α-Nitro Ketones. 2.[1] Conformational Equilibria of 2-Nitrocyclohexanones[2]

Walter W. Zajac, Jr.,* and Hadi Özbal[3]

Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

Received May 14, 1979

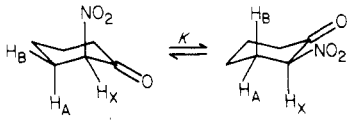
The conformational free energy of the nitro group in 2-nitrocyclohexanone has been determined to be 1.26–1.39 kcal/mol (ca. 90% equatorial), using dipole moment and ^{1}H NMR measurements. The following cyclohexanones were determined to exist exclusively in the conformer in which the nitro group is equatorial: *trans*-2-nitro-3-methyl-, *trans*-2-nitro-3-*tert*-butyl-, *cis*-2-nitro-4-methyl-, *cis*-2-nitro-4-ethyl-, *cis*-2-nitro-4-isopropyl-, *cis*-2-nitro-4-*tert*-butyl-, *trans*-2-nitro-5-methyl-, *trans*-2-nitro-5-*tert*-butyl-, *trans*-2-nitro-3,3,5-trimethyl-, *trans*-2-nitro-3,5,5-trimethyl-, and 2-nitro-3,3,5,5-tetramethylcyclohexanone. The following cyclohexanones were determined to be conformationally mobile, with the position of equilibrium being determined by the *A* value of the substituents: *trans*-2-nitro-4-methyl-, *trans*-2-nitro-4-ethyl-, *trans*-2-nitro-4-isopropyl-, and *cis*-2-nitro-5-methylcyclohexanone. The nitro group adopted the axial position exclusively in the *trans*-2-nitro-4-*tert*-butyl-, *cis*-2-nitro-5-*tert*-butyl-, *cis*-2-nitro-3,3,5-trimethyl- and *cis*-2-nitro-3,5,5-trimethylcyclohexanones.

Introduction

Considerable research has been carried out on the measurement of the conformational equilibria of substituted cyclohexanes[4] and various substituted heterocyclic six-membered rings.[5] A survey of the literature shows that the 2-halocyclohexanones have been studied extensively,[6] but cyclohexanones with other polar substituents have been neglected. Recently, however, we have reported on the conformational equilibria of cyclohexanones substituted in the α position with group IV-A elements.[7]

In most cases, the axial conformer of the cyclohexane derivative is observed to be less stable than the equatorial conformer. However, in the 2-chloro and 2-bromo derivatives of cyclohexanone, as well as the 2-phenylthio and 2-phenylseleno derivatives, the axial orientation of the substituent is more stable.[6,7] Various suggestions as to the reasons for the axial preference of 2-halocyclohexanones have been advanced.[6,8]

As part of our continuing study on the chemistry of α-nitro ketones, we report on the conformational equilibria of 2-nitrocyclohexanone and 19 substituted 2-nitrocyclohexanones. In the NMR spectra of the 2-nitrocyclohexanones the α-proton appears several parts per million downfield from the rest of the protons. This property allowed the use of ^{1}H NMR spectroscopy as the primary method for studying the conformational behavior of the 2-nitrocyclohexanones, utilizing the chemical shift, coupling constant, and bandwidth parameters of the α-proton. Dipole moment measurements and chemical equilibration were also used.



The free-energy difference between two conformations of the 2-nitro ketones is given by eq 1 and the equilibrium

$$\Delta G^\circ = -RT \ln K \quad (1)$$

constant K is given by eq 2, where X is the mole fraction

$$K = X/(1 - X) \quad (2)$$

of one of the conformers present in the equilibrium mixture. One can calculate K from eq 3, where P_a and P_e are

$$K = (P_a - P)/(P - P_e) \quad (3)$$

the magnitudes of a property with an axial and an equational functional group, respectively, and P is the measured property in the mixture. In this study the property P was the α-proton chemical shift, coupling constant, or bandwidth. These properties are average values in a mobile system. The magnitudes of the parameters of the individual conformers must be known. One can obtain these values by lowering the temperature and slowing down the chair–chair interconversion[9] or by using reference compounds similar to the individual conformers but which cannot interconvert (anancomeric compounds).[10] The *tert*-butyl derivatives are generally used for this purpose. Theoretically, low-temperature measurements are more accurate; experimentally, however, they are more difficult to determine. In this investigation the latter method for obtaining the P_a and P_e values was used.

