wt (acetonitrile), 242; neut equiv, 242.[10]

1-(2,2-Dinitropropyl)-4- (or 5-) carboxy-1,2,3-triazole (7).—Azide **5**, 0.75 g, was reacted with propiolic acid in chloroform as described for **4**. **7** (0.95 g, 90.5%) was obtained: mp (after recrystallization from acetonitrile) 157–158° dec; nmr (acetone-d_6) δ 8.67 (s), 5.89 (s), 4.21 (s, COOH); relative areas, 1:2:1.

Anal. Calcd for $C_6H_7N_5O_6$ (245.15): C, 29.40; H, 2.88; N, 28.57. Found: C, 29.71; H, 2.84; N, 28.39.

Reaction of 1 with Potassium Hydroxide in Methanol.—Tosylate **1**, 50 g, was dissolved in 500 ml of warm methanol, the solution was cooled in an ice bath, and a precooled solution of 25 g of potassium hydroxide in 150 ml of methanol was added rapidly with stirring. Potassium tosylate precipitated immediately. The mixture was stirred for 15 min with continued cooling, the precipitate filtered off, and the filtrate freed from most of the methanol at 50° (25 mm). The residue and the previously obtained filter cake were triturated with 500 ml of water, the resulting two-phase mixture was extracted with methylene chloride, the extract was dried ($MgSO_4$), and the solvent was distilled off. A glp chromatogram of the remaining oil showed the presence of at least five compounds. The material was distilled at 0.1 mm and 8.3 g went over at 38–43°. The distillate was a 9:1 mixture of two components which were separated readily by chromatography on silica (G. F. Smith, Columbus, Ohio) with methylene chloride as the eluent. The impurity was eluted first. Thus obtained was 7.4 g (30%) of **8** of good purity: ir 1585, 1355 cm^{-1} (asym and sym NO_2 stretch); nmr (CCl_4) δ 5.64 (double d, J_{HF} = 49, J_{HH} = 4.5 cps), 4.73 (double d, J_{HF} = 10.6, J_{HH} = 4.5 cps), 3.50 (s), 3.47 (s); relative areas, 1:1:3:3; uv λ_{max} (0.01 *N* NaOH) 232.5 nm (ε 10,200) [compare 1-chloro-1-nitroethane, λ_{max} (0.1 *N* NaOH) 237 nm (ε 10,000)].[11]

Anal. Calcd for $C_4H_8FNO_4$: N, 9.15; F, 12.41. Found: N, 8.90; F, 12.71.

Registry No.—**1**, 18138-91-5; **2**, 27396-49-2; **3**, 27396-50-5; **4**, 27396-51-6; **5**, 27396-52-7; **6**, 27378-67-2; **7**, 27378-68-3; **8**, 27396-53-8.

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[10] Base was consumed rapidly past the point of neutralization which was therefore difficult to determine.

[11] M. F. Hawthorne, *J. Amer. Chem. Soc.*, **78**, 4980 (1956).

Nuclear Magnetic Resonance Anisotropic Effects of the Epoxy Group and Averaging of Coupling Constants in *trans*- and *cis*-4,5-Epoxy-*trans*-2-(*p*-chlorophenyl)nitrocyclohexane and Derivatives

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The long-range anisotropic effects of the epoxy group in *trans*- (1) and *cis*-4,5-epoxy-*trans*-2-(*p*-chlorophenyl)-nitrocyclohexane (2) cause deshielding of both axial hydrogens cis to the epoxy group and have little effect on the chemical shift of the axial hydrogen trans to, and two carbons removed from, the epoxy group. The deshielding of the cis axial hydrogen, two carbons removed, is of the same magnitude as the deshielding of the same hydrogen caused by the anisotropic effect of the double bond in the parent alkene. The nmr spectra establish the presence of very high populations of the half-chair conformations with the substituents in equatorial orientations for both epoxides and for the parent alkene. The configurational assignment of the isomeric epoxides has been verified from the nmr spectra of the derived diols, monoacetates, and diacetates from the difference between the spatial 1,3-diaxial deshielding effects of hydroxyl and acetoxy groups. Anisotropic deshielding effects of the epoxy, hydroxyl, and acetoxy groups are responsible for significant averaging of coupling constants, involving geminal hydrogens, observed in the spectra of the epoxides and their derivatives.

