Determination of Rotational Barriers of C(sp²)–C(sp³) Bonds in 2-Arylpiperidines. 3.[1] Proton Dynamic Nuclear Magnetic Resonance Studies and Molecular Mechanics Calculations of the 1,2,2-Trimethyl-6-(3,4,5-trimethoxyphenyl)- and 1,5,5-Trimethyl-2-(3,4,5-trimethoxyphenyl)-4-piperidones

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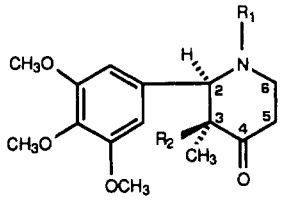
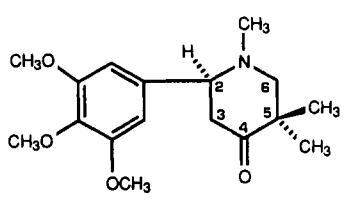
Rotational barriers around the C_2–Ar bond in hydrochlorides of 1,5,5-trimethyl-2-(3,4,5-trimethoxyphenyl)- and 1,2,2-trimethyl-6-(3,4,5-trimethoxyphenyl)-4-piperidones (**4** and **5**) were determined to be 46.0 kJ mol^{-1} at −30 °C and 59.4 kJ mol^{-1} at 40 °C, respectively. Molecular mechanics (MM) calculations on phenyl analogues agree with these values. The barriers for the free bases **4** and **5** (27.7 kJ mol^{-1} and 36.4 kJ mol^{-1}, respectively) were obtained by MM calculations on the analogous 2-phenyl-4-piperidones. The 6-*gem*-dimethyl substituents in **5**·HCl promote a strong long-range effect and thus raise the C_2–Ar rotational barrier, whereas 5-*gem*-dimethyl substitution (**4**·HCl) does not cause this effect. The less constrained phenyl rotation in these 2-arylpiperidones takes place on a twist-boat conformation as suggested by MM calculations.

Introduction

In previous work,[2] we reported upon the rotational barrier determination of 1,3,3-trimethyl-2-(3,4,5-trimethoxyphenyl)-4-piperidone (**1**) hydrochloride, which constitutes one of the few known models whose rotational barrier around a C(sp²)–C(sp³) bond is high enough to be measured by dynamic nuclear magnetic resonance (DNMR) spectroscopy. The rotational barriers of **1** and **1**·HCl were determined by ^{1}H and ^{13}C DNMR ($\Delta G^{\ddagger}$ = 54 kJ mol^{-1} at −7 °C and 69 kJ mol^{-1} at 53 °C, respectively). Several compounds present atropisomerism about C(sp²)–C(sp³) bonds,[3] but only a few known products have high enough barriers to be measured by DNMR spectroscopy if the C(sp²) atom belongs to a phenyl ring with no substituents at either of the ortho positions.[4]



1 R_1=R_2=CH_3
2 R_1=H; R_2=CH_3
3 R_1=R_2=H



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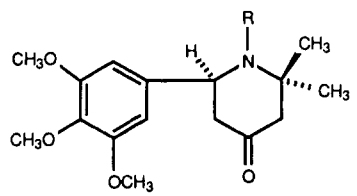

5 R=CH_3
6 R=H

We also mapped in some detail the influence of vicinal substitution on the rotation of the C(sp³)–C(sp²) bond by comparing the rotational barriers in the hydrochlorides of compounds **1**, **2**, and **3**.[1,2,5] Thus, substitution of the axial H_3 proton in compound **3** by a methyl group increases the rotational barrier[4] of the corresponding hydrochloride by about 14 kJ mol^{-1}, whereas substitution of the NH in **2** by an *N*-methyl group raises the rotational barrier[2] of the corresponding hydrochlorides by ca. 22 kJ mol^{-1}.