Results

The ^{1}H NMR parameters determined for the 2-nitrocyclohexanones are listed in Table I.

Chemical Shift. The α-protons of the 2-nitrocyclohexanones behave similarly to those of the 2-halocyclohexanones; that is, the equatorial α-proton appears at a higher field than its axial counterpart.[11] The chemical shifts of the α-proton in the 2-nitrocyclohexanones that have been studied vary over a wide range from 4.59 to 5.45 ppm. For those nitro ketones for which the conformational equilibria lie to one side and the α-proton is equatorial (compounds **13**, **16**, **18**, and **20**), the chemical shifts vary

(1) Part 1: F. E. Elfehail, W. W. Zajac, Jr., J. P. Hazel, and G. T. DeTitta, *Acta Crystallogr., Sect. B*, **33**, 1962 (1977).

(2) Presented at the 172nd ACS National Meeting, San Francisco, 1976.

(3) (a) Taken from the Ph.D. thesis of H. Özbal, Villanova University, 1972; (b) Boğaziçi University, Bebek, Istanbul.

(4) (a) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Wiley-Interscience, New York, 1965. (b) F. R. Jensen and C. H. Bushweller, *Adv. Alicyclic Chem.*, **3**, 139 (1971). (c) B. T. Golding, *MTP Int. Rev. Sci.: Org. Chem., Ser. One*, **5**, 45–85 (1973); B. Fuchs, *MTP Int. Rev. Sci.: Org. Chem., Ser. Two*, **5**, 171–196 (1976). (d) For review of literature through 1975, see *Alicyclic Chem.*, 1–5 (1971–1976).

(5) (a) F. G. Riddell, *Q. Rev., Chem. Soc.*, **21**, 364 (1967). (b) E. L. Eliel, *Acc. Chem. Res.*, **3**, 1 (1970). (c) J. B. Lambert, *ibid.*, **4**, 87 (1971). (d) E. L. Eliel, *Angew. Chem., Int. Ed. Engl.*, **11**, 739 (1972). (e) For a review of literature through 1975, see *Saturated Heterocycl. Chem.*, 1–5 (1973–1978). (f) W. L. F. Armagego, *Stereochem. Heterocycl. Compd., Pt I–II* (1977).

(6) (a) R. C. Bingham, *J. Am. Chem. Soc.*, **97**, 6743 (1975). (b) J. Cantacuzene, R. Jantzen, and D. Ricard, *Tetrahedron*, **28**, 717 (1972), and references therein. (c) See also ref 4a, pp 460–469, and ref 17.

(7) H. Özbal and W. W. Zajac, Jr., *Tetrahedron Lett.*, 4821 (1979).

(8) O. Eisenstein, N. T. Anh, Y. Jean, A. Devaquet, J. Cantacuzene, and L. Salem, *Tetrahedron*, **30**, 1717 (1974); L. Došen-Mičović and N. L. Allinger, *ibid.*, **34**, 3385 (1978).

(9) Reference 4b, pp 149–153.

(10) M. J. O. Anteunis in "Conformational Analysis, Scope and Present Limitations", G. Chiurdoglu, Ed., Academic Press, New York, 1971, p 32; ref 4b, pp 153–155.

(11) K. M. Wellman and F. G. Bordwell, *Tetrahedron Lett.*, 1703 (1963).

0022-3263/80/1945-4154$01.00/0

Table I. ^{1}H NMR Data of α-Protons of 2-Nitrocyclohexanones[a]

