Journal of Organometallic Chemistry, 206 (1981) 131—138
Elsevier Sequoia S.A., Lausanne — Printed in The Netherlands

CONFIGURATION AND CONFORMATION OF LITHIATED IMINES BY DNMR STUDIES AND AB INITIO CALCULATIONS

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(Received July 31st, 1980)

Summary

The *N*-isopropyl imine of lithioacetaldehyde, I, was found to exist as a 50 : 50 mixture of two isomers, as seen below −20°C by ^{1}H and ^{13}C NMR. Comparison of the population ratio and spectral characteristics of the isomers of this and related lithiated imines leads to the conclusion that they are rotamers all of which possess the *syn* configuration. This conclusion is supported by calculations of the barriers to interconversion.

We have previously reported evidence from the alkylation of ketimines [1] and aldimines [2], supported by ab initio calculations [3], that metallation *alpha* to the C=N function yields exclusively the *syn* lithiated imine. All the experimental evidence is based upon the assumption that the alkylation reaction is sufficiently rapid to trap the anionic species, thereby yielding products whose configuration reflects that of the organometallic intermediates. In order to assess the validity of this assumption we have undertaken a study of the ^{13}C and ^{1}H spectra of a number of lithiated imines over the temperature range −60 to +30°C. These DNMR spectra provide clear evidence of a *syn* configuration for each of the lithiated imines examined, through the direct observation of conformational isomers (rotamers) separated by a barrier to rotation of 12 kcal/mol. Since this barrier to rotation about a N(sp^2)—C(sp^3) single bond is of unprecedented magnitude, we have sought confirmatory evidence both from other NMR spectral properties and by extensive ab initio calculations on *N*-isopropyl lithioacetaldimine and the energetics of its barriers to rotation and inversion.

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Experimental

Each of the imines and their lithio derivatives were prepared by the method described below for the solution of I.

A. Synthesis of 4-methyl-3-azaprop-2-ene (acetaldehyde N-isopropylimine)

To a solution of 66 mmol of isopropylamine in 5 ml of *o*-xylene at 0°C was added 66 mmol of acetaldehyde by means of a cold syringe. Anhydrous sodium sulfate, 1 g, was added to absorb the water formed during imine formation. After one hour the solution was warmed to room temperature, filtered and the imine distilled off at 55—58°C. Yields ranged from 50% in the present case to 70—80% for higher boiling imines. All imines were stored under argon at 0°C before use.

B. Preparation of 1-lithio 4-methyl-3-azaprop-2-enide, I

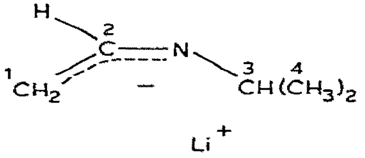
To 3 ml of tetrahydrofuran, freshly distilled from $LiAlH_4$, in a 25 ml syringe-capped flask maintained under a N_2 atmosphere was added 4.2 mmol diisopropylamine. After cooling to —20°C, 4.2 mmol of butyllithium (in hexane, Ventron Corp.) was added. After stirring for ten minutes 4.0 mmol of imine was added and stirring continued for 1 h. The solution was then transferred to the appropriate NMR tube previously flushed with argon in a glove bag under an atmosphere of argon. The tube was sealed with paraffin before removing for transfer to the NMR instrument.

All ^{13}C spectra were recorded on a Varian FT-80 NMR spectrometer operating at a frequency of 20 MHz. The temperatures reported for the coalescence studies on this instrument are accurate to ±4°C. All ^{1}H spectra were recorded on a Varian HA-100 NMR spectrometer operating at 100 MHz. The temperatures reported for studies on this instrument are accurate to ±2°C, both instruments having the probe temperatures monitored by thermocouple measurements before and after obtaining the spectra.

Ab initio calculations were performed using the Gaussian 70 program of Hehre, Ditchfield, Newton and Pople, QPCE 236.

Results and discussion

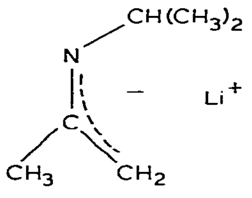
A solution of *N*-isopropyl *alpha*-lithioacetaldimine, I, in THF gave a ^{13}C spectrum at 25°C containing signals assignable to the carbons 1, 2 and 3 in structure I. Unfortunately, the signals for carbon 4 were obscured by solvent. As the temperature was lowered the three observable signals broadened and separated into two peaks in the range 0 to —20°C, giving two sets of sharp signals of essentially equal intensities ($\rho_I = \rho_{II}$) at —40°C. Similarly, a classical coalescence spectrum



(I)

was observed for the formyl proton in the ^{1}H spectrum at —18° C. Obviously two species are present in the solution of I which are interconverting via a process having a free energy of activation of 12.7 kcal/mole. The spectral details are summarized in Table 1.