Epoxidation of *trans*-4-(*p*-chlorophenyl)-5-nitrocyclohexene (**3**)[2] with *m*-chloroperbenzoic acid in ethyl ether yielded the isomeric epoxides *trans*- (**1**) and *cis*-4,5-epoxy-*trans*-2-(*p*-chlorophenyl)nitrocyclohexane (**2**) with a much larger proportion of the trans isomer **1**. The nmr spectra of **1** and **2**, Figure 1, are significantly different. Analysis of the spectra shows that the observed differences are not due to conformational differences, as might be suspected, but result from long-range shielding effects of the epoxy group and from averaging of coupling constants caused by these effects. Complications resulting from averaging of coupling constants due to strong coupling effects in ABX (or higher spin) systems, in which A and B are geminal hydrogens with small chemical shift differences, have been fully described.[3–6] The important thing to keep in mind is that in such systems strong coupling effects tend to average the individual values of J_{XA} and J_{XB}, thus causing changes in the pattern of the signal involved, but the sum of the coupling constants and, therefore, the width of the signal are not affected.[3]

Conformation of Epoxides, Anisotropic Effects, and Averaging of Coupling Constants.—Figure 1 gives portions of the 60-MHz spectra of the two epoxides measured in chloroform-*d*. The width of the signal of H-1 (27.2 Hz at δ 4.89, spectrum A) of the major epoxide **1** and the widths of the signals of H-1 (29 Hz) and H-2 (27.9 Hz) of the minor epoxide at δ 4.68 and 3.34, re-

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[1] NSF Undergraduate Participant, 1968.

[2] A. C. Huitric and W. D. Kumler, *J. Amer. Chem. Soc.*, **78**, 614 (1956).

[3] W. F. Trager, B. J. Nist, and A. C. Huitric, *J. Pharm. Sci.*, **56**, 698 (1967).

[4] R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, **39**, 216 (1961).

[5] J. I. Musher and E. J. Corey, *Tetrahedron*, **18**, 791 (1962).

[6] T. Schaefer, *Can. J. Chem.*, **40**, 1679 (1962).

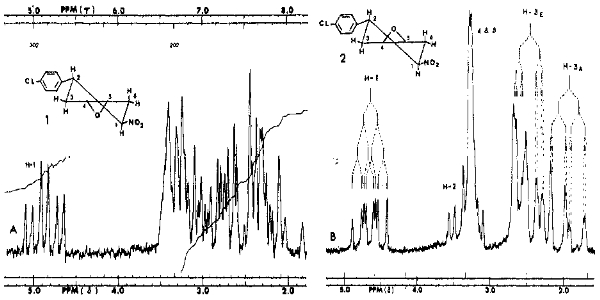


Figure 1.—Portions of the 60-MHz nmr spectra of the major **1** (spectrum A) and minor **2** (B) epoxides in chloroform-*d* at about 33-35° with TMS as internal reference.

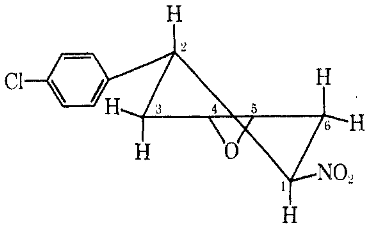
spectively, spectrum B, establish that each of these compounds has a very high population of the half-chair conformation with the nitro and aromatic groups in equatorial orientations as depicted by structures **1** and **2**. These signal widths (the sum of the coupling constants) are consistent with H-1 and H-2 having axial orientations and each being coupled with two adjacent axial and one equatorial hydrogens. In these mobile systems, any contribution from the other half-chair conformation (substituents axial) or any other flexible conformations would decrease the width of the signals of H-1 and H-2. In the other half-chair conformation H-1 and H-2 have equatorial orientations and the width of their signals would be in the order of 9–12 Hz. In compound **1** the signal of H-1 gives an essentially first-order triplet of doublets, $J_{12} \simeq J_{16a} \simeq 11.2$ and $J_{16e} \simeq 4.8$ Hz, but the signal of H-2, which is partially overlapped by the signals of H-4 and H-5, gives a more complex pattern. In the minor epoxide the signal of H-2 at δ 3.34, which is partially overlapped by signals of H-4 and H-5, gives essentially a first-order triplet of doublets, $J_{21} \simeq J_{23a} \simeq 11.6$ and $J_{23e} \simeq 4.6$ Hz, but the signal of H-1 is complicated by averaging of coupling constants and does not yield true coupling constants by first-order approximation. The widths of the signals of the hydrogens on the nitro- and aromatic-bearing carbons of the parent alkene **3** in chloroform-*d* are 26.7 and 27.5 Hz, respectively, indicating a similar high population of the half-chair conformation depicted by structure **3**. For the corresponding alkane **4**, the width of the signal of H-1 is 26 Hz in chloroform-*d*. This compound has been shown to exist essentially in the chair conformation with both substituents in equatorial orientations.[7]

