The Stereochemistry of Protonation of Nitrocycloalkane Nitronate Ions

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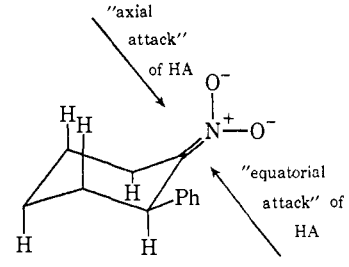
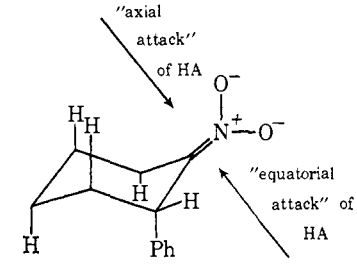
Abstract: The stereochemistry of the protonation of nitronate ions has been found to be relatively insensitive to the acidity of the proton donor, both from direct observations with media of differing acidities and by the success with which calculations of the stereochemical outcome for protonations with methanol can be used to predict the outcome of protonations by acetic acid–acetate buffers. The calculations for methanol protonations were based on a consideration of these protonations as being the microscopic reverse of deprotonations of the corresponding nitroalkanes by NaOMe–MeOH. The predictions of protonation stereochemistry held reasonably well, not only in instances where the deprotonation k_{cis}/k_{trans} ratios corresponded closely with those expected from relative ground-state energies (*e.g.*, 4-*t*-butyl-1-nitrocyclohexane, 4*e*-*t*-butyl-2*a*-phenyl-1-nitrocyclohexane, and 2-phenyl-1-nitrocyclopentane), but also in instances where the k_{cis}/k_{trans} ratios were much higher than expected on the basis of relative ground-state energies (*e.g.*, 2-methyl- and 2-phenyl-1-nitrocyclohexane, 5-nitrobicyclo[2.2.1]hept-2-ene, and 2-nitrobicyclo[2.2.1]heptane). In the latter instances steric effects are believed to direct the stereochemistry of the protonation. For 2-substituted cyclohexanenitronate ions it is, however, the 2 substituent and not the axial hydrogen atoms on the cyclohexane ring that exerts the principal effect on the stereochemical outcome. Removal of the *exo* proton in 2-nitronorbornane is favored by *ca.* 15:1 and protonation of the 2-norbornanenitronate ion on the *exo* side is favored by *ca.* 6:1. The striking parallel between this result and the preference for removal of and return of *exo* groups in the solvolysis of 2-norbornane derivatives is brought out. $A^{1,3}$ strain is discounted as a factor in affecting deprotonation rates or in affecting the stereochemistry of protonation. Ultraviolet spectra of 2-substituted cyclohexanenitronate ions offer no support for the suggestion that the 2 substituent is required to assume an axial position because of $A^{1,3}$ strain. The possible application of these ideas to account for the stereochemistry of protonation of 2-substituted cyclohexane enols is mentioned.

The striking preference for the formation of the less stable isomer on protonation of a number of 2-substituted cyclohexanenitronate ions and cyclohexane enolate ions was first pointed out by Zimmerman in an elegant series of papers.[1] The preference was correctly recognized as being steric in nature and the suggestion was made that the steric factor had its origin in the extent to which the two axial hydrogen atoms on the top side (in the drawing) prevented approach of the proton donor from the "axial side" as compared to the extent to which the three axial hydrogen atoms on the bottom side (in the drawing) prevented attack from the "equatorial side." It was concluded from an examination of models that there was less hindrance to approach from the "equatorial side" of **1a**.[2] The phenyl group was assumed to have no influence on the course of the reaction, since in the ideal chair it lies in the same plane as the $>C{=}NO_2^-$ grouping, and therefore exerts the same influence on approach of the reagent from either the axial or equatorial side.

An alternative explanation for the stereochemistry of protonation has been offered recently by Malhotra and Johnson.[3] They suggest that, because of $A^{1,3}$ strain, the



1a



1b

2-phenylcyclohexanenitronate ion exists in conformation **1b**, instead of **1a**, and that the axial phenyl group hinders protonation from the equatorial side. Axial protonation then leads to the less stable conformation of *cis*-α-phenyl-1-nitrocyclohexane (*i.e.*, 2*a*-phenyl-1*e*-nitrocyclohexane). As support for this view they cited nmr evidence to show that the phenyl group was indeed axial in the 2-phenylcyclohexanenitronate ion, but this interpretation of the nmr spectrum has been questioned.[4] In any event, reaction could still occur *via* **1a**.

In our laboratory the observation that *cis*-2-phenyl-1-nitrocyclohexane is deprotonated 350-fold more

(1) (a) H. Zimmerman, *J. Org. Chem.*, **20**, 549 (1955); (b) H. E. Zimmerman and T. E. Nevins, *J. Amer. Chem. Soc.*, **79**, 6559 (1957); (c) see H. E. Zimmerman, "Molecular Rearrangements," Vol. 1, P. deMayo, Ed., Interscience, New York, N. Y., 1963, Chapter 6.