compd no.	ketone	60 MHz				100 MHz		
		δ	W^b	J_{avg}^{ea-ae}	J_{avg}^{ee-aa}	W^b	J_{avg}^{ea-ae}	J_{avg}^{ee-aa}
1	2-nitrocyclohexanone	5.34	18.3	7.8	10.5	17.6	6.2	11.3
2	*cis*-2-nitro-3-methylcyclohexanone[c]							
3	*trans*-2-nitro-3-methylcyclohexanone	5.11			12.2[d]			12.4[d]
4	*cis*-2-nitro-3-*tert*-butylcyclohexanone[c]							
5	*trans*-2-nitro-3-*tert*-butylcyclohexanone	5.30			11.0[d]			11.0[d]
6	*cis*-2-nitro-4-methylcyclohexanone	5.49	19.3	6.3	13.0	18.3	6.8	12.4
7	*trans*-2-nitro-4-methylcyclohexanone	5.25	14.0	5.2	8.8	13.6	5.0	8.6
8	*cis*-2-nitro-4-ethylcyclohexanone	5.45	19.7	6.6	13.3	18.1[e]	5.6[e]	12.5[e]
9	*trans*-2-nitro-4-ethylcyclohexanone	5.29	14.6	5.6	9.0	14.0[e]	5.4[e]	8.6[e]
10	*cis*-2-nitro-4-isopropylcyclohexanone	5.45	18.8	6.4	12.4	17.8[e]	5.5[e]	12.4[e]
11	*trans*-2-nitro-4-isopropylcyclohexanone	5.09	12.5	5.5	6.7	12.8[e]	5.3[e]	7.4[e]
12	*cis*-2-nitro-4-*tert*-butylcyclohexanone	5.45	19.5	5.8[f]	12.5	18.4	5.7[f]	12.5
13	*trans*-2-nitro-4-*tert*-butylcyclohexanone	5.00	9.3	4.5[g]	4.4[h]	9.6	5.2[g]	4.4[h]
14	*cis*-2-nitro-5-methylcyclohexanone	5.27	14.5	5.5	9.0	14.5	5.5	8.9
15	*trans*-2-nitro-5-methylcyclohexanone	5.39	19.3	7.7	11.6	19.0	6.5	12.5
16	*cis*-2-nitro-5-*tert*-butylcyclohexanone	4.91	8.8	4.4[g]	4.4[h]			
17	*trans*-2-nitro-5-*tert*-butylcyclohexanone	5.39	19.3	6.9[f]	12.4	18.5	6.3[g]	12.3
18	*cis*-2-nitro-3,3,5-trimethylcyclohexanone	4.59[i]						
19	*trans*-2-nitro-3,3,5-trimethylcyclohexanone	5.24[i]						
20	*cis*-2-nitro-3,5,5-trimethylcyclohexanone	4.93		5.2[d]				
21	*trans*-2-nitro-3,5,5-trimethylcyclohexanone	5.11			12.3[d]			12.0[d]
22	2-nitro-3,3,5,5-tetramethylcyclohexanone	5.21[i]						

[a] In $CDCl_3$. [b] $W = J_{AX} + J_{BX}$. [c] Could not be synthesized. [d] Doublet. [e] 220 MHz. [f] J^{ae}. [g] J^{ea}. [h] J^{ee}. [i] Singlet.

Table II. Calculated Conformational Free Energies[a] ($-\Delta G^\circ$) for 2-Nitrocyclohexanones Using ^{1}H NMR Parameters

compd no.	ketone	δ	δ	J	J	W	W	W
1	2-nitrocyclohexanone	0.68[b]	1.29[c]	0.72[b-d]	1.04[b,c,e]	1.19[b,d]	1.34[c,d]	1.39[b,c,e]
7	*trans*-2-nitro-4-methylcyclohexanone	0.08	0.53	0.12	0.04	−0.05	0.0	−0.08
9	*trans*-2-nitro-4-ethylcyclohexanone	0.35	0.80	0.17	0.04	0.03	0.15	0.03
11	*trans*-2-nitro-4-isopropylcyclohexanone	−0.83	−0.32	−0.53	−0.32	−0.47	−0.36	−0.38
14	*cis*-2-nitro-5-methylcyclohexanone	0.30	0.73	0.17	0.13	0.24	0.32	0.17

[a] kcal/mole. [b] *cis*- and *trans*-2-nitro-4-*tert*-butylcyclohexanones as model compounds. [c] *cis*- and *trans*-2-nitro-5-*tert*-butylcyclohexanones as model compounds. [d] 60 MHz. [e] 100 MHz.

from 4.59 to 5.00 ppm. For those nitro ketones for which the conformational equilibria lie to one side and the α-proton is axial (compounds **3**, **5**, **6**, **8**, **10**, **12**, **15**, **17**, **19**, and **21**), the chemical shifts vary from 5.11 to 5.45 ppm. However, within the *cis*-2-nitro-4-alkylcyclohexanone series (compounds **6**, **8**, **10**, and **12**), the chemical shifts remain constant at δ 5.45, demonstrating that an equatorial alkyl substituent 1,3 to an axial hydrogen has little shielding effect. Shielding effects are observed for α-protons that have alkyl substituents attached to the adjacent ring carbon (compounds **3**, **5**, **18**, and **20**).

