Formation and Isomerization of 2-Azaallyllithium Reagents in Deprotonations of *N*-Benzyl Ketimines Containing α-Protons

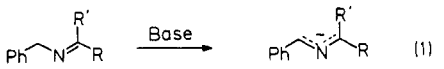
J. Kirk Smith, David E. Bergbreiter,* and Martin Newcomb*[1]

Department of Chemistry, Texas A&M University, College Station, Texas 77843

Received March 25, 1985

Deprotonation of the *N*-benzylimine of 3-pentanone by lithium diisopropylamide (LDA) in tetrahydrofuran occurs at the benzylic position to give a 2-azaallyllithium reagent in high yield. On standing, the 2-azaallyllithium reagent isomerizes to a 1-azaallyllithium reagent. The *N*-benzylimine of 2-butanone can be similarly deprotonated by LDA at the benzylic position in competition with deprotonation at the α-positions to give a 2-azaallyllithium reagent in up to 22% yield. The *N*-benzylimine of acetone is not appreciably deprotonated at the benzylic position by LDA. Kinetic studies of the isomerization of 2-azaallyl- to 1-azaallyllithium reagent from the 3-pentanone imine suggest that this reaction proceeds by a protonation–deprotonation sequence.

Imines serve as useful alternatives to ketones in synthetic sequences since deprotonation of imines yields enolate equivalents,[2] i.e., 1-azaallyllithium reagents, which can be formed with good regiochemical control.[3] In addition, 1-azaallyllithium reagents derived from chiral ketimines can be used effectively in asymmetric synthesis.[4] *N*-Benzyl ketimines have been used in organic synthesis, and in some cases chiral benzyl ketimines derived from ketones and phenethylamine or phenylglycinol methyl ether have been used in asymmetric synthesis.[5] In the course of our studies of the deprotonations of ^{13}C-labeled 3-pentanone imines by lithium dialkylamide bases,[6] we observed that the 3-pentanone *N*-benzylimine was deprotonated rapidly by lithium diisopropylamide (LDA) in tetrahydrofuran (THF) to give an unstable intermediate which rearranged to give the 1-azaallyllithium reagent expected from an α-deprotonation. This intermediate was presumed to be a 2-azaallyllithium reagent. It is well-known that deprotonations of benzylimines containing no acidic α-protons proceed under relatively mild conditions to give 2-azaallyllithium reagents (eq 1).[7] In this report



(1)

R = Ph, R' = H or Ph

we have shown that 2-azaallyllithium reagents can be formed from simple *N*-benzylimines which also contain acidic α-protons. Our results demonstrate the relationship between an *N*-benzyl ketimine's structure and the ratio of α-deprotonation to benzylic deprotonation and suggest a possible mechanism of the observed 2-azaallyllithium reagent to 1-azaallyllithium reagent isomerizations.

Scheme I

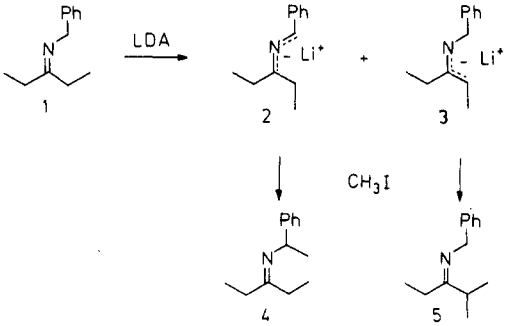


Table I. Products from LDA Deprotonation and Subsequent Methylation of 3-Pentanone *N*-Benzylimine (1) in THF

entry	[1][a]	[LDA][a]	temp, °C	time, h	% yield[b] 4	% yield[b] 5
1	0.14	0.28	−78	1.0	19	4
2	0.20	0.28	−78	1.5	23	4
3	0.19	0.23	−78	4.75	71	15
4	0.24	0.96	−78	24	83	16
5	0.2	0.3	0	0.03	64	36
6	0.2	0.7	0	0.02	54	43
7	0.4	0.6	0	0.05	57	42
8	0.19	0.23	0	2.8	47	51
9	0.24	0.96	0	3.8	37	63
10	0.24	0.25	0	1.8	0	79
11	0.42	0.47	0	4	0	93

[a] Initial molar concentrations of reagents (±5%). [b] Percent yield determined by GC relative to the total amount of imines 1, 4, and 5.

