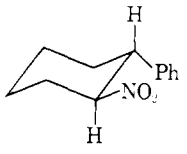
Evidence from Deprotonation Rates for Deformation of the Cyclohexane Chair in 2-Aryl-1-nitrocyclohexanes

F. G. Bordwell and K. C. Yee

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60201. *Received October 17, 1969*

Abstract: Deprotonation rates for the reactions of 30 nitrocycloalkanes with NaOMe–MeOH have been measured spectrophotometrically, usually at more than one temperature. For most *cis–trans* stereoisomeric pairs the k_{cis}/k_{trans} ratios correlated well with those expected on the basis of the observed differences in ground-state energies. The difference in ground-state energies for 2-substituted nitrocyclohexanes was found to be larger than for 4-substituted nitrocyclohexanes. Comparison of ρ-values for 1-aryl-2-nitropropanes (0.87), *cis*-2-aryl-1-nitrocyclopentanes (0.89), *cis*-2-aryl-1-nitrocyclohexanes (0.84), *trans*-2-aryl-1-nitrocyclopentanes (1.45), and *trans*-2-aryl-1-nitrocyclohexanes (1.23) revealed that the aryl groups are much closer to the acidic proton in the *trans* isomers than in the *cis* isomers or open-chain analog. This shows that the chair is deformed in *trans*-2-aryl-1-nitrocyclohexanes, which accounts for the larger difference in ground-state energies in 2-substituted nitrocyclohexanes. Even when this larger difference in ground-state energies for the stereoisomeric pairs of 2-methyl- and 2-phenyl-1-nitrocyclohexane is taken into account the k_{cis}/k_{trans} ratios are still *ca.* four times larger than expected. This is believed to be caused by steric screening of the acidic hydrogen in the *trans* isomer. The k_{endo}/k_{exo} ratios for 5-nitrobicyclo[2.2.1]hept-2-ene and 2-nitrobicyclo[2.2.1]heptane are *ca.* 13 times and 6 times greater, respectively, than expected from the relative ground-state energies. This preference for removal of an *exo* proton must also have its origin in a steric effect.

A few years ago we observed an unusually large retarding effect on the rate of abstraction by methoxide ion of a proton α to a nitro group in nitrocyclohexanes caused by an equatorial β-phenyl group when this group was *cis* to the (axial) proton (*trans* isomer **1**), but not when the equatorial β-phenyl group was *trans* to the (equatorial) proton (*cis* isomer **2**).[1]



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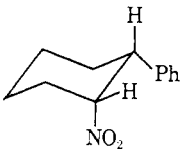
k^{MeO^-}(rel) = 1.0



2

k^{MeO^-}(rel) = 350

This result was surprising because in the ideal cyclohexane chair the steric relationships between the phenyl group and the acidic proton are identical (compare isomers **1** and **2**). It was postulated that the origin of the retarding effect might be found in a deformation of the cyclohexane chair in the *trans* isomer (**1**) caused by bending away from one another of the equatorial phenyl and nitro groups.[2] This could cause a lowering of the ground-state energy of the *trans* isomer, relative to the *cis* isomer, which could result in an increase in the free energy of activation for deprotonation of this isomer. At the same time, in the deformed chair, the phenyl group would be brought into closer proximity to the acidic hydrogen atom and steric hindrance to proton abstraction might be greater in the *trans* isomer than in the *cis* isomer. The rates for a number of additional *cis*- and *trans*-2-aryl-1-nitrocyclohexanes have now been examined in order to test this idea further.

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

(2) The same effect might be achieved in a somewhat flattened cyclohexane chair. R. A. Wohl, *Chimia*, **18**, 219 (1964), has interpreted a number of physical and chemical data on the basis of a chair with angles of 111.5°.

Results

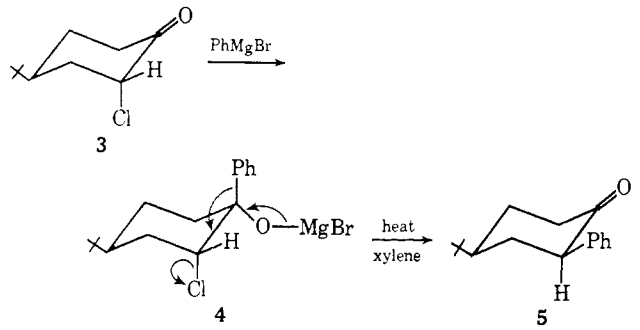
Synthesis of *cis*- and *trans*-4-*t*-Butyl-2-phenylcyclohexanones. These compounds were required as starting materials for the preparation of the four stereoisomeric 4-*t*-butyl-2-phenyl-1-nitrocyclohexanes. The reaction of α-chloro ketones with Grignard reagents has been shown by Tiffeneau to give magnesium salts of chlorohydrins which rearrange on heating.[3a] Rearrangement of the halomagnesium derivative of 1-methyl-*cis*-2-chlorocyclohexanol gave 2-methylcyclohexanone, presumably by displacement during rearrangement of the axial chlorine atom by an axial methyl group with inversion of configuration. The *trans* isomer gave only acetylcyclopentane involving inversion by a ring atom, which is the atom in this isomer that is properly located to effect an inversion at the carbon holding the chlorine atom.[3b] Inasmuch as phenylmagnesium bromide is known to attack 4-*t*-butylcyclohexanone slightly more from the axial side,[4] one expected product from the addition of phenylmagnesium bromide to *trans*-4-*t*-butyl-2-chlorocyclohexanone (**3**) is the bromomagnesium salt of 4*e*-*t*-butyl-2*a*-chloro-1*a*-phenylcyclohexan-1*e*-ol (**4**). Rearrangement is known to proceed well in such reactions,[5] and one would expect the phenyl group in **4** to rearrange by displacing the chlorine atom with inversion giving *cis*-4*e*-*t*-butyl-2*e*-phenylcyclohexanone (**5**).