Separate calculations were made for the conformational energies of the flexible 2-nitrocyclohexanones (compounds **7**, **9**, **11**, **14**), using the two sets of anancomeric compounds *cis*- and *trans*-2-nitro-4-*tert*-butyl- and *cis*- and *trans*-2-nitro-5-*tert*-butylcyclohexanones as the model compounds for the α-proton in the axial and equatorial positions (see Table II).

Only when the *cis*- and *trans*-2-nitro-5-*tert*-butylcyclohexanones are used as reference compounds do the conformational free-energy values compare favorably with the calculations obtained by using the other parameters.

It is obvious from these results that the use of the chemical shift parameter for conformational analysis is useful if the correct reference compounds are chosen, otherwise serious error in the conformational free energy is produced.

Coupling Constants. The α-proton of many of the nitro ketones appears as the X part of an ABX spin system. To determine if the spectra can be treated as first order and if the coupling constants can be obtained directly, the spectra were run at two different frequencies, 60 and 100 Mz. Only small changes were observed in the X part of the spectra, suggesting that the splittings are good approximations of the coupling constants. By use of eq 4 the conformational free energies could be calcu-

$$J_{avg} = XJ^{aa} + (1 - X)J^{ee} \quad (4)$$

lated. Because the magnitude of the difference in the ea and ae coupling constants was on the order of the error of the measurement, eq 5 was not used. Since J^{aa} and J^{ee}

$$J_{avg} = XJ^{ae} + (1 - X)J^{ea} \quad (5)$$

were nearly the same for both the 4-*tert*-butyl and 5-*tert*-butyl compounds at 60 MHz, only one set of calculations was made at this field strength. Results from 60 and 100 MHz are also about the same and the results are listed in Table II. The largest difference is for 2-nitrocyclohexanone, probably because at 60 MHz the spectrum is not truly first order.

Bandwidth. Since the bandwidth is independent of the chemical shift and is a multiple of the participating coupling constants, it can be measured considerably more accurately than the individual coupling constants.

Calculations of the conformational free energies using bandwidths are applicable only to the nitro ketones having two protons on C-3 (compounds **1**, **3**, **5**, **7**, and **14**). The

results of the calculations are summarized in Table II. The results obtained by using the bandwidths are close to each other, regardless of the reference compounds used or the field strengths employed. This is a good indication that conformational energies calculated by using the bandwidth parameter are quite reliable.

Dipole Moments. The dipole moments of 2-nitrocyclohexanone and *cis*-2-nitro-4-*tert*-butylcyclohexanone were determined by the microwave technique[12] to be 5.37 D and 5.61 D, respectively. Unfortunately the *trans*-4-butylcyclohexanone could not be isolated so the dipole moment was calculated by using the coordinates of the skeletal atoms of the ring structure and the unit vectors for the substituents given by Eliel[13] and the bond moments of 2.83 D for the carbonyl group[14] and 3.50 D for the nitro group,[15] respectively.

The experimental and calculated dipole moments of the cis isomer are identical. Therefore the calculated value of 5.37 D for the trans isomer should be very close to the true value. Calculations using the dipole moments result in an equilibrium constant K of 8.16 and a conformational free energy value of −1.26 kcal/mol. The conformational equilibrium contains 89% of the conformer with the nitro group equatorial. The NMR values are in very good agreement with this value.

Chemical Equilibration. Chemical equilibration of the *cis*- and *trans*-4-*tert*-butylcyclohexyl derivatives should give the A value of the substituent directly. The nitrocyclohexanones studied in this investigation were prepared by nitration of the enol acetates of the cyclohexanones with nitric acid. This reaction is a kinetically controlled process.[16] Nitration of 4-*tert*-butyl-1-acetoxycyclohexene (enol acetate of 4-*tert*-butylcyclohexanone) leads to approximately a 50:50 mixture of *cis*- and *trans*-2-nitro-4-*tert*-butylcyclohexanone. The trans isomer rapidly isomerizes to the more stable cis isomer and leads to 91% of the cis isomer at equilibrium. The ratio of isomers was determined by integrating the areas of the peaks of the α-protons and is an average value for ten runs. Attempts to isolate the pure trans isomer were unsuccessful, consequently equilibration could not be approached from both directions. However, assuming that equilibrium had been established, then a $-\Delta G°$ value of 1.4 kcal/mol is obtained for the cis–trans isomerization of 2-nitro-4-*tert*-butylcyclohexanone. This value of 1.4 kcal/mol can be used as the A value for the 2-nitro group in cyclohexanone and is in excellent agreement with the value determined by both the NMR bandwidth method and the dipole moment measurements.