The two species detected could conceivably represent either a pair of *syn-anti* isomers, or two rotational isomers with respect to the N—C bond. In order to distinguish between these alternatives, the structurally related lithioimines II, III and IV were synthesized and the ^{13}C spectra of these species were measured over the temperature range —60 to +25° C.



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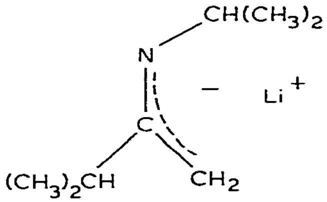

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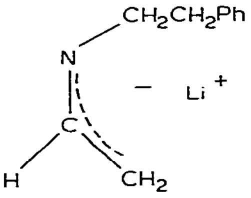

(IV)

For the lithioimines II and III, two species were detectable at —25° C or below. In contrast, IV showed no change in its ^{13}C spectrum down to —60° C (at lower temperatures, solubility problems occurred). The variable temperature spectral characteristics of all the lithioimines summarized in Table 1 indicate a small change in the population ratio of the two species in spite of the replacement of H by methyl or isopropyl groups. This behaviour is not consistent with the presence of a *syn-anti* equilibrium [6], nor is the fact that IV did not exhibit a temperature dependence. A further indication that the two species are not *syn* and *anti* isomers is provided by the ^{1}H vicinal coupling constants in I and V. The values for the vicinal couplings between protons on C(1) and C(2) were 7.5 and 14.5 (±0.1) Hz in both forms. Previous studies on lithiated aldehyde hydrazones have shown that *syn* and *anti* isomers had significantly different *J*'s [7]. Thus the probable origin of the two species is a high barrier to rotation about the N—C bond, albeit of an unusually large magnitude. Indeed, rotational barriers involving an sp^3—sp^2 C—C bond have not been observed previously in metallated propenes [8,9]. It is quite possible they would have lower $\Delta G^{\ddagger}$'s due to a decrease in the ground state steric destabilization when a $\geqslant\underset{|}{\mathrm{C}}\mathrm{H}$ is replaced by $\geqslant\underset{|}{\mathrm{N}}$: . Also those examined * have only involved structures analogous to IV which showed no barrier. Thus, we propose the barrier for the interconversions a $\rightleftharpoons$ b or a $\rightleftharpoons$ c, as depicted in Scheme 1 as responsible for the variation in spectra with temperature. Further experimental evidence was sought by examination of the VT spectra of V, which would in principle exhibit two coalescences between three rotamers (e.g., $CH_3{}^* = C_2H_5$ in Scheme 1). Only two sets of peaks were observable below —10° C, indicative of a single observable coalescence (Table 1 also presents the results for V).

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* An analogous case, that of *Z*-1-isopropylallyl potassium was recently studied [10] but only at room temperature and above.