In the context of our studies of the synthesis of 5,5- and 6,6-dimethyl-substituted 2-aryl-4-piperidones, we have observed[6] the existence of a single, but broad, signal for two aromatic protons of **5**·HCl in the ^{1}H NMR spectrum (60 MHz). The fact that the *gem*-dimethyl groups were far away from the C_2–Ar bond, and therefore could not exert a direct steric hindrance, prompted us to carry out a more accurate study to investigate their effect on the C_2–Ar rotation. In this paper we illustrate restricted rotation around the C(sp²)–C(sp³) bond in 5,5-dimethyl-substituted and 6,6-dimethyl-substituted[7] 2-aryl-4-piperidone hydrochlorides through rotational barrier determination by dynamic nuclear magnetic resonance spectroscopy. We also report here the application of molecular mechanics (MM) calculations to the conformational study of demethoxylated analogues of piperidones **4** and **5** and their corresponding hydrochlorides.

Results

The description of the ^{1}H NMR spectra for **4**, **4**·HCl, **5**, **5**·HCl, **6**, and **6**·HCl are contained in Tables I and II, respectively; Table III shows results of the ^{1}H DNMR experiments on **4**·HCl, **5**·HCl, and **6**·HCl; and the results of MM calculations on **4**, **4**·HCl, **5**, and **5**·HCl are summarized in Table IV. The ^{1}H NMR spectrum (200 MHz) of **5**

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(1) Part 2: Jaime, C.; Rubiralta, M.; Feliz, M.; Giralt, E. *J. Org. Chem.* **1986**, *51*, 3951.
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(7) IUPAC numbering for compounds **5**, **5**·HCl, **6**, and **6**·HCl is not followed intentionally for consistency with all the members of the series.

0022-3263/90/1955-2307$02.50/0

Table I. ^{1}H Nuclear Magnetic Resonance Chemical Shifts[a] of 2-Aryl-4-piperidones 4–6

proton	4	4·HCl	5	5·HCl	6	6·HCl
2-H_a	3.08 dd (11.4, 3.6)	4.15 ddd (14, 9.6, 1.8)	3.57 dd (11.2, 4)	4.15 br d (14.4)	4.15 dd (10, 5.5)	4.40 br ($J_{1/2}$ = 28 Hz)
3-H_e	2.34 dd (15, 3.6)	3.08 br d (15)	2.40 ddd (14, 4, 2.5)	2.71 dt (14.4, 2.5)	2.45–2.55 m	2.66 br d (13.4)
3-H_a	2.80 dd (15, 11.4)	3.70 dd (15, 14)	2.59 ddd (14, 11.2, 0.8)	3.77 t (14.4)	2.45–2.55 m	3.34 t (13.4)
5-H_a	–	–	2.73 br d (13)	*b*	2.52 br d (13)	3.06 d (14.3)
5-H_e	–	–	2.22 dd (13, 2.5)	2.45 dd (14.4, 2.5)	2.27 dd (13, 1.7)	2.28 d (14.3)
6-H_a	2.28 br d (J_{AB} = 11.4 Hz)	3.12 br d (12.6)	–	–	–	–
6-H_e	2.84 d (J_{AB} = 11.4 Hz)	3.69 br d (12.6)	–	–	–	–
$(CH_3)_e$	1.45 s	1.82 s	1.35 s	1.83 s	1.36 s	1.42 s
$(CH_3)_a$	1.06 s	1.22 s	1.03 s	1.39 s	1.21 s	1.17 s
NCH_3	2.09 s	2.68 d (7)	2.06 s	2.54 d (7)	–	–
OCH_3	3.85 s	3.86 s	3.83 s	3.82 s	3.81 s	3.83 s
	3.87 s	3.95 s	3.88 s	3.86 s	3.89 s	3.91 s
				3.92 s		
Ar–H	6.57 s	7.13 br s	6.66 s	6.40 br	6.73 s	6.92 s
				8.07 br		

[a] In parts per million relative to TMS. Measured in $CDCl_3$ solution (21 °C) at 200 MHz in a Varian XL-200 spectrometer. Coupling constants (J) are given in Hertz. [b] Masked by OCH_3 signals. [c] In CD_3OD solution.