Discussion

The two possible conformations of the *trans*-2,3-, *cis*-2,4-, and *trans*-2,5-nitro ketones are diaxial and diequatorial. One would predict the preferred conformation to be the diequatorial one, thereby eliminating the severe syn diaxial interactions. That these nitro ketones (**3**, **5**, **6**, **8**, **10**, **12**, **15**, **17**, and **19**) do exist exclusively in the conformation in which the nitro group and alkyl group are both equatorial is borne out by the NMR data.

Although *trans*-2-nitro-3-*tert*-butylcyclohexanone (**5**) exists exclusively in the diequatorial conformation, the vicinal proton–proton coupling of the diaxial hydrogens is only 11 Hz. The lowering of the value from the expected 12.5 Hz can be attributed to the flattening out of the cyclohexanone ring by the bulky *tert*-butyl group, causing the dihedral angle of the vicinal axial hydrogens to be less than 180°, thereby lowering the coupling constant.[17]

No doubt *trans*-2-nitro-3,3,5-trimethylcyclohexanone (**21**) also exists exclusively in the conformation in which the nitro group and the C-5 methyl are both equatorial. This cannot be corroborated by the NMR data because the only parameter available for the α-proton is the chemical shift. However, there is no reason to think the compound should exist in the alternate conformation with the nitro and methyl groups diaxial. With this the case, one can use the chemical shift value of 5.24 ppm for the α-proton of *trans*-2-nitro-3,3,5-trimethylcyclohexanone (**21**) as a model value for a C-3 geminally substituted 2-nitrocyclohexanone with a nitro group equatorial.

On the basis one would predict the exclusive (at least overwhelmingly preferred) conformation of 2-nitro-3,3,5,5-tetramethylcyclohexanone (**22**) to have the nitro group equatorial since the chemical shift of the α-proton has a value of 5.21 ppm.

Two nitro ketones that exist exclusively in the conformation in which the nitro group is axial are the *trans*-2-nitro-4-*tert*-butyl- and *cis*-2-nitro-5-*tert*-butylcyclohexanones (**13** and **16**). In these compounds the bulky *tert*-butyl group must occupy the equatorial position. Two other compounds in which the nitro group would be expected to be primarily in the axial position are the isomeric *cis*-2-nitro-3,5,5-trimethyl- and *cis*-2-nitro-3,3,5-trimethylcyclohexanones (**18** and **20**). These compounds are conformationally similar in that when the nitro group is equatorial, methyl groups at C-3 and C-5 must both be axial. This creates an unfavorable syn dimethyl diaxial interaction which in cyclohexane is about 3.7 kcal/mol.[18] The alternate conformation in which the nitro group becomes axial and one of the methyl groups becomes equatorial should be overwhelmingly preferred. Unfortunately the only NMR parameter for the 3,3,5-trimethyl compound (**20**) is the α-proton chemical shift which appears as a singlet at 4.59 ppm. The high-field value is consistent with a highly shielded equatorial α-proton, but since there are no model compounds for this type of system one cannot verify experimentally what most probably is the preferred conformation.

For the isomeric 3,5,5-trimethyl compound (**18**), the α-proton appears as a doublet with a coupling constant of 5.2 Hz. Since this is the cis isomer, the coupling must be the average of the vicinal equatorial–axial and axial–equatorial coupling constants. Unfortunately the difference between J^{ae} and J^{ea} is within the experimental error of 0.5 Hz for measuring coupling constants. However, the J^{ea} value at 100 MHz for the model compound is also 5.2 Hz, suggesting that the *cis*-2-nitro-3,5,5-trimethylcyclohexanone (**18**) exists exclusively in the conformation in which the nitro group is axial.