The chemical shifts of the hydrogens on the nitro- and aromatic-bearing carbons of the parent cyclohexene, the corresponding cyclohexane, and the isomeric epoxides are given in Table I. In the parent cyclohexene **3**, in the conformation depicted by structure **3**, H-4 and H-5 have identical geometrical relationships to the double bond and should therefore experience analogous deshielding effects from the magnetic anisotropy of the double bond. This is substantiated by comparison of chemical shifts of these hydrogens with those of the corresponding hydrogens of the saturated compound **4**. Differences of 0.29 and 0.28 ppm are seen for the hydrogen on the nitro- and aromatic-bearing carbons, respectively, between compounds **3** and **4**. In the two isomeric epoxides, when in their established favored conformations, H-1 of **1** and H-2 of **2** have analogous cis geometrical relationships to the epoxy group, and likewise H-2 of **1** and H-1 of **2** have similar trans relationships to the epoxy group. It is interesting to note that the chemical shifts of H-1 in **1** and H-2 in **2** are about identical with those of the corresponding hydrogens in the parent alkene and that the chemical shift of H-1 in **2** is very close to that of H-1 in the corresponding saturated compound **4**.[8] This indicates that when measured in chloroform-*d* the epoxy group in a six-membered ring existing in a given half-chair conformation causes a deshielding of about 0.20 to 0.26 ppm of a cis axial hydrogen two carbons removed from the epoxy group, and that it has little effect on the chemical shift of a trans

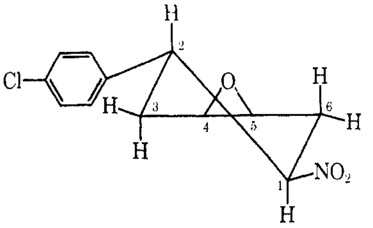
TABLE I

CHEMICAL SHIFTS IN CHLOROFORM-*d* IN δ UNITS (PARTS PER MILLION), INTERNAL TMS

	O_2NCH	ArCH
Parent cyclohexene **3**	4.89	3.36
Major epoxide **1**	4.89	
Minor epoxide **2**	4.68	3.34
Cyclohexane **4**	4.60	3.08



1



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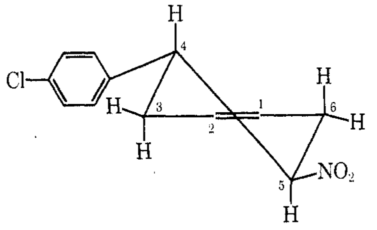

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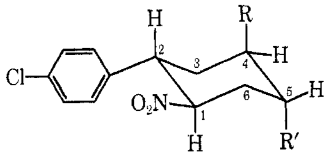

4, R = R′ = H
5, R = R′ = OH
6, R = R′ = OAc
7, R = OAc; R′ = OH
8, R = OH; R′ = OAc

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[7] W. F. Trager, F. F. Vincenzi, and A. C. Huitric, *J. Org. Chem.*, **27**, 3006 (1962).

[8] A similar relationship seems to hold between H-2 of **1** and H-2 of the saturated compound **4**, but the chemical shift of H-2 in **1** cannot be determined with certainty.