Table II. ^{13}C Nuclear Magnetic Resonance Chemical Shifts[a,b] of 2-Aryl-4-piperidones 4–6

carbon	4	4·HCl	5	5·HCl	6	6·HCl
C_2	71.1	70.2	65.0	66.3	55.2	56.8
C_3	45.9	43.4	50.6	47.2	48.4	45.0
C_4	212.2	205.7	208.2	201.3	209.1	202.8
C_5	46.7	45.1	55.5	51.7	52.7	50.2
C_6	68.4	65.1	57.9	65.3	52.8	59.3
$(CH_3)_e$	25.5	26.3	30.8	26.5	30.3	26.8
$(CH_3)_a$	21.7	22.3	15.7	19.5	23.8	23.5
NCH_3	43.1	42.0	33.9	33.2	–	–
m-OCH_3	56.1	56.8	56.1	56.7[c]	54.8	56.8
p-OCH_3	60.7	60.8	60.7	60.7	59.5	60.8
$C_{1'}$	137.3	128.4	137.1	128.7	136.0	129.4
$C_{2'}$	103.9	106.3	104.0	105.8[c]	102.5	106.0
$C_{3'}$	153.4	154.1	153.4	152–156[c]	152.1	153.7
$C_{4'}$	138.3	139.5	139.5	138.9	137.3	138.7

[a] In parts per million relative to TMS. Measured in $CDCl_3$ solution (22 °C) at 50.3 MHz in a Varian XL-200 spectrometer. [b] The assignments are in agreement with off-resonance spectra. [c] Broad signal.

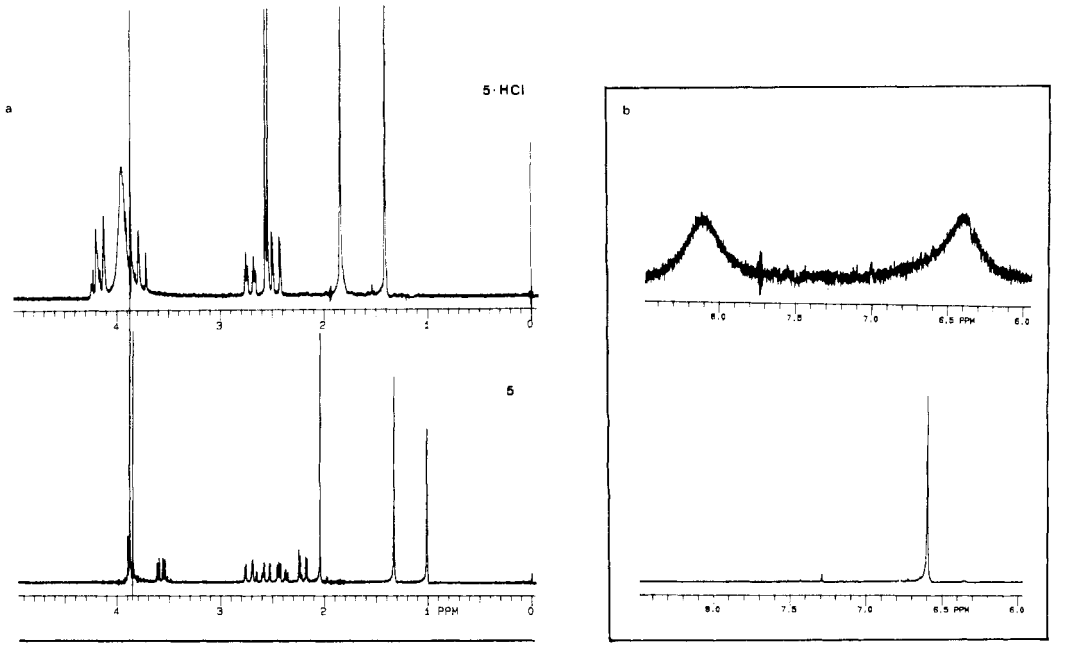

Figure 1. (a) ^{1}H NMR spectra (200 MHz) of 2-aryl-4-piperidones **5**·HCl and **5** in $CDCl_3$ at 18 °C. (b) Expansion of aromatic zone (δ 6–8 ppm).