(2) This view has been widely accepted; see, *e.g.*, E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1966, p 124. In a somewhat analogous situation, attack of small reagents at the carbonyl group of cyclohexanones, it has been concluded, however, that axial approach is less hindered [J. C. Richer, *J. Org. Chem.*, **30**, 324 (1965)], or that equatorial approach is more hindered if the transition state comes "late," but that axial attack may be more hindered if the transition states comes "early" [J. A. Marshall and R. D. Carroll, *ibid.*, **30**, 2748 (1965)].

(3) S. K. Malhotra and F. Johnson, *J. Amer. Chem. Soc.*, **87**, 5492 (1965).

(4) H. E. Zimmerman and P. S. Marino, *ibid.*, **90**, 6091 (1968).

Table I. Comparison of the Stereochemistry of Protonation of Nitronate Ions with Methanol and with Acetic Acid–Acetate Buffer

cis–trans systems	Equilibration[a] (% *trans*)	Methoxide deprotonation[b] (k_{cis}/k_{trans})	Protonation[c] % *cis* obsd (HOAc–LiOAc, H_2O–EtOH)	Protonation[c] % *cis* calcd[d] (MeOH)
4-*t*-Butyl-1-nitrocyclohexane	82	6.15	35	56
4-Phenyl-1-nitrocyclohexane	79[e]	4.90	37[e]	57
2-Methyl-1-nitrocyclohexane	90	39.4	85	82
2-Phenyl-1-nitrocyclohexane	*Ca.* 100	350	*Ca.* 100	79
2-Phenyl-1-nitrocyclopentane	89	4.50	44	35
4*e*-*t*-Butyl-2*e*-phenyl-1-nitrocyclohexane	98	59.0	16	55
4*e*-*t*-Butyl-2*a*-phenyl-1-nitrocyclohexane	50	1.0	50	50
5-Nitrobicyclo[2.2.1]hept-2-ene	64.5[f] (*exo*)	23[g] (*endo*/*exo*)	95[h] (*endo*)	94 (*endo*)
2-Nitrobicyclo[2.2.1]heptane	72[i] (*exo*)	15[g] (*endo*/*exo*)	86[j] (*endo*)	86 (*endo*)

[a] Unless otherwise indicated, equilibration was achieved by refluxing for 4 hr (at *ca.* 78°) in 95% ethanol containing $NaHCO_3$. [b] Rate of deprotonation measured at 25° in NaOMe–MeOH unless otherwise specified; see ref 7. [c] At room temperature (25°). [d] Calculated as described in the text. [e] Reference 4. [f] In *t*-BuOK–*t*-BuOH at 75°; R. J. Ouellette and G. E. Booth, *J. Org. Chem.*, **30**, 423 (1965). [g] Deprotonation with hydroxide ion in 50% (v/v) H_2O–dioxane at 28°; P. W. K. Flanagan, Ph.D. Dissertation, Ohio State University, 1957. The ratio measured in 50% (v/v) H_2O–dioxane is 19.7 at 0°, 18.4 at 9.9°, and 15 at 28°. See also H. Shechter, P. W. K. Flanagan, H. Stone, J. G. Traynham, and F. J. Williams, Jr., Abstracts, 136th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1959, p 33P. [h] Protonation with dilute acetic acid (see Ouellette and Booth in footnote *f*). [i] R. J. Sundberg and P. A. Bukowick, *J. Org. Chem.*, **33**, 4098 (1968). [j] Composition obtained on oxidation of the oxime (see footnote *i*).

rapidly than its *trans* isomer was traced to a retarding effect in the *trans* isomer.[5] To account for this it was suggested that in the *trans* (but not the *cis*) isomer the nitro and phenyl groups bend away from one another causing a deformation (or flattening) of the chair.[6] This view has since been supported by experimental evidence.[7] It was further suggested that at least part of the cause of slow deprotonation of the *trans* isomer might be due to the closer proximity of the phenyl group and the acidic hydrogen in the deformed chair than in the *cis* isomer (normal chair). It follows that if interference of the phenyl group to removal of the acidic hydrogen causes retardation of deprotonation in the *trans* isomer this same factor must then cause retardation of protonation to form the *trans* isomer in the microscopic reverse reaction (protonation of the nitronate ion by methanol). This then offered a possible explanation for the preferential formation of the *cis* isomer on protonation of 2-phenylcyclohexanenitronate ion by acetic acid–acetate buffers.[1] To test this idea the stereochemistry of the protonation of the 4-*t*-butylcyclohexanenitronate ion was examined. Here, with the 2 substituent absent, it was found that the stereochemical outcome of the protonation was just reversed. Now the more stable *trans* isomer, presumably resulting from axial protonation, was the major product. This result, which has since been confirmed using the 4-phenylcyclohexanenitronate ion,[4] clearly showed that it was the phenyl group and not the axial hydrogen atoms that was dictating the high stereoselective result in the case of the protonation of the 2-phenylcyclohexanenitronate ion.[5] This conclusion has now been supported by additional work on this and related systems.