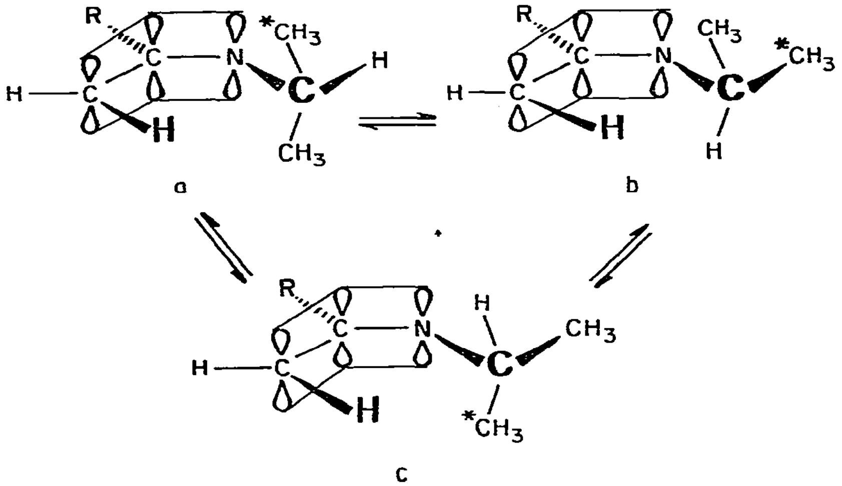
TABLE 1

^{13}C CHEMICAL SHIFTS AND COALESCENCE DATA

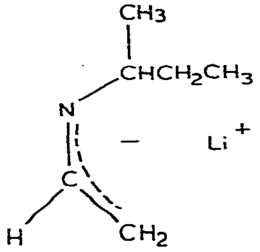
	Temperature (°C)	^{13}C Shifts [a, b]			Coalescence Studies				
		C(1)	C(2)	C(3)	Nucleus	$\Delta\nu$	ρ_I/ρ_{II}	T_c (°C)	$\Delta G^{\ddagger}$ (kcal/mol) [c]
I	27	66.1	155.1	53.2	C(2)	100	1	−8	12.6
	−35	63.3 (obsc.)	157.7, 152.6	58.0, 48.2	H (formyl)	20	1	−18	12.9
II	27	67.5	160.9	52.7	C(2)	80	2	−20	12.1
	−60	62.2 (obsc.)	160.0, 163.9	(obsc.)					
III	27	61.3	171.1	52.5	C(1)	200	2	−10	12.1
	−60	64.0, 53.9	171.1, 169.8	(obsc.)					
IV	27	67.6	155.6	56.4					
	−60	67.8	154.8	55.3				None	
V	−27	66.2	155.0	60.1	H	19	1	−24	12.6
					C(2)	110	1	−5	12.7
	−60	62.4 (obsc.)	158.3, 152.6	65.6, 55.4	C(3)	204	1	1	12.6

[a] ^{13}C shifts expressed in ppm from TMS, using the shift for the alpha C of THF (δ = 69.00 ppm) as standard. [b] The low temperature assignments were confirmed by deuteration experiments and by off-resonance decoupling. [c] $\Delta G^{\ddagger}$ calculated from the expression [4], $\Delta G^{\ddagger} = 4.57\ T_c\ (10.32 + \log T_c/2.22\ \Delta\nu)$, which retains its validity yielding $\Delta G^{\ddagger}_{av}$ when $\rho_I \neq \rho_{II}$ [5].

SCHEME 1

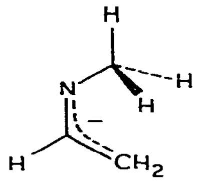


Confirmatory evidence of a totally theoretical nature is provided by ab initio calculations on the anions of *N*-methyl and *N*-isopropyl acetaldimine. We

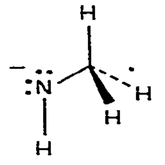


(V)

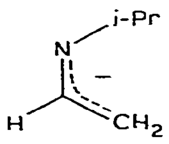
reported earlier that rotational barriers in alkylamides are about 1.0 kcal/mol higher than those in the corresponding amines, but coordination with Li^+ lowers these barriers to approximately the same values as in the amines [10]. Previous calculations of the rotational barriers in VI [3] indicate that the staggered conformation shown is the most stable, as is also observed for methylamide, VII [10]. The barriers to rotation to eclipsed conformations are 3.8 and 2.8 kcal/



(VI)



(VII)



(VIII)

mol, respectively, in these two species at the 4-31G/4-31G level [10,11]. For the *N*-isopropyl anion, VIII, only partial geometry optimizations were carried out using the minimal STO-3G basis set for two approximately staggered and