shows a narrow single signal at δ 6.66 for the ortho aromatic protons and two singlets at δ 3.83 and 3.88 due to the para and the two "equivalent" meta methoxy groups, respectively. Surprisingly, the NMR spectrum of **5**·HCl (Figure 1) recorded under the same experimental conditions exhibits two broad signals ($W_{1/2}$ = 50 Hz) centered at δ 6.40 and 8.07 for the now nonequivalent ortho aromatic protons, and a broad signal at δ ~3.95 for the two meta methoxy

Table III. ^{1}H Dynamic Nuclear Magnetic Resonance Data of 2-Aryl-4-piperidones

compd	solvent	Ar–H_a	Ar–H_b	T, °C	$\Delta\delta$, Hz	T_c, °C	k_c, s^{-1}	$\Delta G^{\ddagger}$, kJ mol^{-1}
4·HCl	$CDCl_3$	6.45	7.79	−59	268	−30	595	46.0
5·HCl	$CDCl_3$	6.40	8.07	21.8	333	40	739	59.4
6·HCl	$CDCl_3$	6.97 br		<−58	–	<−58	–	–

Table IV. Relative Energy for All the Existing Conformers of 5·HCl, 5, 4·HCl, and 4 as Calculated by the MM2 Program as Well as the Lowest Calculated Phenyl Rotation Barrier ($\Delta H^{\ddagger}$(rot)) Relative to the C1 Conformer of Each Compound

	relative conformer energy, kJ mol^{-1}															lowest $\Delta H^{\ddagger}$(rot)
compd	C1	C2	C3	C4	TB1	TB2	TB3	TB4	TB5	TB6	TB7	TB8	TB9	TB10	TB11	TB12	
5·HCl	0.0	15.05	7.44	18.35	28.09	17.55	19.56	31.43	30.85	36.74	30.01	28.09	33.65	48.86	37.33	35.28	47.77[a]
	(71.69)[d]	(48.65)	(47.73)	(51.00)	(48.65)	(91.58)[d]	(47.77)	[e]	[e]	[e]	[e]	[e]	[e]	[e]	(57.81)	(64.54)	
5	0.0	16.88	10.41	20.44	24.45	18.72	16.89	28.09	32.69	33.48	30.18	28.88	36.45	47.36	39.75	32.39	36.41
	(67.13)[d]	(48.49)[c]	(47.77)	(50.20)	(39.83)	[e]	(36.41)	(37.57)	[e]	[e]	(66.21)	(53.96)	(51.96)	[e]	[e]	(66.21)	
4·HCl	0.0	26.92	25.33	6.69	25.33	25.75	14.25	*b*	*b*	22.57	25.12	25.41	40.46	45.98[c]	26.88	*b*	33.98
	(54.59)[d]	(46.02)	(54.80)	(36.37)	(47.73)	[e]	(33.98)			(65.21)	[e]	(54.80)	[e]	(82.39)	(45.94)		
4	0.0	28.05	27.59	7.56	23.70	27.92	13.25	*b*	*b*	22.24	26.96	27.59	44.22	46.90[c]	28.05	*b*	27.75
	(66.88)[d]	(48.82)	(58.39)	(40.42)	(43.13)	(53.80)[e]	(27.75)			(68.30)	(67.55)	(58.39)	[e]	(48.82)	(48.82)		

[a] Rotation on C3 gives a barrier similar to that on TB3. [b] Do not exist as a defined energy minimum. [c] Actually a boat conformation. [d] Not continuous. [e] Conformer has changed upon rotation.