Results

The pK_a's of nitroalkanes in methanol are much smaller than that of methanol itself, which means that protonation of alkanenitronate ions by methanol is very slow. It is impractical in most systems, therefore, to study the stereochemistry of protonation of nitronate ions by methanol. This difficulty can be circumvented, however, if for a pair of *cis–trans* stereoisomers rates of deprotonation by methoxide ion and the relative ground-state energies are both known. Since *cis–trans* stereoisomers give the *same* nitronate ion the difference in free energies of activation ($\Delta G^{\ddagger}$) of protonation by methanol to give *cis* and *trans* isomers (the microscopic reverse of deprotonation) will be given by the equation $\Delta G^{\ddagger} = \Delta G^{*} - \Delta G^{\circ}$ where ΔG^{*} is the difference in free energy of activation for deprotonation of the *cis* and *trans* isomers at 25° (obtainable from the rate data), and ΔG° is the difference in ground-state energies of the *cis* and *trans* isomers (obtainable from equilibration data).[8] Knowing the value of $\Delta G^{\ddagger}$ one can then calculate the percentage of *cis* and *trans* isomers that would be formed on protonation of the nitronate ion with methanol. The calculated values for the per cent of *cis* isomer are compared in Table I with the per cent of *cis* isomer observed on protonation of the nitronate ion with acetic acid–acetate buffer.

The correspondence between the per cent of *cis* (or *endo*) isomer formed on protonation in acetic acid–acetate buffer (or like) medium with that calculated for protonation in methanol (assuming microscopic reversibility) is remarkably good, particularly considering the variation in the solvents and temperatures in some instances. The good agreement obtained suggests that the stereochemistry of protonation is relatively insensitive to the acidity of the protonating medium. This conclusion is confirmed by a number of other observations.

4-*t*-Butylcyclohexanenitronate ion was found to give essentially the same ratio of *trans*- and *cis*-4-*t*-butyl-1-nitrocyclohexanes (*ca.* 25% *cis*, 75% *trans*) on protonation at −50° with ethanolic sulfuric acid to a congo red end point followed by: (a) immediate addition of water, (b) stirring for 1 hr then adding HOAc–NaOAc–H_2O, or (c) stirring for 5 min then

(5) F. G. Bordwell and M. M. Vestling, *J. Amer. Chem. Soc.*, **89**, 3906 (1967).

(6) (a) E. L. Eliel, *J. Chem. Educ.*, **37**, 126 (1960); (b) R. A. Wohl, *Chimia*, **18**, 219 (1964).

(7) F. G. Bordwell and K. C. Yee, *J. Amer. Chem. Soc.*, **92**, 5933 (1970) (paper II in the present series).

(8) The treatment is analogous to that used when *cis–trans* isomers give the same carbonium ion; see (a) H. L. Goering and C. B. Schewene, *ibid.*, **87**, 3516 (1965); (b) H. C. Brown and M. H. Rei, *ibid.*, **90**, 6216 (1968).

adding HOAc–NaOAc–H_2O. The yield of by-product ketone was 50% in (a), 35% in (b), and 16% in (c) showing that the difference in medium had a marked effect on the overall course of the reaction, but not on the stereochemistry.[9] Protonation by adding the solution of 4-*t*-butylcyclohexanenitronate ion in NaOMe–MeOH or in *t*-BuOK–*t*-BuOH directly to a HOAc–LiOAc–H_2O–EtOH buffer solution gave, in the present work, *ca.* 35% of *cis*- and 65% of *trans*-4-*t*-butyl-1-nitrocyclohexane (*ca.* 5% of ketone was formed under these conditions). About the same ratio of these products (31% *cis*, 69% *trans*) was also formed on oxidation of 4-*t*-butylcyclohexanone oxime with trifluoroperoxyacetic acid in wet acetonitrile buffered with disodium hydrogen phosphate using the Emmons–Pagano nitroalkane synthesis.[10,11] It has recently been pointed out that the stereochemistry obtained in the Emmons–Pagano oxidation of 2-substituted cyclohexanone oxime and norbornan-2-one oxime parallels that observed for the protonation of the cyclohexanenitronate ions in other buffered media.[12] We have observed this parallelism in a number of other systems.

Discussion

Protonation of Substituted Nitrocyclohexane and Nitrocyclopentane Nitronate Ions. From the data just presented it would appear that the stereochemistry of protonation by HOAc–LiOAc–H_2O–EtOH does not differ greatly from protonation by MeOH.[13] Deprotonation of a nitroalkane by methoxide ion can, therefore, be used as a model, in at least some instances, for the microscopic reverse of the protonation of the corresponding nitronate ion by a buffer medium.