axial hydrogen two carbons removed.[9] Spectra A and B indicate that there is also deshielding of the adjacent cis pseudoaxial hydrogens H-6a in **2** and H-3a in **1**. There is apparently little effect on the chemical shift of the adjacent trans pseudoaxial H-3a in **2**. At least, the observed difference of 0.52 ppm between the chemical shifts of the equatorial and axial hydrogens on C-3 is normal. First-order treatment of the signals of H-3a centered at δ 1.93, H-3e at 2.45, and H-2 at 3.34, in spectrum B gives the following apparent coupling constants: $J_{3a3e} \simeq 15.5$, $J_{23a} \simeq J_{21} \simeq 11.6$ Hz; $J_{23e} \simeq 4.6$, $J_{3a4} \simeq J_{3e4} \simeq 1.5$ Hz. The signal of H-2, although partially overlapped with the signals of H-4 and H-5, shows essentially a first-order triplet of doublets, as expected from coupling with axial H-1, axial H-3a, and equatorial H-3e, providing that there is a sufficient difference between the chemical shifts of geminal H-3a and H-3e. In contrast to H-2, the signal of H-1 gives an eight-peak multiplet. The complexity of the signal arises from averaging of coupling constants J_{16a} and J_{16e} because of the small difference in chemical shifts between geminal H-6a and H-6e. The signals of the geminal hydrogens on C-6 appear as a pair of complex components, about 8–9 Hz apart, centered at about δ 2.60. They partially overlap the signal of H-3e. The observed pattern is explainable on the basis of a small difference in chemical shift between the two geminal hydrogens and an averaging of their coupling constants with H-1. The outer components of the highly skewed doublets resulting from geminal coupling are not discernible. The signal of H-1 gives $J_{12} \simeq 11.7$ Hz, and averaging of J_{16a} and J_{16e} to yield separations of 9.7 and 7.7 Hz, respectively. The computer reproduced spectrum[10] of H-1 matched the observed spectrum exactly when the difference of 4 Hz was used between the chemical shifts of H-6a and H-6e with the equatorial hydrogen at lower field. The other values used were $J_{gem} = -15.5$, $J_{aa} = 11.7$, and $J_{ae} = 5.7$ Hz.[11] Decoupling of H-1, by double resonance, caused a partial merging of the two components of the C-6 hydrogens without causing any change in the signals of the hydrogens on C-3. Strong irradiation in the region of the C-6 hydrogens caused a collapse of the signal of H-1 essentially into a doublet with separation of about 11.5 Hz. Clean decoupling becomes more difficult the larger the coupling constants with the hydrogen being decoupled (the wider its signal). The near equivalence of chemical shifts of H-6a and H-6e is attributed to a deshielding effect of H-6a by the *cis*-epoxy group. The anisotropy of the nitro group may also play a role, but the fact that the signals of H-1 in **4** and in **1** are essentially first-order, six-peak multiplets indicates that the role of the epoxy group is the most important. The fact that the signal of H-2 in **1** appears to be complicated by averaging of coupling constants is consistent with a deshielding of axial H-3a by the adjacent *cis*-epoxy group.

Proof of Configuration.—The configurations of the epoxides **1** and **2** were established from the nmr spectra of their diol, diacetate, and monoacetate derivatives by taking advantage of the spatial 1,3-diaxial deshielding effects of a hydroxyl group on ring hydrogens[12-16] and of the larger deshielding effect of a hydroxyl group compared to the corresponding acetoxy group.[13,15,17] The diol was obtained by acid-catalyzed hydrolysis of either epoxide or from a mixture of the two. The monoacetates were prepared by treating each epoxide with potassium acetate in acetic acid, and the diacetate was prepared from the diol or the monoacetates. The relevant portions of the 60-MHz spectra of the four derivatives, in pyridine, are given in Figure 2. The widths of the signals of H-1 or H-2, or both when discernible, are of the order of 27–28 Hz, consistent with H-1 and H-2 having axial orientations and being coupled with two axial and one equatorial hydrogens. This establishes a high time-average population of the chair conformation with the nitro and aromatic group in equatorial orientations for each derivative. The narrow signals of H-4 and H-5 indicate that these hydrogens have the equatorial orientation and establish that in each derivative the hydroxyl and acetoxy group have the trans-diaxial relationship while the nitro and aromatic groups have the trans-diequatorial orientations. The structures of these products indicate that the epoxide opening occurred *via* a transition state which can be visualized as having the aromatic and nitro groups essentially

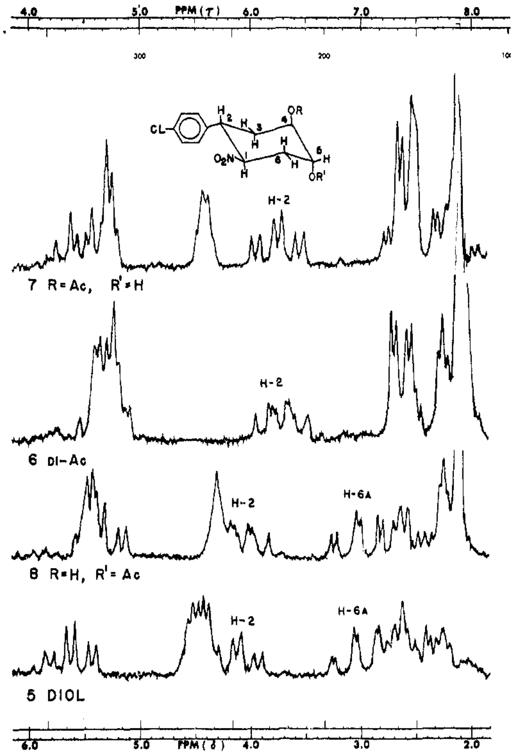

Figure 2.—Portions of the 60-MHz nmr spectra of the diol **5**, the diacetate **6**, and the major **7** and minor **8** monoacetates in pyridine at about 33–35° with TMS as internal reference.