The remaining nitro ketones (**1**, **7**, **9**, **11**, and **14**) studied are conformationally mobile and the conformational free-energy values calculated from the NMR parameters are tabulated in Table II. As one can see from the values listed for a given compound, there can be as much as a

(12) V. I. Minkin, O. A. Osipov, and Yu. A. Zhadanov, "Dipole Moments in Organic Chemistry", Plenum Press, New York, 1970, pp 31–39.
(13) Reference 4a, p 454.
(14) N. L. Allinger, J. Allinger, L. A. Freiberg, R. F. Czaja, and N. A. Lebel, *J. Am. Chem. Soc.*, **82**, 5876 (1960).
(15) T. Urbanski, D. Gürne, R. Kolinski, H. Piotrowska, A. Jonczyk, B. Serafin, M. Szretter-Szmid, and M. Witanowski, *Tetrahedron, Suppl.*, **20**, 195 (1964).
(16) H. Özbal and W. W. Zajac, Jr., 178th ACS Meeting, Washington, 1979, ORGN 254.
(17) A. Lectard, A. Lichanot, F. Metra, J. Gaultier, and C. Hauw, *J. Mol. Struct.*, **34**, 113 (1976).
(18) N. L. Allinger and M. A. Miller, *J. Am. Chem. Soc.*, **83**, 2145 (1961).

Table III. Calculated Conformational Free-Energy Values[a] for Alkyl Groups on a Cyclohexanone Ring

compd no.	ketone	ΔG°_{calcd} [b]	$\Delta G^\circ_{NO_2}$	ΔG°_{alkyl} (alkyl)
7	*trans*-2-nitro-4-methylcyclohexanone	0.08	1.39	1.47 (4-Me)
9	*trans*-2-nitro-4-ethylcyclohexanone	−0.03	1.39	1.36 (4-Et)
11	*trans*-2-nitro-4-isopropylcyclohexanone	0.38	1.39	1.77 (4-*i*-Pr)
14	*cis*-2-nitro-5-methylcyclohexanone	−0.17	1.39	1.22 (3-Me)

[a] kcal/mole. [b] Values from Table II, column 7.

0.7-kcal difference in the ΔG° value. The most reliable NMR parameter used is the bandwidth at 100 MHz (vide supra).

For the *trans*-2-nitro-4-alkylcyclohexanone series, as the size of the alkyl group increases the percentage of conformer with the nitro group equatorial decreases. By use of eq 6 and a ΔG° value in Table II and the $-\Delta G^\circ$ value

$$\Delta G^\circ_{obsd} = \Delta G^\circ_{NO_2} + \Delta G^\circ_{alkyl} \quad (6)$$

of 1.39 kcal/mol for the 2-nitro group on a cyclohexanone ring, the ΔG° value of the alkyl groups on a cyclohexanone ring can be determined. The results are summarized in Table III.

When a carbonyl group is introduced into a six-numbered ring the hydrogens at C-2 and C-6 are moved outward, relieving the syn diaxial hydrogen interaction and thereby lowering the ΔG° value for the 4-alkyl substituent in a cyclohexanone ring when compared to the ΔG° value of the 4-alkyl substituent in the cyclohexane ring. This is the so-called 4-alkyl ketone effect[19] and our results are consistent with this interpretation. Our calculated ΔG° values for the 4-methyl, 4-ethyl, and 4-isopropyl groups in the *trans*-2-nitro-4-alkylcyclohexanones are all lower by at least 0.3 kcal/mol than those for the alkylcyclohexanones.

The introduction of a substituent at the 3-position in a cyclohexanone ring causes the removal of one syn CH_3/H interaction and should result in a substantial lowering of the ΔG° for that substituent when compared to the cyclohexane ring system. This 3-alkyl ketone effect[20] has been estimated to be rather substantial, 0.6 kcal/mol. We have calculated a ΔG° value of 1.22 kcal/mol for a methyl group at position 3 in a cyclohexanone, which is a reduction of at least 0.5 kcal/mol when compared to the cyclohexane ring system. Our results are in good agreement with the prediction of a lowering of the ΔG° value for the 3-substituted cyclohexanone.

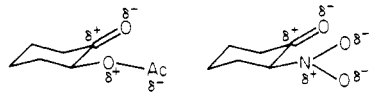
It is interesting to compare the ΔG° value for the nitro group in a number of six-membered-ring compounds that have been studied, (see Table IV). For all the cases studied the nitro group has a ΔG° value of at least −1 kcal/mol, except in the 1,3-dioxane system when the nitro group is at position 5, where it prefers the axial orientation by about 0.6 kcal/mol. Thus far this appears to be the only example of the nitro group behaving anomalously (i.e., exhibiting a "conformational effect"[28] in a simple six-membered ring).