It was shown in the previous paper that the rates of methoxide ion deprotonation of these and other stereoisomeric nitrocycloalkanes in most instances could be correlated by assuming that the heights of the transition state barriers for the two stereoisomers were about equal and that the difference in rates was primarily caused by differences in ground-state energies. If the assumption of equality of transition state barriers were literally true it would require that in the reverse reaction, protonation of the nitronate ion, equal amounts of the stereoisomers be formed. Examination of Table I shows that this prediction holds exactly in only one instance, protonation of 4*e*-*t*-butyl-2*a*-phenyl-1-nitrocyclohexane, where the equilibrium constant is 1, the k_{cis}/k_{trans} ratio is 1, and equal amounts of the two stereoisomers (1*a*-nitro and 1*e*-nitro) are formed on protonation. This result is no doubt fortuitous since it seems unlikely that the barriers will ever be exactly of the same height. This would be equivalent to saying that the energy paths for "axial approach" or "equatorial approach" of the proton donor to a cyclohexanenitronate ion such as **1a** or **1b** are exactly the same. This, we believe, is not a bad first approximation, but it is clear from the earlier work and the other entries in Table I that neither the relative rates of deprotonation of *cis*–*trans* isomers[7] nor the relative rates of formation of *cis*–*trans* isomers on protonation are dependent on ground-state energy effects alone. For 4-*t*-butyl-, 4-phenyl-, and 4*e*-*t*-butyl-2*e*-phenyl-1-nitrocyclohexanes the observed k_{cis}/k_{trans} deprotonation ratios are in each instance about 1.2 times that predicted on the basis of ground-state energies, as judged by the equilibration data.[7,14] One would expect, then, that a slightly larger amount of *cis* than *trans* isomer would be obtained on protonation. This expectation was not realized, but the difference in % *cis* calculated and observed is not large for the 4-*t*-butyl- and 4-phenyl-1-nitrocyclohexanes (56 *vs.* 35% and 57 *vs.* 37%). For 4*e*-*t*-butyl-2*e*-phenyl-1-nitrocyclohexane the discrepancy between the per cent *cis* calculated and observed is more serious (55 *vs.* 16%).[15]

2-Phenyl-1-nitrocyclopentane is the only entry in Table I where k_{cis}/k_{trans} is smaller than that calculated from ground-state energies.[7] Here one predicts that less *cis* than *trans* isomer will be formed on protonation, and this prediction is borne out.

For 2-methyl- and 2-phenyl-1-nitrocyclohexanes the observed k_{cis}/k_{trans} ratios are about fourfold greater than predicted on the basis of ground-state energies. This we ascribe to steric hindrance to deprotonation caused by the close proximity of the methyl or phenyl group to the acidic hydrogen atom in the deformed cyclohexane chair.[7] This same steric effect, whatever its nature, should inhibit protonation of the nitronate ion in the microscopic reverse reaction leading to an appreciably larger amount of the *cis* than the *trans* isomer, as observed (Table I). This is illustrated in Figure 1 for the 2-methyl-1-nitrocyclohexane system, which provides the better example because there is enough of the *cis* isomer present at equilibrium to allow a reasonable estimate of the relative ground-state energies.

The equilibration data (90% *trans*) show a ground-state energy difference ($\Delta G°$) of 1.3 kcal/mol at 25°. The free-energy difference for deprotonation is $\Delta G^* = RT \ln (k_{cis}/k_{trans}) = 2.2$ kcal/mol. The free-energy difference for protonation is then $\Delta G^{\pm} = \Delta G^* - \Delta G° = 0.9$ kcal/mol. The calculated ratio for the rate of formation of *cis vs. trans* isomer for protonation of the 2-methylcyclohexanenitronate ion by methanol is then *ca.* 4.6 (82% *cis*); 85% is observed to be formed on protonation with acetic acid–acetate buffer (Table I). In view of the approximations made the agreement is much better than could have been expected, and is probably fortuitous. It does give us confidence, however, in the conclusion that deprotonation of nitroalkanes by methoxide in methanol provides a

(9) M. M. Vestling, Ph.D. Dissertation, Northwestern University, June 1967.

(10) A. C. Huitric and W. F. Trager, *J. Org. Chem.*, 27, 1926 (1962).

(11) W. D. Emmons and A. S. Pagano, *J. Amer. Chem. Soc.*, 77, 4557 (1955).

(12) R. J. Sundberg and P. A. Bukowick, *J. Org. Chem.*, 33, 4098 (1968).

(13) The pK_a of acetic acid in ethanol is *ca.* 9.5 (R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 46). Thus the pH of the buffered medium in ethanol is not as far apart from that of methanol as one might have at first supposed.

(14) It must be noted that equilibrations were carried out in a solvent different from that in deprotonation (usually EtOH rather than MeOH) and at a different temperature (usually 78° rather than 25°). It was found, however, that essentially the same results were obtained by equilibration of 2-phenyl-1-nitrocyclopentane by refluxing in 95% ethanol in the presence of sodium bicarbonate for 4 hr (89% *trans*, 11% *cis*) as for equilibration at 25° in methanol in the presence of a trace of sodium methoxide for 14 days or 5 months (90% *trans*, 10% *cis*). Also, R. J. Ouellette and G. E. Booth, *J. Org. Chem.*, 30, 423 (1965), report only very small differences in equilibrium constants for equilibrations carried out at 50, 75, and 100°. It appears, therefore, that the differences in solvent and temperature employed do not lead to *large* changes in equilibrium constants.