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[9] The assumption is made that there is little difference in the time-average populations of rotamers of the nitro and aromatic groups between the epoxides, the cyclohexene, and the cyclohexane in the conformations described, with both substituents in equatorial orientations.

[10] K. B. Wiberg and B. J. Nist, "The Interpretation of NMR Spectra," W. Benjamin, New York, N. Y., 1962.

[11] The theoretical value of 5.7 Hz for J_{ae} exceeds observed J_{23e} by about 1 Hz. It was obtained by difference from the width of the signal of H-1, with the assumption that J_{12} and J_{16a} are equal. This assumption may not be exactly correct, but the results clearly demonstrate the complications by averaging of coupling constants.

[12] A. C. Huitric, J. B. Carr, and W. F. Trager, *J. Pharm. Sci.*, **55**, 211 (1966).

[13] D. B. Roll and A. C. Huitric, *ibid.*, **55**, 942 (1966).

[14] K. Tori and T. Komeno, *Tetrahedron*, **21**, 309 (1965).

[15] N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, pp 19, 185.

[16] P. V. Demarco, E. Farkas, D. Doddrell, B. L. Mylari, and E. Wenkert, *J. Amer. Chem. Soc.*, **90**, 5480 (1968).

[17] K. Tori and E. Kondo, *Steroids*, **4**, 713 (1964).

equatorial. A transition state involving the other half-chair conformation, with the aromatic and nitro groups axial, would yield a diol which would differ from structure **5** by having the trans-diequatorial hydroxyl groups. Similar all-equatorial products would be obtained from such transition states in the formation of the monoacetates, but in addition the relative skeletal positions of the hydroxyl and acetoxy groups would be inverted in the product from a given epoxide. There is no evidence that any such products were formed.

The determination of the direction of epoxide opening also establishes that epoxides **1** and **2** yield the monoacetates **7** and **8**, respectively. The monoacetates were characterized by comparing the chemical shifts of H-1 and H-2 with those of the diol and diacetate in pyridine. The monoacetate obtained from the major epoxide gives spectrum **7**. The similarity in chemical shifts of H-2 with that of the diacetate (spectrum **6**) and of H-1 with that of the diol (spectrum **5**) establishes that this monoacetate has the acetoxy group at C-4, structure **7**. This characterizes the major epoxide as structure **1**. The monoacetate obtained from the minor epoxide gives spectrum **8**. The similarity in chemical shifts of H-2 with that of the diol and of H-1 with that of the diacetate establishes that the compound has the acetoxy group at C-5. This characterized the minor epoxide as structure **2**.

TABLE II

CHEMICAL SHIFTS IN PYRIDINE IN δ UNITS (PARTS PER MILLION), INTERNAL TMS

	H-1	H-2	H-6a
Diol **5**	5.62	4.12	3.04
Di-Ac **6**	5.32	3.72	
Monoacetate **7** (from major epoxide)	5.52	3.75	
Monoacetate **8** (from minor epoxide)	5.35	4.08	3.02
Cyclohexane **4**	4.87	3.12	