Results

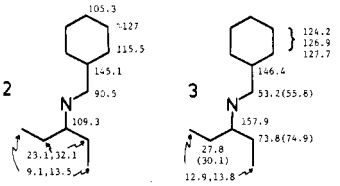
Treatment of 3-pentanone *N*-benzylimine (**I**) with LDA in THF gave the 2-azaallyllithium reagent **2** and the 1-azaallyllithium reagent **3**. Subsequent methylation gave products **4** and **5**, respectively (Scheme I). The results for deprotonation experiments run for various times at −78 and 0 °C are collected in Table I. At −78 °C the benzyl anion **2** was formed first (entries 1–4). The low total yields of **4** and **5** in entries 1 and 2 result from incomplete deprotonation of **1**. Little isomerization of **2** to **3** was observed in 24 h at −78 °C (entry 4). At 0 °C, deprotonation at the α-position competed more efficiently with benzylic deprotonation (entries 5–7), and at long reaction times at 0 °C partial isomerization of **2** to **3** was apparent (entries 8 and 9). 1-Azaallyllithium reagent **3** was the only anionic product present when essentially stoichiometric amounts of base and imine at both 0.2 and 0.4 M concentrations of reagents were employed (entries 10 and 11).

(1) Camille and Henry Dreyfus Teacher–Scholar, 1980–1985.
(2) Whitesell, J. K.; Whitesell, M. A. *Synthesis* **1983**, 517–536.
(3) (a) Smith, J. K.; Bergbreiter, D. E.; Newcomb, M. *J. Am. Chem. Soc.* **1983**, *105*, 4396–4400. (b) Smith, J. K.; Newcomb, M.; Bergbreiter, D. E.; Williams, D. R.; Meyers, A. I. *Tetrahedron Lett.* **1983**, *24*, 3559–3562. (c) Hosomi, A.; Araki, Y.; Sakurai, H. *J. Am. Chem. Soc.* **1982**, *104*, 2081–2083.
(4) Bergbreiter, D. E.; Newcomb, M. In "Asymmetric Syntheses"; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Chapter 9.
(5) (a) Meyers, A. I.; Poindexter, G. S., Brich, Z. *J. Org. Chem.* **1978**, *43*, 892–898. (b) Fraser, R. R.; Akiyama, F.; Banville, J. *Tetrahedron Lett.* **1979**, 3929–3932. (c) Saigo, K.; Kasahara, A.; Ogawa, S.; Nohira, H. *Tetrahedron Lett.* **1983**, *24*, 511–512.
(6) Smith, J. K.; Bergbreiter, D. E.; Newcomb, M. *J. Org. Chem.* **1981**, *46*, 3157–3158.
(7) (a) Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 627–639. (b) Kauffmann, T.; Habersaat, K.; Köppelmann, E. *Chem. Ber.* **1977**, *110*, 638–644. (c) Kauffmann, T.; Eidenschink, R. *Chem. Ber.* **1977**, *110*, 645–650. (d) Young, R. N.; Ahmad, M. A. *J. Chem. Soc., Perkin Trans. 2* **1982**, 35–38. (e) Vo-Quang, L.; Vo-Quang, Y.; Pouet, M. J.; Simonnin, M. P. *Tetrahedron* **1981**, *37*, 4343–4352 and references cited in each.

0022-3263/85/1950-4549$01.50/0

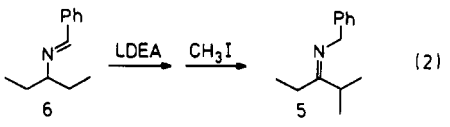
Formation of the 2-azaallyllithium reagent **2** and its isomerization to **3** could be followed by ^1H NMR or ^{13}C NMR spectroscopy. When **1** was added to a THF solution of LDA at −78 °C and ^1H NMR spectra were recorded as the mixture was allowed to warm toward room temperature, we observed a rapid loss of the aryl signals and of the benzylic signal at δ 4.45 from **1**. New signals which we attribute to **2** were observed. The downfield signals from **2** resemble those seen in the ^1H NMR spectra of 1-phenylallyllithium reagents.[8a] Specifically, the para proton was shifted to δ 5.6 (t), the meta and ortho proton signals were distinct from one another at δ 6.5 (t) and 6.1 (d), respectively, and the signal from the one remaining benzylic proton was at δ 5.5 (s, overlapping the para signal). On standing, the signals from **2** were replaced by those from **3**; δ 6.8–7.2 (m, aryl), 4.0 (s, benzylic). When a partially isomerized reaction mixture containing equal area signals at δ 4.0 (the two-proton benzylic signal from **3**) and δ 5.5 (the one-proton benzylic signal for **2**) was methylated, a 2:1 ratio of products **4** and **5** was obtained as expected.