(15) The observed result is somewhat suspect here because of the unusual ease of epimerization of the *cis* to *trans* isomer.

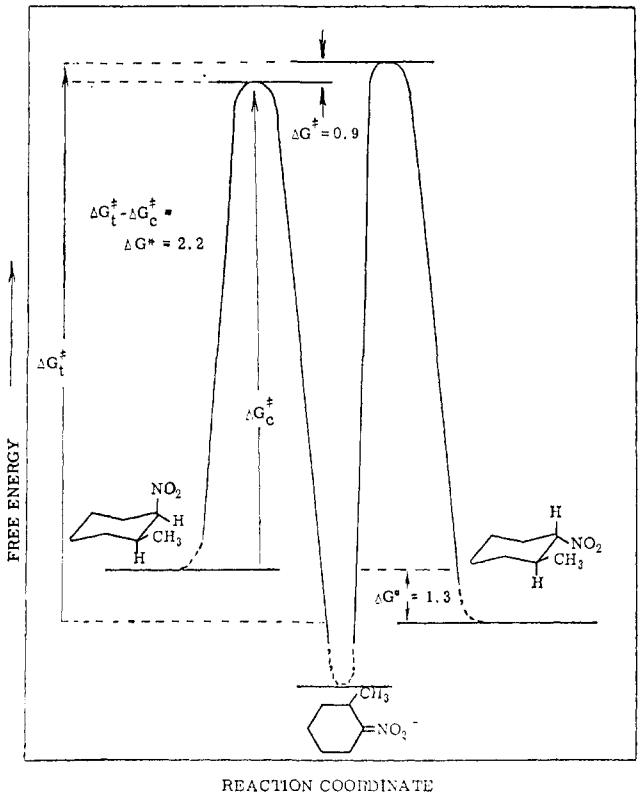


Figure 1. Free energy *vs.* reaction coordinate diagram for the reaction of the 2-nitro-1-methylcyclohexanes in sodium methoxide–methanol at 25° (all numbers in kilocalories/mole).

reasonable model of the microscopic reversal of protonation of nitronate ions by acetic acid–acetate buffers.

Protonation of Bicycloheptane and Bicycloheptene Nitronate Ions. The k_{endo}/k_{exo} deprotonation ratios for 5-nitrobicyclo[2.2.1]hept-2-ene and 2-nitrobicyclo-[2.2.1]heptane (2-nitronorbornane) are *ca.* 6 and 13 times those predicted on the basis of ground-state energies.[7] These effects are considerably larger than for 2-substituted nitrocyclohexanes and point to the operation of a sizable steric factor favoring removal of an *exo* relative to an *endo* proton in these systems. The data in Table I show that this same factor is operating in what we consider to be the microscopic reverse step, protonation of the nitronate ion, favoring return of the proton to the *exo* position. In fact, the per cent of observed *exo* protonations (*endo* isomer formed) by proton donors corresponds closely with those calculated for water protonations (Table I).

The preference for removal and return of an *exo* proton for these nitrobicyclo systems bears a striking resemblance to the preference for removal and return of an *exo* grouping in the solvolysis of *exo vs. endo* norbornyl acetates, tosylates, etc. In the solvolyses the rate preferences are larger. Here $k_{exo}/k_{endo} \cong$ 9000/1 at 25° for acetolysis of the acetate,[8a] and the preference for formation of an *exo* acetate product is *ca.* 1500/1.[8a] For 2-nitronorbornane $k_{exo}/k_{endo} \cong$ 15/1 at 25°,[16] and the protonation ratio is *ca.* 6/1 (Table I).[12]

(16) P. W. K. Flanagan, Ph.D. Dissertation, Ohio State University, 1957. The ratio, measured in 50% (v/v) H_2O–dioxane is 19.7 at 0°, 18.4 at 9.9°, and 15 at 28°. See also, H. Shechter, P. W. K. Flanagan, H. Stone, J. G. Traynham, and F. T. Williams, Jr., Abstracts, 136th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1959, p 33P.

The ground-state energies of *exo*- and *endo*-norbornyl acetates differ by *ca.* 1 kcal/mol, those of *exo*- and *endo*-2-nitronorbornanes differ by *ca.* 0.6 kcal/mol. The favored explanations for the high degree of preference for groups leaving from and returning to the *exo* position during solvolysis appear to be: (a) formation of a nonclassical norbornyl cation which is formed with anchimeric assistance and reacts by stereoelectronic control[17] or (b) the transition state for loss of the group from an *endo* position is strained relative to loss of the group from an *exo* position.[8b] For 2-nitronorbornane the nonclassical ion explanation is clearly inadmissible. On examination of rates, removal of the *endo* proton appears to be normal, relative to nitrocyclohexane (67 *vs.* 78 M^{-1} min^{-1} at 28°) and slow compared to nitrocyclopentane (67 *vs.* 325 M^{-1} min^{-1} at 28°).[16] On the other hand, removal of the *exo* proton is accelerated relative to either nitrocyclohexane (1010 *vs.* 78 M^{-1} min^{-1} at 28°) or nitrocyclopentane.[16] The enthalpies of activation are 11.5 kcal/mol for *endo*, 11.7 for nitrocyclopentane, 12.8 for *exo*, and 13.1 for nitrocyclohexane.[16] Explanation (b) is probably correct, but the exact nature of the steric effects involved remain to be defined.[18]