Averaging of Coupling Constants in the Acetates.—Spectrum **5**, of the diol, gives essentially first-order signals for H-1 and H-2 with observed coupling constants of $J_{12} \simeq J_{16a} \simeq J_{23a} \simeq 11.6$ Hz, $J_{16e} \simeq 4.5$ Hz, and $J_{23e} \simeq 4.2$ Hz. Comparison of the chemical shifts of H-1 and H-2 of the diol with the alkane **4** shows a deshielding of 1.0 ppm of H-2 by the axial C-4 hydroxyl group and of 0.75 ppm of H-1 by the axial C-5 OH group. Similar deshielding effects will be experienced by axial H-3a and axial H-6a, and the chemical shifts of these axial hydrogens are expected to be at lower field than those of their geminal equatorial partners. The signal (triplet of doublets) centered at δ 3.04 is attributed to H-6a. The observed pattern results from the geminal coupling with H-6e being about equal to $J_{6a1} \simeq$ 11–13 Hz, and $J_{6a5} \simeq$ 3–4 Hz.[18] When an acetoxy replaces an axial OH group, the 1,3-diaxial deshielding is reduced such that an acetoxy group at C-5 will cause the chemical shifts of the geminal hydrogens at C-3 to be more closely equivalent; an axial acetoxy at C-4 will have a similar effect on the geminal C-6 hydrogens. The complex patterns of the signals of H-2 in the diacetate **6** and monoacetate **8** are attributed to averaging of J_{23a} and J_{23e} because of small differences in the chemical shifts of the C-3 geminal hydrogens.[19] Similarly, the small difference in chemical shifts of the geminal C-6 hydrogens in **7** causes the complex pattern of H-1. The similarity in chemical shifts of H-6a of the minor acetate and the diol further substantiates that the minor acetate has the OH group at C-4.

Experimental Section[20]

***trans*-4,5-Epoxy-*trans*-2-(*p*-chlorophenyl)nitrocyclohexane (1) and *cis*-4,5-Epoxy-*trans*-2-(*p*-chlorophenyl)nitrocyclohexane (2).**—A solution of 10 g (0.042 mol) of *trans*-4-(*p*-chlorophenyl)-5-nitrocyclohexene (**3**)[2] and 17.1 g of 85% *m*-chloroperbenzoic acid (0.084 mol) in 200 ml of anhydrous ethyl ether was kept at room temperature, and the progress of the reaction was followed by thin layer chromatography (tlc) on silica gel. A solvent mixture of equal volumes of chloroform and hexane gave good separation of the alkene from the epoxides, with the alkene having the largest R_f value. There was no evidence of starting alkene after 4 days. The ether solution was then washed successively with aqueous 20% sodium bisulfite, water, saturated sodium bicarbonate solution, and water. Removal of the solvent gave 6.5 g of colorless solid, mp ~103–107°. The nmr spectrum indicated a mixture of epoxides with a large predominance of isomer **1** which could be obtained by recrystallization of the mixture in 2-propanol, mp 107.5–109°. Tlc on silica gel (ethyl ether) showed separation of the isomers. The minor isomer **2** was obtained in pure form by ascending dry-column chromatography using silica gel (0.05–0.2 mm) deactivated to Brockmann activity II[21] and equilibrated with 5% ethyl ether. Anhydrous ethyl ether was used as solvent. A mixture of epoxides (5.7 g) which had been enriched in **2** by crystallization of **1** was deposited on 20 g of silica gel, and this material was placed at the bottom of 5 × 95 cm nylon tubing column equipped for ascending chromatography. The solvent was brought to 8 cm from the top in 5 hr. Positions of the compounds on the column were approximated with the aid of a uv lamp;[22] the column was sliced in sections and the compounds were eluted by soaking in ether. Three 6-cm sections, with R_f values[23] of 0.49, 0.55, and 0.62, contained pure **2** (analyzed by tlc and nmr). The next section contained a mixture of **1** and **2**, and pure **1** was found in the upper part of the column. The separated isomers were recrystallized from 2-propanol, mp 107.5–109°, for the major epoxide **1**, and 108.5–109.5° for **2**. A mixture of the two epoxides gives a depression in the melting point.

Anal. Calcd for $C_{12}H_{12}ClNO_3$: C, 56.81; H, 4.77; N, 5.52. Found (**1**): C, 56.61; H, 4.87; N, 5.50. Found (**2**): C, 56.83; H, 4.92; N, 5.51.

***trans*-2-(*p*-Chlorophenyl)-*cis*-4-acetoxy-*trans*-5-hydroxynitrocyclohexane (7) and *trans*-2-(*p*-Chlorophenyl)-*cis*-4-hydroxy-*trans*-5-acetoxynitrocyclohexane (8).**—The monoacetates were prepared by allowing a solution of about 500 mg of the epoxide and 650 mg of potassium acetate in 10 ml of glacial acetic acid to stand at room temperature for 3 or 4 days. The solution was

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[18] The assignment of H-6a has been verified by decoupling of H-1 at 100 MHz. The 100-MHz spectrum also gives distinct signals for H-4 and H-5 at δ 4.38 and 4.50, respectively. Differentiation between H-4 and H-5 was done by decoupling of H-6a, causing a narrowing of the signal at δ 4.50 without affecting the signal at 4.38. The 100-MHz spectrum also shows the signal of equatorial H-3a as a six-peak multiplet (doublet of triplets, $J_{gem} \simeq 13$, $J_{3e2} \simeq J_{3e4} \simeq 3.5$ Hz) centered at δ 2.13. Decoupling of H-2 causes a decrease in the multiplicity of this signal and does not affect the signal assigned to H-6a.