In practice, the major product (30%) was indeed **5**, but this was accompanied by *ca.* 8% of the *trans* isomer (**6**). An additional amount of **5** (18%) was obtained from a reaction of phenylmagnesium bromide with *cis*-4-*t*-butyl-2-chlorocyclohexanone; 20% of **6** was also obtained from this reaction.

(3) (a) M. Tiffeneau and B. Tchoubar, *Compt. Rend.*, **199**, 360 (1934); (b) T. A. Geissman and R. I. Akawic, *J. Amer. Chem. Soc.*, **73**, 1993 (1951).

(4) G. D. Meakins, R. K. Percy, E. E. Richards, and R. N. Young, *J. Chem. Soc.*, 1106 (1968).

(5) A. S. Hussey and R. R. Herr, *ibid.*, 24, 843 (1959).



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Preparation and Structures of Nitroalkanes. Nitroalkanes were prepared by the Emmons–Pagano method.[6] Structures for the *cis* and *trans* isomers for 2-aryl-1-nitrocyclohexanes,[7-9] 2-methyl-1-nitrocyclohexanes,[9] 4-*t*-butyl-1-nitrocyclohexanes,[8b] and 4-phenyl-1-nitrocyclohexanes[10] have been established by chemical means[7] and by nmr.[8,9] The nmr data show that the *trans* structure can be assigned to that isomer in which the nmr peak for C*H*NO_2 is broader and at a position farther upfield;[8,9] the *trans* isomer is also known to be present in larger quantity at equilibrium.[7] In the present work these considerations were used in assigning structures to the 2-aryl-1-nitrocyclopentanes and for 4*e*-*t*-butyl-2*e*-phenyl-1-nitrocyclohexanes.

The two isomeric 4*e*-*t*-butyl-2*a*-phenyl-1-nitrocyclohexanes had identical nmr spectra, except for the positions of the *t*-butyl resonances. The C*H*NO_2 peak was in each instance an apparent doublet at 5.07 ppm; this absorption is somewhat upfield from the signals for even the equatorial C*H*NO_2 signals in other 2-aryl-1-nitrocyclohexanes.[8] The isomers reacted with excess sodium methoxide in methanol to give the same nitronate ion. Isomerization of the 54° isomer or the 84° isomer gave the same 50–50 mixture. Evidently the isomers each exist in a twist form. In this form the C*H*NO_2 proton might be split strongly by one of three adjacent protons, and only weakly by the remaining two protons. This could explain the apparent doublet pattern.

Kinetic Studies. Rates of deprotonation by methoxide ion in methanol were determined spectrophotometrically by the method described previously.[11] For nitrocyclohexane itself it was necessary to use a concentration of methoxide ion above 0.05 *M* in order for the reaction to go to completion.[12] A still higher methoxide ion concentration (*ca.* 0.5 *M*) was required for *trans*-2-aryl- and *trans*-2-methyl-1-nitrocyclohexanes, and 4*e*-*t*-butyl-2*e*-phenyl-1*e*-nitrocyclohexane failed to give any apparent reaction even at this concentration. For these compounds, which have pK_a's high enough to make the back reaction sufficiently fast to cause problems, rates were determined also with *t*-BuOK–*t*-BuOH. The results of the rate studies are summarized in Tables I, II, and III.

(6) W. D. Emmons and A. S. Pagano, *J. Amer. Chem. Soc.*, 77, 4557 (1955).
(7) H. E. Zimmerman and T. E. Nevins, *ibid.*, 79, 6559 (1957).
(8) (a) W. F. Trager, F. F. Vincenzi, and A. C. Huitric, *J. Org. Chem.*, 27, 3006 (1962); (b) A. C. Huitric and W. F. Trager, *ibid.*, 27, 1926 (1962).
(9) R. J. Sundberg and P. A. Bukowick, *ibid.*, 33, 4098 (1968).
(10) H. E. Zimmerman and P. S. Marino, *J. Amer. Chem. Soc.*, 90, 6091 (1968).
(11) F. G. Bordwell, W. J. Boyle, Jr., and K. C. Yee, *ibid.*, 92, 5926 (1970) (paper I in the present series).
(12) The pK_a of nitrocyclohexane in methanol is *ca.* 14.5; W. J. Boyle, Jr., unpublished results.

The rates for a number of *cis*- and *trans*-2-aryl-1-nitro cyclohexanes and 2-aryl-1-nitrocyclopentanes were measured in order to determine Hammett correlations (Table II).

The four stereoisomers of 4-*t*-butyl-2-phenyl-1-nitrocyclohexane were studied in order to examine the effect of "conformation holding" substituents at both the 2 and 4 positions on the rates. The isomers with axial phenyl substituents reacted at "normal" rates and have been included in Table I. The isomers with equatorial phenyl groups reacted very slowly with sodium methoxide and were therefore measured with *t*-BuOK–*t*-BuOH (Table III).