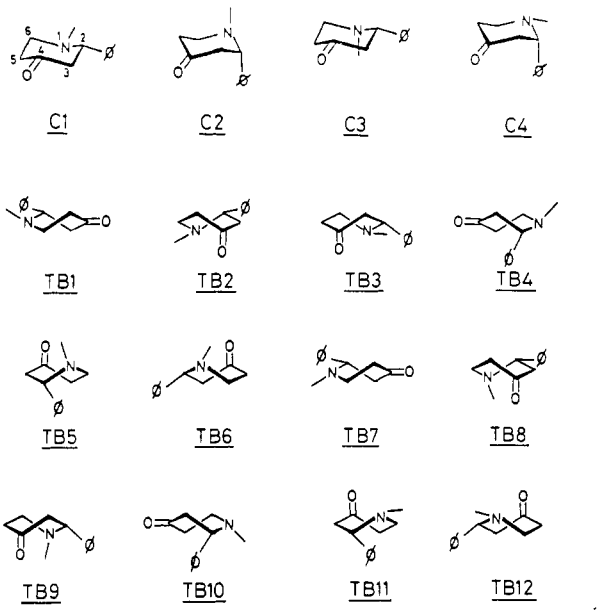

Figure 2. All possible chair and twist-boat conformers of the parent piperidones **4**·HCl and **5**·HCl. TB1 and TB6 belong to C1/C2 family and TB7 to TB12 to the C3/C4 family. Compound **4**·HCl is obtained by adding a 5,5-dimethyl substituent while a 6,6-dimethyl leads to **5**·HCl.

groups. In addition, **5**·HCl presents the meta methoxy groups as well as $C_2(C_6)$ and $C_3(C_5)$ phenyl carbons as broad signals in its ^{13}C NMR spectrum (see Table II). All these facts indicate that for 5,5- and 6,6-disubstituted 2-aryl-4-piperidones, even if the C(sp^2)–C(sp^3) bond is not flanked by one or two methyl groups, the barrier can be high enough to observe restricted rotation on the NMR time scale. Moreover, the presence of coupling between the N–H and the N–Me groups even at +40 °C clearly suggests the existence of a single configuration for **5**·HCl. The chemical shift of the N–Me allows us to assign an equatorial position for the N–Me group.

Molecular mechanics calculations on the hydrochloride of the demethoxylated analogue of **5** were performed[6] by using the MM2(77) program[8a–c] and lacking parameters were simply transferred from the MM2(85) program.[8d] This molecule can, a priori, adopt four different chair and 12 twist-boat conformations (Figure 2), and the phenyl ring rotation must be simulated in all conformers in order to obtain reliable results. Even if the inversion of configuration of the nitrogen atom is slow compared to the rotation around the C(sp^3)–C(sp^2) bond (N^+–methyl appears as a doublet even at 40 °C), both cis and trans isomers were calculated in order to obtain a more complete overview of the system's behavior. In our definition of the ground state, the phenyl ring was initially considered to exist in the "perpendicular" conformation and then was allowed to optimize its position. Phenyl ring rotation was simulated by driving the C(sp^2)–C(sp^2)–C(sp^3)–H dihedral angle from +180° to −180° at 10° steps using the one-bond drive technique.

In spite of the fact that C1 was shown to be the most stable conformation, rotation on this conformer gives rise to a barrier of 71.69 kJ mol^{-1}. The lowest energy pathways for phenyl rotation were shown to be either on a C3 conformation or on a TB3 twist-boat conformation (the energy

(8) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982. (c) Allinger, N. L.; Yuh, N. Y. *QCPE* **1980**, *12*, 395. (d) Available from QCPE (PC version) or from Molecular Design Ltd., 2132 Farallon Dr., San Leandro, CA 94577.