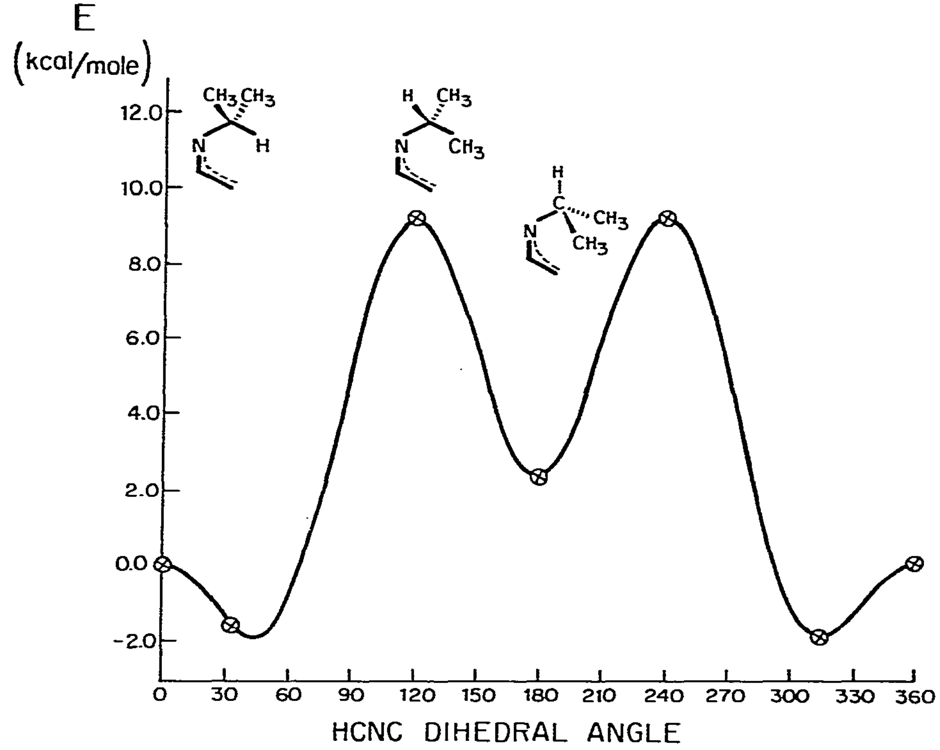


Fig. 1. Energies of rotamers as a function of dihedral angle ϕ(ϕ = 180° for H—C—N—C in antiperiplanar arrangement).

two eclipsed conformations and the results are summarized in Figure 1 and Table 2. Three staggered conformations correspond to energy minima, while the three eclipsed are energy maxima. Using a three term Fourier analysis of these rotational barriers *, the true energy minima can be estimated to lie at rotational angles of 45° and 315°, separated by a 1.9 kcal/mol barrier at 0° C. The global maximum is 11.1 kcal/mol above the absolute minimum, in good accord with the measured free energies of rotation of 12—13 kcal/mol (Table 1). The less stable staggered conformation, a, which has an energy 4.0 kcal/mol above that of b(c), is higher in energy than is found experimentally, where ΔG(a) = ΔG(b) = ΔG(c). We attribute some of this error to incomplete optimizations utilized here, but the role of lithium and solvation should be important as well. For example, in our earlier calculations on methylamide and ethylamide, the rotational barriers were reduced by 0.8 and 1.0 kcal/mol, respectively, upon coordination to Li^+. This was attributed to unfavorable steric interactions of Li with H or Me, in the favored conformation. In VIII, Li—Me interactions will be greater in conformation b = c than in a, regardless of the precise location of Li. We have reported earlier that the energies of VIII with Li^+ π-bonded to the allyl anion system, or σ-bonded to N, are similar in energy, and that Li is close to N

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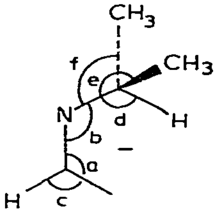
* 4-31G/4-31G refers to 4-31G energy calculations on geometries fully optimized at the 4-31G level [12]. Calculations were carried out with GAUSSIAN 70, QCPE 236.

TABLE 2

STO-3G OPTIMIZED ANGLES FOR SYN-VIII [a]



Dihedral Angle CNCH (°)	Parameter (°)						Energy (a.u.)
	a	b	c	d	e	f	
0	137.0	114.8	112.6	114.8	110.8	110.8	−246.36176
33	136.0	113.8	113.1	113.1	109.7	113.8	−246.36424
120	141.6	122.6	110.5	108.3	108.0	121.7	−246.34704
180	138.5	117.2	111.9	106.2	115.0	115.0	−246.35791

[a] Bond lengths for the imine anion portion of the molecule are obtained from the 4-31G optimized geometry reported earlier for VI. The isopropyl group is standard ($r(CC) = 1.54$ Å, $r(CC) = 1.09$ Å, $<CCH = 109.5°$) except for angles e and f, which were optimized in each conformation.

in both of these species. Thus Li^+ coordination is expected to lower the energy difference between a and b = c.

The origin of this relatively high a ⇌ b barrier found experimentally and theoretically is obviously the steric compression between an isopropyl methyl and the $CHCH_2$ moiety which occurs in the transition state between a and b. We did not carry out optimizations of the *anti*-VIII. Using a standard isopropyl group and the imine anion geometry obtained for VI, the highest barrier to rotation about the N—C bond is calculated to be 15.8 kcal/mol. Using the corresponding standard geometries for *syn*-VIII, this barrier is 45.4 kcal/mol! Thus, barriers to N—C rotation in the *anti* species are much lower than those in the *syn*, so only *syn*-VIII is expected to have the high barriers observed experimentally.

We have also found that the barriers to *N*-inversion and rotation about the N═C bond, to give *syn—anti* isomerization of the imine anions, are 37 and 21 kcal/mol [13], respectively, so that these processes are not the ones being observed in solution.

In summary, we have demonstrated the presence of exceptionally high rotational barriers in lithiated imines. Since such barriers could only arise in a *syn* isomer, our original conclusion that for lithiated imines the *syn* configuration predominates (>95%) at −78°C in THF solution is confirmed.

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