Discussion

Most of the effects of substituents on rates recorded in Table I are relatively small. Comparison of the rates for deprotonation by methoxide ion shows that a *trans*-4-*t*-butyl group has a slight retarding effect relative to nitrocyclohexane (1.6-fold) and that a *trans*-4-phenyl group has a slight accelerating effect (1.4-fold). The *cis*-4-*t*-butyl and 4-phenyl isomers react more rapidly than does nitrocyclohexane, no doubt because 1,3-diaxial interactions between the axial nitro group and the axial protons are relieved in the transition state (steric assistance).[13] A *cis*-2-phenyl group has a slight accelerating effect (2.6-fold) and a *cis*-2-methyl group has essentially no effect. These compounds react at about the same rate as does 2-nitropropane: substitution of a β-phenyl group into 2-nitropropane causes a slight acceleration (1.5-fold), no doubt due to the inductive effect of the phenyl group.

The small effects just described contrast sharply with the strong retarding effect produced by substitution of a *trans*-2-phenyl group (350-fold retardation, relative to its *cis* isomer, 85-fold retardation relative to *trans*-4-*t*-butyl-1-nitrocyclohexane). This retardation is caused primarily by an increase in the activation energy (Table I). A *trans*-2-methyl group has a similar but smaller effect (40-fold retardation, relative to its *cis* isomer).

On the other hand, substitution of a *trans*-2-phenyl group into nitrocyclopentane brings about only a 4.2-fold rate retardation, caused entirely by a decrease in activation entropy. A *cis*-2-phenyl group causes almost no rate change, although the activation energy is increased by *ca.* 1 kcal/mol.

The large retarding effects observed with *trans*-2-phenyl- and *trans*-2-methyl-1-nitrocyclohexane appear to be due to ring deformation. It has been recognized for some time that deformation of the cyclohexane chair may occur rather easily since angle and torsional deformations are generally much less expensive, in terms of energy, than are van der Waal interactions.[14] Deformation of the *trans* isomer for 1,2-disubstituted cyclohexanes is also known to occur much more readily than in the *cis* isomer.[14] The first recognition of this phenomenon appears to have been Eliel's observation from entropy considerations that the methyl groups in *cis*-1,2-dimethylcyclohexane interfered with one

(13) Nitrocyclohexane exists to the extent of about 80% in the conformation in which the nitro group is equatorial; see W. F. Trager and A. C. Huitric, *J. Org. Chem.*, 30, 3257 (1965).
(14) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1967, pp 126–127.

Table I. Rates of Deprotonation of Nitroalkanes by Sodium Methoxide in Methanol

Nitroalkane	T, °C	k,[a] M^{-1} sec^{-1}	E_a, kcal/mol	ΔS^*, eu	r[b]
Nitrocyclohexane	16.5	1.57×10^{-1}			
	24.9	3.34×10^{-1}	16.7	−6.7	0.999
	36.3	1.00			
cis-4-*t*-Butyl-1-nitrocyclohexane[c]	8.8	2.33×10^{-1}			
	25.1	1.24	17.1	−2.6	
trans-4-*t*-Butyl-1-nitrocyclohexane[c]	8.8	4.30×10^{-2}			
	25.0	2.09×10^{-1}	16.2	−9.3	
cis-4-Phenyl-1-nitrocyclohexane[d]	25.0	2.24			
trans-4-Phenyl-1-nitrocyclohexane[d]	25.0	4.59×10^{-1}			
cis-2-Phenyl-1-nitrocyclohexane	25.0	8.71×10^{-1}	16.9	−4.1	0.998
	35.2	2.06			
	47.1	6.22			
trans-2-Phenyl-1-nitrocyclohexane	25.0	2.47×10^{-3}	19.3	−7.6	0.999
	35.1	7.24×10^{-3}			
	46.7	2.23×10^{-2}			
	47.1	2.38×10^{-2}			
cis-2-*p*-Chlorophenyl-1-nitrocyclohexane[c]	25.1	1.57	17.7	−0.2	0.999
	39.1	5.78			
	50.2	1.61×10			
trans-2-*p*-Chlorophenyl-1-nitrocyclohexane[c]	25.1	7.12×10^{-3}	18.3	−9.0	0.999
	39.0	2.88×10^{-2}			
	50.0	7.67×10^{-2}			
4*e*-*t*-Butyl-2*a*-phenyl-1*a*-nitrocyclohexane[e]	25.1	2.10×10^{-1}			
4*e*-*t*-Butyl-2*a*-phenyl-1*e*-nitrocyclohexane[e]	25.0	2.01×10^{-1}			
cis-2-Methyl-1-nitrocyclohexane	25.0	3.97×10^{-1}			
trans-2-Methyl-1-nitrocyclohexane	25.0	1.01×10^{-2}			
2-Nitropropane	16.0	1.42×10^{-1}			
	25.1	3.20×10^{-1}	16.0	−8.9	0.999
	36.1	8.66×10^{-1}			
1-Phenyl-2-nitropropane	25.0	5.0×10^{-1}			
Nitrocyclopentane	25.1	1.43	14.9	−9.9	
	47.1	8.03			
cis-2-Phenyl-1-nitrocyclopentane	14.4	5.10×10^{-1}			
	24.6	1.35	16.2	−5.4	
trans-2-Phenyl-1-nitrocyclopentane	13.7	1.25×10^{-1}			
	24.9	3.34×10^{-1}	14.8	−13.2	0.999
	37.0	8.85×10^{-1}			
	45.6	1.66			

[a] Average of three or more runs; standard deviations were generally within ±3%. [b] Correlation coefficient for Arrhenius plots. [c] Original sample kindly furnished by Professor A. C. Huitric. [d] Sample kindly furnished by Professor H. E. Zimmerman. [e] The assignment of this structure is arbitrary with respect to the disposition of the nitro group; the molecule probably exists in a twist form (see Experimental Section).