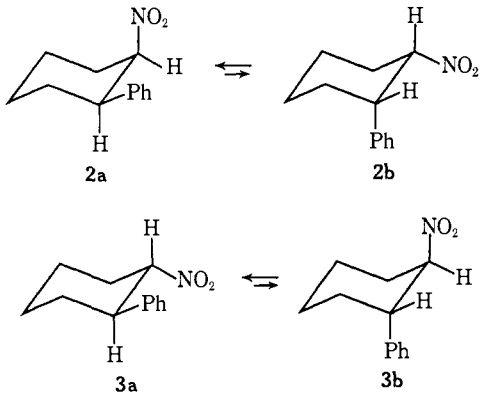
Arguments from Rate Data Against Deprotonations or Protonations *via* Conformation with an Axial Phenyl. The explanation adopted herein for the stereoselective protonation of 2-substituted cyclohexanenitronate ions differs from that of Malhotra and Johnson,[3] as well as that of Zimmerman.[1,4] Because 2-substituted nitrocyclohexanes and cyclohexanenitronate ions are not ideal chairs it is the 2 substituent (and not the axial hydrogen atoms on the cyclohexane ring[1,4]) that provide the major influence on the rates of deprotonation and the stereochemistry of protonation. The deformation of the chair does not go so far as to require an axial phenyl group in the 2-phenylcyclohexanenitronate ion.[3] Acceptance of the transition state conformation for protonation as one in which the phenyl group is axial would require also that in the microscopic reverse deprotonation reaction the 2-Ph or 2-R substituent be in an axial position. This has indeed been suggested as an explanation for the slow rate of deprotonation of *trans*-2-phenyl-1-nitrocyclohexane.[12] Following the argument used by House and Richey[19a] and by Johnson[19b] to explain the low rate of deprotonation of *trans*-2-methylcyclohexyl chloromethyl ketone, Sundberg and Bukowick[12] suggest that, because of $A^{1,3}$ strain in the transition state for deprotonation, *cis*- and *trans*-2-phenyl-1-nitrocyclohexanes react *via* conformations **2b** and **3b**, respectively. The slower rate for the *trans* isomer was ascribed to the difficulty of attainment of conformation **3b** which has two axial groupings.[20]

(17) (a) S. Winstein, *J. Amer. Chem. Soc.*, 87, 381 (1965); (b) G. A. Olah, Abstracts, 21st National Organic Symposium, June 1969, Salt Lake City, Utah, pp 99–101.

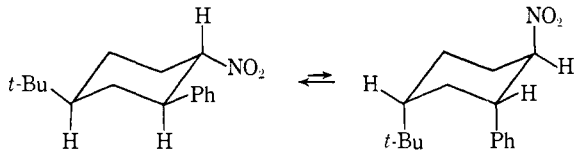
(18) If this evidence for a steric effect for removal of an *exo vs.* an *endo* grouping can be extended to solvolysis reactions and Olah's nmr evidence[17b] for a nonclassical norbornyl cation proves definitive, these data portend a fate for the norbornyl nonclassical ion controversy comparable to that of many earlier scientific controversies, namely, that each point of view has some truth on its side.

(19) (a) H. O. House and, F. A. Richey, *J. Org. Chem.*, 32, 2151 (1967); (b) F. Johnson, *Chem. Rev.*, 68, 375 (1968).

(20) If we assume that the energy barriers between **2a** ⇄ **2b** and between **3a** ⇄ **3b** are small compared to the deprotonation barriers, which seem likely, this suggestion violates the Curtin–Hammett principle;



There are a number of reasons that this alternative explanation appears to be unacceptable, aside from the Curtin–Hammett principle.[20] Firstly, conformations **2b** and **3b** differ only in that **2b** has an equatorial nitro group whereas **3b** has an axial nitro group. This amounts to a difference of only 0.8 kcal/mol in energy,[10] which could account for only a fourfold difference in rates. The actual rate difference between **2** and **3** is 350-fold.[7] Secondly, $A^{1,3}$ strain will appear in the transition state for deprotonation only to the extent that the transition state is product-like. Evidence has been presented in an earlier paper to show that the transition state for methoxide deprotonations of nitroalkanes is *not* product-like.[21] Thirdly, the rate and activation parameters for deprotonation of 4*e*-*t*-butyl-2*e*-phenyl-1*e*-nitrocyclohexane (**4a**) by *t*-BuOK in *t*-BuOH are very similar to those for **3** under these conditions.[7] If deprotonation of **3** is slow because the free energy of activation is less for reaction *via* conformation **3b** than for **3a**, then the rate for **4** should be *much* slower since it must either react *via* conformation **4a**, which is presumed to be subject to a large $A^{1,3}$ strain,[12,20] or *via* conformation **4b** (or a twist form), which should be much more difficult to attain than is conformation **3b**.