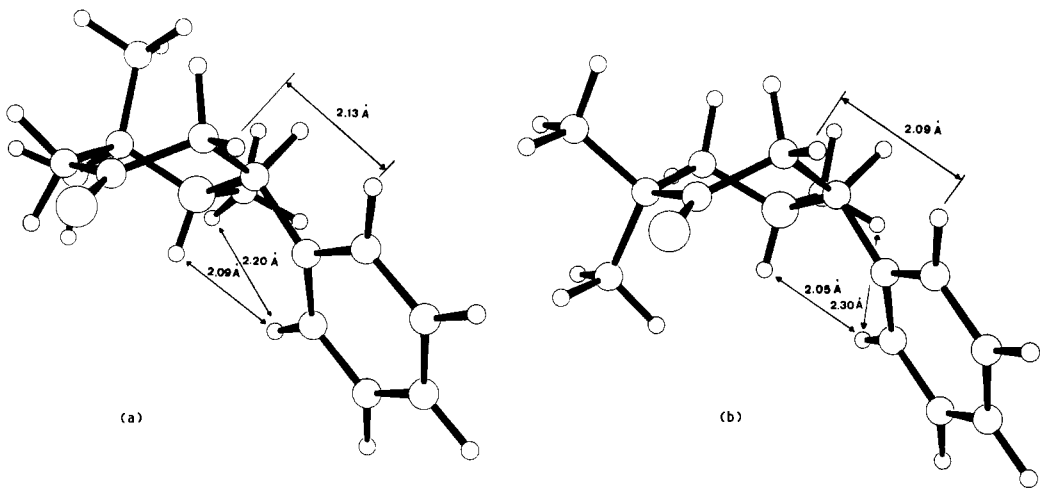

Figure 3. ORTEP[10] representation of the 2-aryl-4-piperidones 4·HCl and 5·HCl on a TB3 saddle point containing the main geometrical features, as obtained by the BIGSTRN-3[11] program. (a) 5·HCl. (b) 4·HCl.

difference between these two pathways is only 0.04 kJ mol^{-1}). Rotation on TB1 and C2 gives rises to a calculated $\Delta H^{\ddagger}$ of 48.65 kJ mol^{-1}, while rotation on other conformers produces higher barriers (Table IV). The MM2 calculated rotational barrier for 5·HCl (47.8 kJ mol^{-1}) is in agreement with the experimental value (59.4 kJ mol^{-1}), obtained from dynamic NMR experiments (see Table III). Moreover, NMR spectra clearly indicate that 5·HCl exists in a single N configuration, and MM calculations show that phenyl rotation takes place on a single N configuration, as well (TB3 and C1 have the same N configuration, with the *N*-methyl group equatorial).

The free base of piperidone **5** presents a single singlet for the two aromatic protons at δ 6.66 in the ^{1}H NMR spectrum. Its theoretical study, carried out by molecular mechanics calculations, showed that the phenyl rotation also occurs in a TB3 conformer, and the calculated barrier (36.4 kJ mol^{-1}) was 11.2 kJ mol^{-1} lower than in its hydrochloride.

As expected from the previous result obtained for 2·HCl, the hydrochloride of the *N*-demethyl analogue of **5** (**6**·HCl) showed a single singlet at δ 6.97 for the two aromatic protons in its ^{1}H NMR spectrum at room temperature, which evolves toward a broad signal, when the spectrum is recorded at −58 °C. The coalescence temperature is then below −58 °C, and the barrier is lower than 40.6 kJ mol^{-1}. A N–Me group seems to be necessary to observe restricted rotation in the hydrochlorides of 2-aryl-4-piperidones.

However, in order to demonstrate the influence of *gem*-dimethyl groups on the C_2–Ar bond rotation, we have experimentally and theoretically studied piperidone **4**, in which the substituents are the most distant from the C_2–Ar bond. The ^{1}H NMR spectrum of **4** hydrochloride showed two singlets at δ 6.45 and 7.79 for the two aromatic protons at −59 °C, and the experimental rotational barrier, determined by ^{1}H DNMR, was 46 kJ mol^{-1}. This value, 13.4 kJ mol^{-1} lower in 5·HCl, gives evidence that the *gem*-dimethyl substituents exert an important effect on the barrier magnitude. The MM2 calculated rotational barrier for 4·HCl was 33.9 kJ mol^{-1}, also around 13 kJ mol^{-1} lower than the calculated value for 5·HCl.[9]

Table V. Pseudodihedral Angle and Distance for the $H_3 \bullet\bullet\bullet X_6$ [$X_6 = CH_3$ (5·HCl), H (4·HCl)] Unit in the Ground State and in the Rotational Barrier Geometry ($TB_3^{\ddagger}$) for the TB3 Conformers of 5·HCl and 4·HCl[a]

	5·HCl			4·HCl		
	TB3	TB3‡	|Δ|	TB3	TB3‡	|Δ|
$\theta(H_3\cdots X_6)$	20.3	15.3	5.0	16.5	10.8	5.7
$l(H_3\cdots X_6)$	3.240	2.786	0.454	2.456	2.265	0.191

[a] Angles in degrees and distances in angstroms.