Table II. Hammett Correlations from the Rates of Deprotonation of Stereoisomeric 2-Aryl-1-nitrocycloalkanes by Sodium Methoxide in Methanol at 25°

Nitroalkanes	Substituents	ρ	r[a]
cis-2-Aryl-1-nitrocyclopentanes	4-Me, H, 4-Br, 3-CF_3	0.89	0.996
trans-2-Aryl-1-nitrocyclopentanes	4-Me, H, 4-Br, 3-CF_3	1.45	0.984
1-Aryl-2-nitropropanes	13 substituents[b]	0.87	0.979
cis-2-Aryl-1-nitrocyclohexanes	4-MeO, 4-Me, H, 4-Cl, 3-Cl	0.84	0.992
trans-2-Aryl-1-nitrocyclohexanes	4-MeO, 4-Me, H, 4-Cl, 3-Cl	1.23	0.965

[a] Correlation coefficient. [b] See ref 11.

Table III. Rates of Reactions of 2-Phenyl-1-nitrocyclohexanes with *t*-BuOK in *t*-BuOH at 25°

Nitrocyclohexane	T, °C	k, M^{-1} sec^{-1}	E_a, kcal/mol	ΔS^*, eu	r[a]
trans-2-Phenyl-1-nitrocyclohexane	25.1	1.40	11.5	−21.4	0.980
	34.7	3.17			
	40.4	3.54			
	45.1	4.95			
4*e*-*t*-Butyl-2*e*-phenyl-1*a*-nitrocyclohexane	25.0	2.96×10^{1}	9.6	−21.5	0.997
	34.7	4.67×10^{1}			
	45.0	8.25×10^{1}			
4*e*-*t*-Butyl-2*e*-phenyl-1*e*-nitrocyclohexane	25.2	5.03×10^{-1}	11.0	−24.9	0.993
	34.8	7.96×10^{-1}			
	40.4	1.23			
	45.0	1.58			

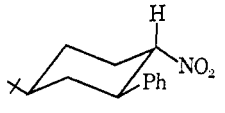
[a] Correlation coefficient for the Arrhenius plot.

another, whereas those in *trans*-1,2-dimethylcyclohexane did not. It was suggested that the chair in *trans*-1,2-dimethylcyclohexane was deformed in such a way as to allow the two methyl groups to move away from one another.[15] Electron-diffraction data showed that the chair in cyclohexane itself was flattened to the point where the ring angles are *ca.* 111.5°, rather than the tetrahedral angle.[16] This alone is sufficient to bring *cis* groups closer to one another than *trans*, and Wohl's interpretations[2] were made on this basis.

The data in Table II provide convincing evidence for chair deformation (or flattening) in *trans*-2-aryl-1-nitrocyclohexanes. For ideal chairs the relationship between the aryl group and the acidic hydrogen atom should be exactly the same in *cis*- and *trans*-2-aryl-1-nitrocyclohexanes. The ρ values should also be identical. Instead, the ρ value for the *trans* isomer is much greater (1.23 *vs.* 0.84) as expected for a deformed chair where the bending of the aryl group away from the nitro group causes it to come closer to the acidic hydrogen atom (field effect). Judging from the ρ values, the steric relationship between the aryl group and the acidic hydrogen atom appears to be nearly the same in *cis*-2-aryl-1-nitrocyclopentanes, 1-aryl-2-nitropropanes, and *cis*-2-aryl-1-nitrocyclohexanes (ρ's 0.89, 0.87, and 0.84, respectively). The aryl group is much closer to the acidic hydrogen atom in *trans*-2-aryl-1-nitrocyclopentanes (ρ = 1.45), as would be expected.

The sharp increase in rate of deprotonation (600-fold) of *trans*-2-phenyl-1-nitrocyclohexane for *t*-BuOK–*t*-BuOH relative to NaOMe–MeOH is expected in view of the large increase in base strength (*ca.* 3 pK_a units). The drop of almost 8 kcal/mol in activation energy is remarkably large. It no doubt reflects the lack of solvation around *t*-BuOK relative to NaOMe. The sharp decrease in ΔS^* can be correlated in a general way with the change in solvents. Strongly negative activation entropies appear to be the rule for ionic reactions occurring in poorly ionizing solvents.[17]

Substitution of a 4-*t*-butyl group into *trans*-2-phenyl-1-nitrocyclohexane causes a 2.8-fold drop in rate, which suggests that the 4-*t*-butyl group causes some change in the ring conformation or flexibility of the deformed chair. This seems to be true also for 4*e*-*t*-butyl-2*e*-phenyl-1*a*-nitrocyclohexane (**8**) since deprotonation occurs only 60-fold faster than with the 1*e*-nitro isomer, **7** (the difference is 350-fold with the *t*-butyl group absent) and is only 21-fold faster than



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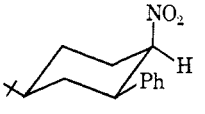

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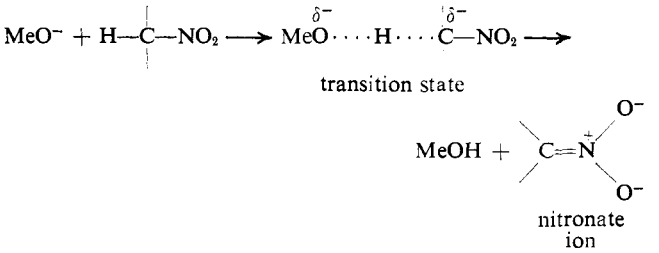
for *trans*-2-phenyl-1-nitrocyclohexane. Alternatively, one might look on the smaller rate differences as manifestations of the greater reactivity and, therefore, lesser selectivity of *t*-BuOK–*t*-BuOH as compared to NaOMe–MeOH.