[19] The near equivalence of the geminal C-3 hydrogens of the minor monoacetate **8** is clearly seen in the 100-MHz spectrum where the signals of these two hydrogens overlap to give a signal centered at δ 2.15 (also overlapped by the acetoxy methyl hydrogens). At 100 MHz the signal of equatorial H-6e appears as a six-peak multiplet ($J_{gem} \simeq 13$, $J_{6e1} \simeq J_{6e3} \simeq 3.5$ Hz) centered at δ 2.51. Decoupling of H-1 changes the multiplicities of the signals of H-6a and H-6e, while irradiation at the position of H-2 causes changes in the pattern of the overlapping H-3a and H-3e signals without causing any changes in the signals of H-6a and H-6e.

[20] Melting points were determined on a Kofler micro hot stage. The nmr spectra were obtained with a Varian A-60 spectrometer, unless otherwise stated, in the solvents reported, with TMS internal standard, at an operating temperature of about 33–35°.

[21] B. Loev and M. M. Goodman, *Chem. Ind.* (*London*), 2026 (1967).

[22] About 0.5% of G.E. Electronic Phosphor, type 118-2-7, was blended with the silica gel as a fluorescent indicator.

[23] These values are taken from the center of the sections.

then added to 100 ml of water, the mixture extracted with ether, the ethereal extract washed with sodium bicarbonate solution and dried (Na_2SO_4), and the solvent removed. The product was recrystallized from a mixture of benzene and hexane. Epoxide **1** yielded the monoacetate **7**, mp 161–162°, and the minor epoxide **2** gave monoacetate **8**, mp 168.5–170°.

Anal. Calcd for $C_{14}H_{16}ClNO_5$: C, 53.59; H, 5.14; N, 4.46. Found (**7**): C, 53.39; H, 5.14; N, 4.41. Found (**8**): C, 53.80; H, 5.21; N, 4.45.

***trans*-2-(*p*-Chlorophenyl)-*cis*-4-*trans*-5-dihydroxynitrocyclohexane (5).**—A mixture of 1.5 g of epoxide **1** (or a mixture of the two epoxides), 7.5 ml of H_2O, and 2 drops of concentrated H_2SO_4 in 15 ml purified dioxane was allowed to stand for 2 days. The mixture was added to 60 ml of water and extracted with ether. The product was recrystallized from a mixture of benzene and hexane, mp 204–205°.

Anal. Calcd for $C_{12}H_{14}ClNO_4$: C, 53.03; H, 5.19; N, 5.16. Found: C, 52.96; H, 5.51; N, 5.09.

The diacetate **6** was prepared from **5** with acetic anhydride in dry pyridine by the usual manner and recrystallized from a mixture of benzene and hexane, mp 162–163°.

Anal. Calcd for $C_{16}H_{18}ClNO_6$: C, 54.02; H, 5.10; N, 3.94. Found: C, 53.91; H, 5.14; N, 3.78.

Registry No.—**1**, 27390-71-2; **2**, 27390-72-3; **4**, 17321-89-0; **5**, 27390-74-5; **6**, 27390-75-6; **7**, 27390-76-7; **8**, 27390-77-8.

Orientation in the 1,3-Dipolar Cycloaddition Reactions of Heteroaromatic Nitrogen Methylides with Dipolarophiles[1]

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The orientation in the 1,3-dipolar cycloaddition reactions of several ring-substituted nitrogen methylides with dipolarophiles was investigated. The cycloaddition reactions of 3-substituted pyridazinium methylides with dimethyl acetylenedicarboxylate (DAC) and cyanoacetylene afforded the corresponding cycloadducts. In reactions of 3,6-dialkoxypyridazinium methylides with DAC, one of two alkoxyl groups was expelled in the formation of the adducts. A mixture of isomeric adducts was obtained in the reactions of 3-substituted pyrazinium methylides and 3-substituted pyridinium methylides, in which the major product was produced by cyclization at the C-2 position. An isomeric mixture of the adducts was also obtained by the reaction of 3,4-dimethylpyridinium methylide; however, the major product was afforded by cyclization at the C-6 position. Although the thermal addition of 4-carbomethoxypyridinium methylide to DAC afforded the cycloadduct, the methylide was photochemically too stable to undergo the photocycloaddition.