4a **4b**

	3	**4**
$k_{t\text{-BuOK}}^{25°}$, M^{-1} sec^{-1}	1.4	0.50
E_a, kcal/mol	11.5	11.0
ΔS^*, eu	−21.4	−24.9

We conclude that alkoxide ion initiated deprotonations of **3** and **4** proceed *via* conformations **3a** and **4a**, and that the transition states do *not* resemble the corresponding nitronate ions in structure. The low reactivity of these compounds is caused by a lowering of the ground-state energy through deformation of the ring and the consequent steric hindrance to deprotonation caused by the closer approach of the phenyl group to the acidic hydrogen atom.[22] The same explanation can be applied to the slow deprotonation of *trans*-2-phenylcyclohexyl phenyl ketone.[19,20]

Structural Evidence Concerning the 2-Phenylcyclohexanenitronate Ion Derived from Ultraviolet Spectra. It has been suggested that nitronate ion **1a** is subject to severe $A^{1,3}$ strain and that it actually exists, therefore, in (the relatively unstable) conformation **1b**.[3] On this basis one would expect the nitronate ion from **4** to be even more strained since it must either exist in a conformation analogous to **1a**, which is subject to $A^{1,3}$ strain, or one analogous to **4b**, which is subject to severe interactions between axial, or pseudoaxial, *t*-butyl and phenyl groups. One might expect a strain of this type to be reflected in the ultraviolet spectrum, since the position of λ_{max} and, particularly, the size of ϵ is known to be subject to steric effects.[23] Table II presents a comparison of pertinent spectra.

Table II. Ultraviolet Spectra of Nitroalkane in NaOMe–MeOH and in *t*-BuOK–*t*-BuOH

Nitroalkane[a]	NaOMe, *M*	λ_{max},[b] nm	ϵ_{max}[c]
2-Nitropropane	0.0276	227	10,000
Nitrocyclopentane	0.00552	232	10,700
2-Phenyl-1-nitrocyclopentane	0.276	237	11,800
2-Methoxy-2-phenyl-1-nitrocyclopentane	0.0242	246	12,000
Nitrocyclohexane	0.0276	237	10,000
4-*t*-Butyl-1-nitrocyclohexane	0.0552	235	12,000
4-Phenyl-1-nitrocyclohexane	0.0552	237	13,000
2-Phenyl-1-nitrocyclohexane	0.276	238	11,700
2-*p*-Methoxyphenyl-1-nitrocyclohexane	0.0456	235	12,900
2-*p*-Methoxyphenyl-1-nitrocyclohexane	0.0456	237	11,500
2-*o*-Methylphenyl-1-nitrocyclohexane	0.0380	239	3,000
2-*p*-Chlorophenyl-1-nitrocyclohexane	0.0276	235 (sh)	12,400
2-*m*-Chlorophenyl-1-nitrocyclohexane	0.0276	237	12,000
2-Methyl-1-nitrocyclohexane	0.0912	235	11,600
4*e*-*t*-Butyl-2*e*-phenyl-1-nitrocyclohexane	0.276	237	9,900
4*e*-*t*-Butyl-2*a*-phenyl-1-nitrocyclohexane	0.276	233	9,600

Nitroalkane[a]	*t*-BuOK	λ_{max}, nm	ϵ_{max}
4-*t*-Butyl-1-nitrocyclohexane	0.000912	242	12,400
2-Phenyl-1-nitrocyclohexane	0.00188	243	12,000
4*e*-*t*-Butyl-2*e*-phenyl-1-nitrocyclohexane	0.00188	243	12,000
4*e*-*t*-Butyl-2*a*-phenyl-1-nitrocyclohexane	0.000912	236	10,400
2-Methoxy-2-phenyl-1-nitrocyclohexane	0.00366	252	10,000

[a] Since *cis*–*trans* isomers give the same nitronate ion no stereochemistry is indicated, although data for both isomers were obtained (K. C. Yee, Ph.D. Dissertation, Northwestern University, Aug 1969). [b] Secondary maxima are not shown. [c] Some variation in ϵ_{max} was observed in different determinations and for some compounds with different concentrations of alkoxide; the highest observed values were chosen for this table.

There is little evidence from the λ_{max} or ϵ_{max} values recorded in Table II that substitution of a 2-aryl group

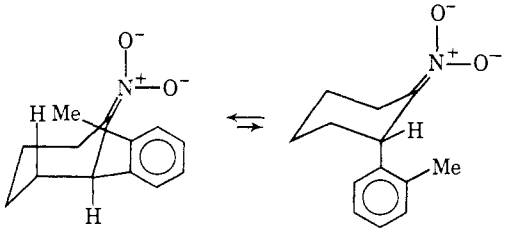
see, E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., p 151.