Correlation of Rates and Ground-State Energies. In attempting to correlate the relative rates of stereoisomeric nitroalkanes with structure it is important to know as much as possible about the transition state structure. The evidence available concerning this point was summarized in the preceding paper in this series and the conclusion was reached that for deprotonations by hydroxide (or methoxide) ion the transition state is *not* product-like. Yet the relatively large observed k_H/k_D ratio indicates that breaking of the H–C bond has progressed about half-way at the transition state. This leads to a picture of the transition state where bond making and bond breaking have progressed to about an equal extent, but where the developing negative charge is concentrated on carbon rather than being delocalized to the nitro group. In other words the carbon atom has acquired an appreciable negative charge without being rehybridized. Apparently rehybridization is too costly from an energy standpoint.



When applied to stereoisomeric nitroalkanes this pictoralization could lead to the conclusion that the transition state energies of the stereoisomers should be quite similar, which would mean that the rates of deprotonation would correlate with the relative ground-state energies of the nitroalkanes. Proceeding on this hypothesis we have determined the relative ground-state energies for the isomeric pairs shown in Table I by equilibration and measurement of the isomer distribution. Making the oversimplifying assumption that the transition state energies for the individual isomers are equal allows the relative deprotonation rates to be calculated from the difference in ground-state energies ($\Delta G°$). A comparison of k_{cis}/k_{trans}

$$\log k_{cis}/k_{trans} = \Delta G°/RT$$

calculated in this way with the observed values is shown in Table IV for most of the stereoisomeric pairs listed in Table I and for other pairs where data from the literature are available.

Examination of Table IV shows that, considering the approximations made, the agreement between calculated and observed values is remarkably good for the systems 4-*t*-butyl-1-nitrocyclohexane, 4-phenyl-1-nitrocyclohexane, 2-phenyl-1-nitrocyclopentane, 4*e*-*t*-butyl-2*a*-phenyl-1-nitrocyclohexane, 1-methoxy-2-nitro-1-phenylcyclohexane, and 1-methoxy-2-nitro-1-phenylcyclopentane. It seems safe to conclude from these data that the transition state energies for the individual stereoisomers in these systems do not differ greatly, and that the rates are indeed primarily reflections of differences in ground-state energies.

Comparison of the equilibrium data for 4-*t*-butyl- and 4-phenyl-1-nitrocyclohexanes with that for 2-phenyl-, 2-methyl-, and 4*e*-*t*-butyl-2*e*-phenyl-1-nitrocyclohexanes shows that introduction of a 2 substituent causes the ground-state energy of the *trans* isomer to decrease appreciably relative to the *cis* isomer (Table IV). This must be caused, at least in part, by the ability of the

(15) E. L. Eliel, *J. Chem. Educ.*, 37, 126 (1960).
(16) O. Hassel and M. Davis, *Acta Chem. Scand.*, 17, 1181 (1963).
(17) See A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, p 138.

Table IV. Comparison of Observed *cis/trans* Rate Ratios with those Calculated on the Basis of Ground-Energy Effects

cis/trans system	Equilibration[a] (% *trans*)	ΔG,[b] kcal/mol	k_{cis}/k_{trans} Calcd[c]	k_{cis}/k_{trans} Obsd[d]
4-*t*-Butyl-1-nitrocyclohexane	83	0.95	4.9	6.2
4-Phenyl-1-nitrocyclohexane	79	0.79	3.8	4.9
2-Methyl-1-nitrocyclohexane	90	1.31	9.0	40
2-Phenyl-1-nitrocyclohexane	99[e]	2.75	99	350
2-Phenyl-1-nitrocyclopentane	89	1.25	8.1	4.5
4*e*-*t*-Butyl-2*e*-phenyl-1-nitrocyclohexane	98	2.32	49	59[f]
4*e*-*t*-Butyl-2*a*-phenyl-1-nitrocyclohexane	50	0.0	1.0	1.0
1-Methoxy-2-nitro-1-phenylcyclohexane	57[g]	0.16	1.3	1.4[h]
1-Methoxy-2-nitro-1-phenylcyclopentane	70[i]	0.50	2.3	2.6
5-Nitrobicyclo[2.2.1]hept-2-ene	64.5[j] (*exo*)	0.35	1.8 (*endo/exo*)	23[k] (*endo/exo*)
2-Nitrobicyclo[2.2.1]heptane	72[l] (*exo*)	0.57	2.6 (*endo/exo*)	15[k] (*endo/exo*)