As for compounds **5** and 5·HCl, the most stable conformer of 4·HCl turned out to be the C1 chair, where both phenyl and *N*-methyl groups are equatorial, although phenyl rotation on this conformer gives a barrier of 54.59 kJ mol^{-1}. The lowest energy for the phenyl rotation pathway was rotation on the twist-boat conformation TB3.

In the same way, the MM2 calculated barrier for the free base **4** turned out to be 6.2 kJ mol^{-1} lower than for its hydrochloride (see Table III). Compound **4** also prefers the C1 conformation as its ground state, and the lowest energy phenyl rotation barrier is on the TB3 twist-boat conformation (Table III).

Discussion

A careful analysis of MM2 calculated transition state geometries (Figure 3) indicates that interactions between H_{ortho} and N^+–methyl or C_3 substituents are responsible for the barrier heights. Considering only phenyl rotations on the TB3 conformers of 5·HCl and 4·HCl, a difference of 13.9 kJ mol^{-1} is observed. Thus, two questions arise: (i) What is the reason for this difference if the geometry around the C_2–Ar bond is almost the same in both compounds? (ii) What is the *gem*-dimethyl effect on the rotational barrier?

The TB3 conformer of 5·HCl is 5.3 kJ mol^{-1} higher in energy than that of 4·HCl (see Table III), but 8.6 kJ mol^{-1} still remains unexplained. It must be noted here that TB3 in 5·HCl presents an axial methyl on C_6 suffering one flagpole interaction with the axial H_3 atom, while in the TB3 conformer of 4·HCl, only the H_6–H_3 flagpole interaction is observed. In order to obtain a qualitative estimation of the strength of these flagpole interactions, the pseudodihedral angle formed by H_3–$C_3\cdots C_6$–X_6 [$X_6 = CH_3$ (5·HCl), H (4·HCl)] and the H_3 to X_6 distance have been measured in both transition-state conformations (Table V).

The larger nonbonding flagpole interaction can be detected by a larger decrease in the nonbonding distance and

(9) A systematic difference of about 12.5 kJ mol^{-1} between calculated and experimental barriers was obtained. The provisional parameterization of torsional constants involving the N^+ atom may be responsible, at least in part.

(10) Johnson, C. K. ORTEP-II. Oak Ridge National Laboratory Report, ORNL-5138, 1976.

(11) Nachbar, R. B., Jr.; Mislow, K. Available in QCPE program No. 514 and described in *QCPE Bull.* 1986, *6*, 96.

in the pseudodihedral angle. As shown in Table V, the TB3 flagpole interaction is clearly stronger in 5·HCl, and this is probably the ultimate cause responsible for the long-range effect of the 6-*gem*-dimethyl groups on the $C(sp^3)$–$C(sp^2)$ rotation barrier and, particularly, of the noteworthy differences in behavior between compounds 4·HCl and 5·HCl.

The *gem*-dimethyl group compresses the N–Me one (the C_6–N–Me bond angle is 114.1° in TB3). However, the buttressing of the *gem*-dimethyl is energetically less severe than the repulsion coming from the H_{ortho}–Me nonbonded interaction in the TB3* (the C_6–N–Me bond angle closes to 111.7°).

Conclusions

The barriers to rotation in two different 2-aryl-4-piperidone hydrochlorides have been determined by ^1H DNMR ($\Delta G^* = 46.0$ kJ mol^{-1} at −30 °C and 59.4 kJ mol^{-1} at 40 °C for 4·HCl and 5·HCl, respectively). Compound 5·HCl seems to exist in a single configuration with the N–Me group in equatorial position. Molecular mechanics calculations have proved to be useful in the determination of the global rotational process and also help in finding the interactions producing the barriers. Although the absolute values obtained in the MM2 calculations agree rather well with the experimental ones, they must be handled with care. Nevertheless, the theoretical calculations also perfectly reproduce the experimental trends with the proper relative order.[9]

The flagpole interactions existing in the cyclohexane moiety of the target compounds as well as the H–H unbonded interactions about the pivot bond are the main factors responsible for the barrier heights.