(21) F. G. Bordwell, W. J. Boyle, Jr., and K. C. Yee, *J. Amer. Chem. Soc.*, **92**, 5926 (1970) (paper I in this series).

(22) The ultimate result of bending the nitro and phenyl groups away from one another in **3a** is conversion to a twist form and thence to conformation **3b**. Our view is that the ring is merely deformed; we do not believe that deprotonation occurs *via* **3b** as is implied in the discussion of our views in ref 12.

(23) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," Wiley, New York, N. Y., 1962, Chapter 15.

into the cyclohexanenitronate ion introduces $A^{1,3}$ strain. Examination of a space-filling molecular model of the 2-phenylcyclohexanenitronate ion shows no steric interference between $C{=}NO_2^-$ and the phenyl group as long as the latter is oriented so that its plane is perpendicular to that of the nitronate ion. Crowding is sufficient to prevent rotation of the phenyl past the nitronate, which restricts the orientation of the groups to one in which one of the oxygen atoms of NO_2^- points directly into the π cloud of the benzene ring, but comparison with the spectra of 4-*t*-butylcyclohexanenitronate ion, 4-phenylcyclohexanenitronate ion, or the *p*-MeO, *p*-Me, *p*-Cl, or *m*-Cl derivatives of the 2-phenylcyclohexanenitronate ion indicates that this has little or no perturbing effect on ϵ_{max} or λ_{max}. This system is, nevertheless, highly sensitive to steric effects as may be judged by the effect of adding an *ortho*-methyl group (ϵ_{max} decreases from 11,700 to 3000). Here examination of models shows extreme crowding for conformation **5a**. This can be avoided by rotations to give the boat or conformation **5b**. This would not, however, produce such a drastic decrease in ϵ_{max}, judging from the spectrum of the 4*e*-*t*-butyl-2*a*-phenylcyclohexanenitronate ion (Table II) which must have the phenyl group in an axial (or pseudoaxial) position. Instead, it would appear that the molecule exists in conformation **5a** and that the strain is relieved by twisting the $C{=}NO_2^-$ grouping.[24]



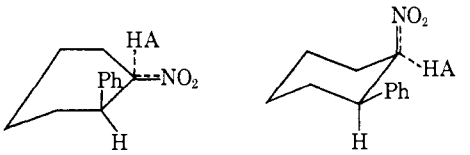
5a **5b**

One must conclude from this that there is relatively little $A^{1,3}$ strain in the 2-phenylcyclohexanenitronate ion, itself, and that it exists in conformation **1a**, rather than in conformation **1b**.

Introduction of a 4-*t*-butyl group into 2-phenyl-1-nitrocyclohexanenitronate ion causes a small drop in ϵ_{max}, but this is the same order of magnitude as the increases in ϵ_{max} for substitution of a 4-*t*-butyl or 4-phenyl group into the cyclohexanenitronate ion. The reason for these changes is not clear, but there is certainly no reason to believe that there is a drastic change in the structure of the nitronate ions from **3** and **4**, as would be required by the $A^{1,3}$ strain hypothesis. Nevertheless, there is evidence from pK_a data that small $A^{1,3}$ strains are present in the nitronate ions derived from **3** and **4**.[25]

Conclusion

According to our view the preferred transition state for protonation of the 2-phenylcyclohexanenitronate ion will resemble that for deprotonation of *cis*-2-phenyl-1-nitrocyclohexane. In this transition state the H–C bond has been appreciably formed and the C=N bond has been appreciably broken. This can occur without undue strain if protonation occurs from the equatorial side, as Zimmerman originally proposed. On the other hand, axial approach of the proton donor (microscopic reverse of deprotonation of *trans*-2-phenyl-1-nitrocyclohexane) will force the NO_2 group into a pseudoequatorial position and the phenyl group into a pseudoaxial position where it interferes with the approach of the proton donor.



transition state for axial protonation (steric hindrance between HA and Ph)

transition state for equatorial protonation (no steric hindrance between HA and Ph)

This is a modification of Zimmerman's views in that a greater degree of bonding is visualized at the transition state and in that the steric effect for axial approach is exerted between the phenyl group and the proton donor, rather than between the axial hydrogen atoms and the proton donor. These views obviously can be extended to account for the effect of 2-phenyl and like substituents on the rates of deprotonation of ketones[19] and to account for the stereochemistry of the protonation of enols.[1]

Acknowledgment. This work was supported by the National Science Foundation (GP 7065).

(24) Another example of a severe steric effect on the absorption of the $C{=}NO_2^-$ group is found in the series $ArCMe{=}NO_2^-$ where the *o*-Me derivative has a shoulder at 260 nm (ϵ_{max} 5300) as compared to λ_{max} 287 nm (ϵ_{max} 13,000) for the *p*-Me derivative—see ref 21.

(25) Unpublished results of W. J. Boyle, Jr., and K. C. Yee.