[a] In refluxing sodium bicarbonate–95% ethanol. [b] Difference in ground-state energies at 25°. [c] Assuming $\Delta G^\circ = \Delta G^*$. [d] Rate ratio in NaOMe–MeOH at 25° unless otherwise specified. [e] Determined by ir; see H. E. Zimmerman and T. E. Nevins, *J. Amer. Chem. Soc.*, 79, 6559 (1957). [f] In *t*-BuOK–*t*-BuOH at 25°. [g] The equilibration was carried out in refluxing sodium bicarbonate–95% ethanol and the equilibrated product was analyzed at the period of 15–30 min by nmr. The resonance for methoxy group of 1-methoxy-*trans*-2-nitro-1-phenylcyclohexane (*trans* isomer) is at 174 cps in CCl_4 and that for *cis* isomer is at 185 cps. The composition of equilibration product was based on the integration of these peaks. [h] Rate ratio in *t*-BuOK–*t*-BuOH at 38.6°. [i] The equilibration was carried out in refluxing sodium bicarbonate–95% ethanol and the equilibrated product was analyzed at the period of 10–20 min by nmr. The resonance for methoxy group of 1-methoxy-*trans*-2-nitro-1-phenylcyclopentane (*trans* isomer) is at 177 Hz in $CDCl_3$ and that for *cis* isomer is at 183 Hz. The composition of equilibration product was based on the integration of these peaks. [j] Equilibration at 75° in *t*-BuOK–*t*-BuOH; see R. J. Ouellett and G. E. Booth, *J. Org. Chem.*, **30**, 423 (1965). [k] Rate ratio in 50% (v/v) H_2O–dioxane at 28°; see P. W. K. Flanagan, Ph.D. Dissertation, Ohio State University, 1957; see also H. Shechter, P. W. K. Flanagan, H. Stone, J. G. Traynham, and F. T. Williams, Jr., Abstracts of Papers, 136th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 13–18, 1959, p 33*P*. [l] R. J. Sundberg and P. A. Bukowick, *J. Org. Chem.*, **33**, 4098 (1968).

nitro and phenyl (or methyl) groups to bend away from one another in the *trans* (but not the *cis*) isomer.[14] The equilibration data for the 4*e*-*t*-butyl-2*e*-phenyl-1-nitrocyclohexane and 2-phenyl-1-nitrocyclohexane systems is not as reliable as for the other systems because very little of the *cis* isomer is present at equilibrium, which makes analysis more difficult. Comparison with the 2-methyl-1-nitrocyclohexane system, where analysis is more accurate, lends confidence, however, to the conclusion that in these systems k_{cis}/k_{trans} is appreciably higher, at least for the 2-methyl- and 2-phenyl-1-nitrocyclohexane systems, than can be accounted for on the basis of ground-state effects alone. The operation of another effect is indicated. The effect must be one wherein the rate for the *trans* isomer is retarded over that expected since the rate for the *cis* isomer appears to be "normal" (see above). It is significant that this effect appears in the *trans* isomer, for which the ground-state energy has been lowered by deformation of the cyclohexane chair. It seems likely that the retarding effect is associated with this chair deformation, which causes the phenyl group to come much closer to the acidic hydrogen atom (ρ = 1.23 as compared to ρ = 0.84 for the *cis* isomer, see above). Some kind of steric hindrance by the phenyl group to proton removal appears to be indicated.[18] (The only disturbing part about this explanation is that one might then have expected an even larger retarding effect for *trans*-2-aryl-1-nitrocyclopentanes, but this did not materialize.)

There is also a disagreement between calculated and observed k_{cis}/k_{trans} for 2-phenyl-1-nitrocyclopentanes, although not as marked as for 2-phenyl-1-nitrocyclohexanes. Here the *cis* isomer appears to be less reactive than expected.

(18) R. J. Sundberg and P. A. Bukowick, *J. Org. Chem.*, **33**, 4098 (1968), have suggested that deprotonation is retarded for *trans*-2-phenyl-1-nitrocyclohexane because it reacts in a conformation wherein the phenyl and nitro groups are axial. Reasons for rejecting this proposal are given in the next paper in this series, F. G. Bordwell and K. C. Yee, *J. Amer. Chem. Soc.*, **92**, 5939 (1970).

Large discrepancies between the calculated and observed k_{endo}/k_{exo} rate ratios appear in the 5-nitrobicyclo[2.2.1]hept-2-ene and 2-nitrobicyclo[2.2.1]heptane systems (Table IV). Here the *endo* isomers, in which the *exo* proton is abstracted, appear to be much more reactive than expected on the basis of relative ground-state energies. This observation is in line with reports from several laboratories that the *exo* protons in norbornan-2-one systems are much more readily abstracted than are the *endo* protons.[19] Once again a steric effect of some kind is indicated. This point will be discussed further in the next paper in this series.

Experimental Section[20]

***cis*- and *trans*-4*e*-*t*-Butyl-2-phenylcyclohexanones.** A solution of 26 g (0.14 mol) of (mainly) *trans*-4-*t*-butyl-2-chlorocyclohexanone[21] in *ca.* 50 ml of anhydrous ether was added to a solution containing a slight excess of phenylmagnesium bromide at such a rate that gentle reflux was maintained. After reflux for an additional hour the ether was replaced by *ca.* 75 ml of dry xylene. After a 14-hr reflux the reaction mixture was cooled and poured into cold 5% HCl. The reaction mixture was extracted with ether and the recovered product (29.6 g 43%) was taken up in chloroform and chromatographed on silica gel. Chromatographic separation gave 2.5 g (8%) of the liquid *trans* isomer and 9.5 g (30%) of the *cis* isomer, a solid, mp 81–83° after two crystallizations from pentane.