Indolidines and polyazaindolidines of the 10-π-electron system are of interest for the studies on azulene heteroanalogs, and recent studies[2,3] have focused on the convenient one-step synthesis of these aromatic heterocycles by 1,3-dipolar cycloaddition reactions.

Although the mechanism of 1,3-dipolar cycloaddition reactions has been extensively discussed by Huisgen and Firestone,[4] little is known about the orientation in 1,3-dipolar cycloaddition reactions of ring-substituted heteroaromatic nitrogen methylides with dipolarophiles. Recent results[3,5] in the 1,3-dipolar photocycloaddition reactions of isoelectronic 3-methyl-1-carbethoxyiminopyridinium ylide disclose significant differences between ground state and the excited state properties. In continuation of these studies,[3,5] this paper deals with an extension of the 1,3-dipolar cycloaddition of a series of ring-substituted heteroaromatic nitrogen methylides with dipolarophiles.[6]

Results and Discussion

Pyridazine (**1**), substituted pyridazine derivatives (**2–6**), and β-substituted pyridine derivatives (**26** and **27**) reacted with tetracyanoethylene oxide (TCNEO) to give crystalline compounds **7**, **8–12**, **30**, and **32**, respectively. Their compositions corresponded to 1:1 adducts of the base and dicyanomethylene. The infrared spectra of these compounds exhibit common strong nitrile absorptions at 2225 and 2220 cm^{-1}, indicating a high degree of ionic character in the dicyanomethylides.[7] Pyrazinium *N*-phenacylide (**22**) and pyridinium *N*-phenacylides (**31**, **33–35**) were prepared by treatment of the corresponding phenacyl bromides with aqueous potassium carbonate.[3] The structures of these ylides are based on the structural elucidation of 1,3-dipolar cycloaddition products as discussed below. The physical data of the dicyanomethylides **7–12** and **32** are summarized in Table I.

1,3-Dipolar Cycloaddition of Pyridazinium Methylides with DAC and Cyanoacetylene.—The 1,3-dipolar cycloaddition reactions of pyridazinium dicyanomethylide (**7**) and 3-substituted pyridazinium dicyanomethylides **8** and **10** with DAC afforded the cycloadducts **13–15**, respectively, in 50–70% yields. The spectrum of **13** shows a doublet at τ 1.87 (1 H, H_4, $J_{4,3}$ = 6.0 Hz),[8] double doublets at τ 2.74 (1 H, H_3, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 3.0 Hz), a doublet at τ 1.90 (1 H, H_2, $J_{2,3}$ = 3.0 Hz),[8] and singlet signals of two methyl protons at τ 5.88 and 5.99. In contrast, the spectra of **14** and **15** exhibit two ring proton signals at τ 1.70–1.80 (1 H) and τ 2.93–3.35 (1 H) as each doublet with the coupling constant of 9–10 Hz. Since the coupling constants of compound **13** are considerably different from those of compounds **14** and **15**, the structural elucidation of **13** was

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[1] Studies of Heteroaromaticity. XLIII.

[2] For a recent review, see V. Boekelheide and N. A. Fedoruk, *J. Amer. Chem. Soc.*, **90**, 3830 (1968), and references cited therein.

[3] T. Sasaki, K. Kanematsu, and Y. Yukimoto, *J. Chem. Soc. C*, 481 (1970).

[4] (a) R. Huisgen, *J. Org. Chem.*, **33**, 2291 (1968); (b) R. A. Firestone, *ibid.*, **33**, 2285 (1968).

[5] T. Sasaki, K. Kanematsu, A. Kakehi, I. Ichikawa, and K. Hayakawa, *ibid.*, **35**, 426 (1970).

[6] Contrary to extensive studies on the 1,3-dipolar cycloaddition reactions of the zwitterionic methylides with DAC, the same reactions of 1-alkoxycarbonyliminopyridinium ylides will be presented later [see Studies of Heteroaromaticity. LI (submitted for publication in *J. Org. Chem.*)].

[7] W. J. Linn, O. W. Webster, and R. E. Benson, *J. Amer. Chem. Soc.*, **87**, 3651 (1965).

[8] The assignment of the H_2 and H_4 signals is based on the magnitude of $J_{4,3}$ in **13** and of $J_{3,4}$ in **14** and **15**; it may be the reverse of that given.