Registry No. 4, 73608-62-5; 4·HCl, 88091-29-6; 5, 75306-47-7; 5·HCl, 88091-33-2; 5·HCl (demethoxylated analogue), 125329-75-1; 6, 88091-30-9; 6·HCl, 88091-31-0.

Alkylation of (Fluorocarbethoxymethylene)tri-*n*-butylphosphorane: A Facile Entry to α-Fluoroalkanoates[1]

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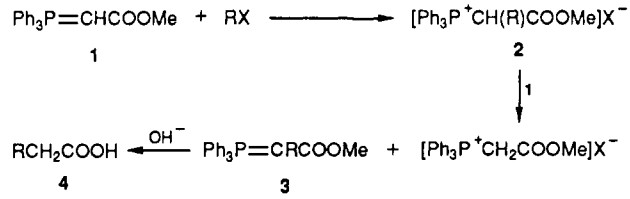
(Fluorocarbethoxymethyl)trialkylphosphonium bromides **6**, prepared from ethyl bromofluoroacetate and tertiary phosphines, react with *n*-butyllithium in THF to give the corresponding phosphoranes **7**. Reaction of the pregenerated (fluorocarbethoxymethylene)tri-*n*-butylphosphorane **7a** with primary alkyl iodides and activated alkyl bromides followed by in situ hydrolysis of the alkylated salts provides the fluoroalkanoates **9** in a one-pot reaction. In the case of secondary alkyl halides, no substitution was observed, the main reaction being decomposition of the phosphorane. However, the anion obtained from diisopropyl (fluorocarbethoxymethyl)phosphonate **10b** reacts with $CH_3CH(Ph)Br$ and $(CH_3)_2CHI$ to afford the corresponding alkylated phosphonates in good yields. Displacement of the phosphonate moiety either by base-induced hydrolysis or by reduction was unsuccessful.

Introduction

Elucidation of the mechanism of toxicity of fluoroacetate in living organisms led to a new wave of research into the preparation and properties of fluoro esters. The use of fluorine-substituted esters as analytical probes and diagnostic tools in metabolic processes has added to their stature as important compounds in biochemistry.[2] All of these applications are mainly due to the high electronegativity of fluorine, the increased bond strength of the carbon–fluorine bond, and the enhanced lipid solubility of fluorine substituted compounds.[3]

Although numerous literature methods exist to incorporate a fluorine atom adjacent to a carbonyl group, the limitations associated with them restrict their practicality. Extreme reaction conditions and special apparatus are required to effect a metathesis reaction between a halo ester and a metal fluoride or other fluoride ion source.[4]

Scheme I



The condensation reaction between fluoroacetates and alkylating agents under basic conditions employs toxic materials.[5] The explosion hazard associated with perchloryl fluoride limits its synthetic utility in the fluorination reactions.[6] Fluorination with hypofluorites limits the presence of functionalities that are susceptible to oxidation.[7] The strong Lewis acidity of specific fluorinating agents such as antimony fluorides, phosphorus fluorides, and fluorinated sulfuranes precludes their application toward a large number of bioactive molecules that are sensitive to acid, base, or both.[8]

(1) (a) Presented in part at the 21st Midwest Regional Meeting of the American Chemical Society, Kansas City, MO, November 1986, Abstract no. 709. Taken in part from the Ph.D. Thesis of A.T., University of Iowa, 1989. (b) A preliminary report of this work has appeared: Thenappan, A.; Burton, D. J. *Tetrahedron Lett.* **1989**, *30*, 3641.

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(3) Filler, R., Ed. *Biochemistry Involving Carbon-Fluorine Bonds*: ACS Symposium Series 28; American Chemical Society: Washington, DC, 1978; Chapter 1.

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