A similar preparation using 41 g (0.218 mol) of (mainly) *cis*-4-*t*-butyl-2-chlorocyclohexanone[21] gave 10.3 g (20%) of *trans* isomer (from fractions 4 and 5) and 9.4 g (18%) of *cis* isomer (from fractions 10–12).

Oxidation of *cis*- and *trans*-4-*t*-Butyl-2-phenylcyclohexanone Oxime. The nitroalkanes were prepared by oxidation of the cor-

(19) (a) A. F. Thomas and B. Willham, *Tetrahedron Lett.*, No. 18, 1309 (1965), and D. E. Sunko, *ibid.*, No. 49, 4665 (1965), have found from exchange studies that norcamphor, isofenchane, and camphor are monodeuterated principally in the *exo* position; (b) T. T. Tidwell, 157th National Meeting of the American Chemical Society, Minneapolis, Minn., April 14–18, 1969 reports an *exo/endo* rate ratio of 20:1 for proton abstraction from the 3 position of camphor; (c) A. F. Thomas, R. A. Schneider, and J. Meinwald, *J. Amer. Chem. Soc.*, **89**, 68 (1967).

(20) Additional experimental details may be found in the Ph.D. Dissertation of K. C. Yee, Northwestern University, Aug, 1969. Microanalyses were by Micro-Tech, Skokie, Ill.

(21) N. L. Allinger, J. Allinger, L. A. Freiberg, R. F. Czaja, and N. A. LeBel, *J. Amer. Chem. Soc.*, **82**, 5876 (1960).

Table V. Properties of 2-Aryl-1-nitrocyclopentanes

Y-C_6H_4	Mp, °C	Molecular formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H	Nmr, ppm $CHNO_2$
trans-Ph	Liquid	$C_{11}H_{13}NO_2$	69.03	6.85	69.02	7.02	Apparent quartet, 4.90 (J = 6.5–7.5 Hz)
cis-Ph	62–62.5	$C_{11}H_{13}NO_2$	69.03	6.85	69.26	6.95	Multiplet 5.14 (W_H = 20 Hz)
trans-*p*-BrPh	Liquid	$C_{11}H_{12}NO_2Br$	48.91	4.48	49.16	4.59	Apparent quartet, 4.85 (J = 6.5–7.5 Hz)
cis-*p*-BrPh	49.0–49.5	$C_{11}H_{12}NO_2Br$	48.91	4.48	49.18	4.65	Apparent doublet of triplets 5.15 (J = 6.5–3.0 Hz)
trans-*m*-CF_3Ph	Liquid	$C_{12}H_{12}F_3NO_2$	55.60	4.67	55.82	4.66	Apparent quartet, 4.90 (J = 7.0 Hz)
cis-*m*-CF_3Ph	Liquid	$C_{12}H_{12}F_3NO_2$	55.60	4.67	55.66	4.69	Multiplet, 5.16 (W_H = 20 Hz)
trans-*p*-MePh	Liquid	$C_{12}H_{15}NO_2$	70.22	7.37	70.48	7.49	Apparent quartet, 4.85 (J = 6.5–7.0 Hz)
cis-*p*-MePh	66.5–67.5	$C_{12}H_{15}NO_2$	70.22	7.37	70.37	7.45	Apparent doublet of triplets 5.14 (J = 6.0–7.0, 3.0–3.5 Hz)

responding ketone oximes by the Emmons–Pagano procedure.[6] Details are given for 4-*t*-butyl-2-phenyl-1-nitrocyclohexane isomers in order to illustrate the method used for product isolation. A mixture of 4.16 g (0.017 mol) of *trans*-4-*t*-butyl-2-phenylcyclohexanone oxime, mp 131–135°, 0.34 g of urea, and 13.3 g (0.094 mol) of disodium hydrogen phosphate in 60 ml of acetonitrile was oxidized with a solution of trifluoroperoxyacetic acid prepared from 0.94 ml (0.034 mol) of 90% hydrogen peroxide and 5.8 ml (0.039 mol) of trifluoroacetic anhydride in 9 ml of acetonitrile.[6,22] The conditions and work-up were comparable to those described,[6] except that the residual liquid was dissolved in a minimum amount of chloroform and the solution added to a column (4 × 60 cm) slurry packed with silica gel (350 g) and 1% ether–hexane (500 ml). Elution was carried out with 6 l. of 1% ether–hexane (500-ml fractions). Removal of solvent from fractions 10 and 11 gave 3.8 g (85%) of liquid, showing strong ir NO_2 absorptions at 6.43 and 7.30 μ. The nmr showed two resonances of equal intensities for the *t*-butyl group, one at 46, the other at 52 cps. Solidification in Dry Ice–acetone and fractional crystallization from pentane gave two isomers.

Isomer A melted at 83.5–84.0°; ir λ_{max}^{KBr} 3.45, 3.50, 6.46 (NO_2), 6.68, 6.88, 7.38 (NO_2), 13.80, and 14.20 μ; nmr $\delta_{TMS}^{CCl_4}$ 7.36 (m, Ar-H, 5 H), 5.07 (apparent doublet, C*H*NO_2, W_H = 10.8 Hz, 1 H), *ca.* 2.94 (m, C*H*Ph, W_H = 28 Hz, 1 H), 2.07–1.17 (m, methylene H, 7H), 0.765 (s, *t*-butyl H, 9 H).

Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.38; H, 9.03, N, 5.35.