Table IV. Conformational Free-Energy Values[a] for the Nitro Group in Six-Membered Rings

nitro compd	$-\Delta G^\circ$	ref
nitrocyclohexane	1.05	21
2-nitrocyclohexanone	1.39	*b*
2-nitro[2.2.1]bicycloheptane[c]	1.38 (100 °C)	22
5-nitro-1,3-dioxane	−0.63	23
4-nitropiperidine	*d*	25
5-nitro-1,3-oxazine	*d*	26
5-nitrohexahydropyrimidine	*d*	27

[a] kcal/mole. [b] Value from Table II, column 7. [c] Exo isomer more stable. [d] See ref 24.

In conclusion it appears that the increased preference of the nitro group to occupy the equatorial position in 2-nitrocyclohexanone compared with nitrocyclohexane has its origin in the attractive electrostatic interaction of the polar nitro and carbonyl groups. A similar explanation[29] is used to account for the observation that 2-acetoxycyclohexanone exists almost exclusively with the acetoxyl group equatorial ($-\Delta G^\circ$ = 2.5 kcal/mol).



Experimental Section

The nitro ketones in this study were prepared by nitration of the ketone enol acetates.[3a,16]

The ^1H NMR spectra were determined on either a Varian Associates A-60, HA-100, or HA-220 spectrometer. The spectra were determined in deuteriochloroform with Me_4Si as an internal standard.

Acknowledgment. We are indebted to Dr. Kermit Ramey, ARCO Chemical, Glenolden, PA, for determining the 100- and 220-MHz NMR spectra and Dr. Ernest DiCarlo, St. Joseph's University, Philadelphia, for the dipole moment measurements. We also thank Professor Ernest L. Eliel, University of North Carolina, and Professor Kenneth Williamson, Mt. Holyoke College, for critically reading the manuscript prior to publication.

Registry No. **1**, 4883-67-4; **2**, 74609-63-5; **3**, 74609-64-6; **4**, 74609-65-7; **5**, 74609-66-8; **6**, 74609-67-9; **7**, 74609-68-0; **8**, 74609-69-1; **9**, 74609-70-4; **10**, 74609-71-5; **11**, 74609-72-6; **12**, 74609-73-7; **13**, 74609-74-8; **14**, 74609-75-9; **15**, 74609-76-0; **16**, 74609-77-1; **17**, 74609-78-2; **18**, 74609-79-3; **19**, 74609-80-6; **20**, 74609-81-7; **21**, 74609-82-8; **22**, 74609-83-9.

(19) J. C. Richter, L. A. Pilato, and E. L. Eliel, *Chem. Ind. (London)*, 2007 (1961).
(20) N. Allinger and L. A. Freiberg, *J. Am. Chem. Soc.*, **84**, 2201 (1962).
(21) Reference 4b, p 178.
(22) R. J. Oulette, J. D. Rawn, and S. N. Jressaty, *J. Am. Chem. Soc.*, **93**, 7117 (1971).
(23) M. Kaloustian, N. Dennis, S. Mager, S. A. Evans, F. Alcudia, and E. L. Eliel, *J. Am. Chem. Soc.*, **98**, 956 (1976).
(24) Although the ΔG° values for the nitro group in the parent heterocycles were not determined, conformational data from some N-substituted derivatives indicates that the nitro group has a large $-\Delta G^\circ$ in these ring systems also. One exception is in the 5-nitrohexahydropyrimidinium trifluoroacetate in which the nitro group is axial because of hydrogen-bonding stabilization with the axial ammonium proton.[27]
(25) H. Piotrowska, W. Sas, and J. Winiarski, *Bull. Acad. Polon. Sci.*, **26**, 277 (1978).
(26) D. Gürne, L. Stefaniak, T. Urbanski, and M. Witanowski, *Tetrahedron, Suppl.*, **20**, 211 (1964).
(27) H. Piotrowska, W. Sas, and T. Urbanski, *Rocz. Chem.*, **51**, 1541 (1977).
(28) N. S. Zefirov, *Tetrahedron*, **33**, 3193 (1977).
(29) M. J. T. Robinson, *Tetrahedron*, **30**, 1971 (1974).