Isomer B melted at 54.5–55.5°; ir λ_{max}^{KBr} 3.39, 3.48, 6.45 (NO_2), 6.69, 6.84, 7.30 (NO_2), 13.65, 13.80, and 14.30 μ; nmr $\delta_{TMS}^{CCl_4}$ 7.40 (m, Ar-H, 5 H), 5.05 (apparent doublet, C*H*NO_2, W_H = 10.6 Hz, 1 H), *ca.* 2.94 (m, C*H*Ph, 1 H), 0.865 (s, *t*-butyl H, 9 H). A mixture containing 70% isomer B and 30% isomer A (nmr) was used for microanalysis.

Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87. Found: C, 73.49; H, 8.89.

Equilibration of either isomer A or B in refluxing saturated sodium bicarbonate–95% ethanol solution gave a 50–50 mixture of isomer A and B.

Isomers A and B are 4*e*-*t*-butyl-2*a*-phenyl-1*a*-nitrocyclohexane and 4*e*-*t*-butyl-2*a*-phenyl-1*e*-nitrocyclohexane, but a definite assignment of structure cannot be made on the basis of the available evidence.

Oxidation of 6.2 g (0.0254 mol) of *cis*-4-*t*-butyl-2-phenylcyclohexanone oxime was carried out in the same manner except that *ca.* twice as much acetonitrile was used in an (unsuccessful) attempt to bring the oxime into solution. (A run with phenylacetonitrile gave no better results.) Chromatography in the manner described above gave (fraction 5) 1.45 g of a blue liquid, which solidified: mp 81.5–82.0° (pentane); ir λ_{max}^{KBr} 3.40, 3.50, 5.58, 5.62 (CO, equal intensity), 6.38, 6.90, 7.36, 8.10, 8.40, 8.50, 8.70, 9.04, 9.35, 11.60, 12.50, 13.10, 13.30, 13.76, 14.16, and 14.25 μ; nmr $\delta_{TMS}^{CCl_4}$ 7.05–6.70 (m), 3.40–1.80 (m), 1.10 (singlet). This compound was not identified.

Anal. Found: C, 37.59; H, 3.82; N, 2.37.

Fraction 6 gave 1.15 g of a pale green liquid from which 4*e*-*t*-butyl-2*e*-phenyl-1*e*-nitrocyclohexane, mp 98.5–100° (pentane), was isolated: ir λ_{max}^{KBr} 3.39, 3.47, 6.44 (NO_2), 6.65, 6.76, 6.86, 7.24 (NO_2), 7.45, 7.70, 8.12, 9.10, 9.26, 10.15, 10.90, 12.60, 12.88, 13.05, 13.50, and 14.20 μ; nmr $\delta_{TMS}^{CDCl_3}$ 7.25 (s, Ar-H), 4.67 (doublet of triplets, axial-C*H*NO_2, J = 10.5, 4.3 Hz), 3.20 (doublet of triplets, axial-C*H*Ph, J = 11.2, 4.0 Hz), 2.44–1.16 (m, methylene H), 0.90 (s, *t*-butyl H); the corresponding peaks in CCl_4 are 7.17, 4.50, 3.12, 2.30–1.27, 0.87.

Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.27; H, 8.77; N, 5.37.

Fraction 7 gave 0.28 g of yellow liquid which solidified (mp 47–70°) in a Dry Ice–acetone bath. Crystallization from pentane gave crystals of 4*e*-*t*-butyl-2*e*-phenyl-1*a*-nitrocyclohexane: mp 107–108; ir λ_{max}^{KBr} 3.36, 3.46, 6.42 (NO_2), 6.65, 6.75, 6.85, 6.90, 7.27, 7.43, 7.68, 7.97, 8.10, 8.45, 9.05, 9.60, 9.70, 10.48, 11.05, 11.60, 11.92, 12.50, 12.88, 13.25, and 14.27 μ; nmr $\delta_{TMS}^{CCl_4}$ 7.20 (s, Ar-H), 4.84 (quartet, equatorial-C*H*NO_2, J = 3.2, W_H = 9.5 Hz), 3.00 (triplet of doublets, axial-C*H*Ph), J = 12.4 Hz), 2.84–1.67 (m, methylene H), 0.97 (s, *t*-butyl H).

Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.39; H, 8.81; N, 5.22.

Low yields of nitroalkanes are often obtained with sterically hindered oximes.[6,9]

Equilibration with refluxing EtOH–$NaHCO_3$ gave 98% *trans* and 2% *cis* (analysis by vpc).

2-Aryl-1-nitrocyclopentanes. Some of the properties of the 2-aryl-1-nitrocyclopentanes are summarized in Table V.

2-Aryl-1-nitrocyclohexanes. The parent compounds and their *cis* and *trans* *m*-Cl, *p*-Cl, *m*-CH_3, and *p*-CH_3 derivatives have been described previously.[8,23,24]

Analytical data had not been reported for *trans*-2-*p*-methoxyphenyl-1-nitrocyclohexane, mp 83–86°.[24]

Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.47; H, 7.29.

The *cis* isomer, mp 83–84°, was prepared from the *trans* isomer by dissolving in NaOMe–MeOH and treatment with HOAc–LiOAc–H_2O–EtOH buffer.[7]

Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.39; H, 7.29.

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(22) We are indebted to the Inorganic Chemical Division of the FMC Corporation for a generous gift of 90% hydrogen peroxide.

(23) A. C. Huitric, W. G. Clark, Jr., K. Leigh, and D. C. Staiff, *J. Org. Chem.*, 27, 715 (1962).

(24) We are indebted to Professor A. C. Huitric for gifts of these compounds.