Similar results were observed in ^{13}C NMR spectral studies of the deprotonation of **1**. Imine **1** was treated with excess LDA at −80 °C, and ^{13}C NMR spectra of the reaction mixture were recorded periodically over several hours. The signals from **1** were smoothly replaced by signals from **2**. After 3 h at −80 °C there was less than 5% isomerization of **2** to **3**. However, upon warming, the spectrum of **2** was replaced by the spectrum of **3**. Methylation of the reaction mixture at this point gave only the 2-methyl-3-pentanone *N*-benzylimine (**5**). Deprotonation of **1** with lithium diethylamide (LDEA) at −80 °C also gave 2-azaallyllithium reagent **2**; the deprotonation was complete within a few minutes, and isomerization of **2** to **3** was ca. 50% complete in 25 min at −80 °C.[9] The ^{13}C NMR spectrum of **2** resembled that of 1-phenylallyllithium,[8a] and the ^{13}C NMR spectrum of **3** which we observed was similar to that previously reported by Fraser.[8b] The ^{13}C NMR chemical shifts for **2** (at −80 °C) and **3** (at 25 °C) are shown below;



chemical shifts are reported relative to the β-carbon of THF which we assign as δ 25.0. An ^1H-coupled spectrum of **2** was not obtained, and it is possible that the assignment of the charged carbon at δ 109.5 and one of the aryl signals are inverted. An off-resonance ^1H-decoupled spectrum of **3** confirmed the assignments for this azaallyllithium reagent; the chemical shift values reported by Fraser[8b] for **3** are shown in parentheses.

The intermediacy of 2-azaallyllithium reagent **2** in the formation of **3** was further confirmed by the direct generation of **2** by deprotonation of *N*-benzylidene-1-ethylpropylamine (**6**). Treatment of **6** with lithium diethylamide in THF at 0 °C for 2 days followed by methylation gave the *N*-benzylimine of 2-methyl-3-pentanone (**5**) in ca. 40% yield as the major product observed by GC (eq 2). The yield of the *N*-phenethylimine product **4** observed in this reaction was low (< 1%) because the isomerization of **2** to **3** was faster that the rate of formation of **2**. The reaction of **6** with LDA was observed to be slower than that with lithium diethylamide.[9]



(2)

Scheme II

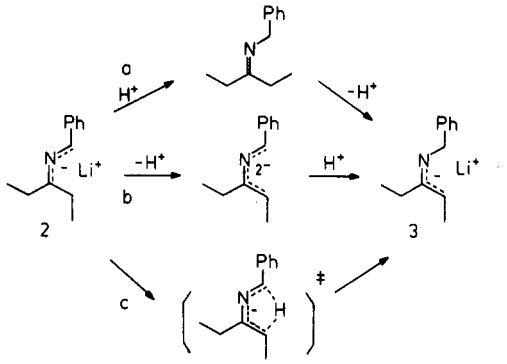


Table II. Rate Constants for Isomerization of 2 to 3 in THF at 0 °C

entry	[1][a]	[LDA][a]	% 2[b]	$10^5 k_{2\rightarrow3}, s^{-1}$ [c]	half-lives[d]
1	0.2	0.3	64	3.6 ± 0.6	1
2	0.2	0.7	55	3.9 ± 0.3	2
3	0.4	0.6	58	8.7 ± 0.1	3
4	0.2	0.15	64	8.2 ± 0.7	3[e]

[a] Molar concentrations of reagents used in formation of **2** (±5%). [b] Initial percentage of **2** relative to total azaallyllithium reagent concentration. [c] First-order rate constant found for four to seven points; the error stated is one standard deviation. [d] Number of half-lives over which data was collected. [e] This reaction accelerated after one half-life; the rate constant was calculated only for points in the first half-life.

2-Azaallyllithium reagent **2** could isomerize to 1-azaallyllithium reagent **3** by several simple mechanisms as shown in Scheme II. In the first case (path a), protonation of **2** by a dialkylamine or another neutral molecule of imine could give the neutral imine **1** which could then be deprotonated at the benzylic position to return anion **2** or at the α-position to give **3**. Despite the kinetic preference for formation of **2**, the thermodynamically favored **3** would predominate eventually. In the second pathway (b), a second deprotonation of **2** could give a dilithium dianion which upon protonation could give monolithium reagents **2** or **3**. The dianion intermediate in pathway b might be expected to be accessible since other linearly conjugated four-atom dianions are known including dianions from oximes and hydrazones.[10] The third pathway (c) is a 1,4-sigmatropic hydrogen shift which, although an allowed process, has little precedent.[11]

To study the isomerization pathway, we deprotonated **1** with LDA at 0 °C. Aliquots of the reaction mixtures were removed at various times and alkylated with iodomethane. The resulting product mixtures were analyzed by GC for yields of alkylation products **4** and **5**, and from this data

(8) (a) O'Brien, D. H. In "Comprehensive Carbanion Chemistry"; Buncel, E., Durst, T., Eds.; Elsevier: Oxford, 1980; Part A; Chapter 4. (b) Fraser, R. R.; Chuaqui-Offermanns, N. *Can. J. Chem.* **1981**, *59*, 3007–3011.

(9) The higher kinetic basicity of LDEA relative to that of LDA in deprotonations of imines and related species has been noted previously; see footnote 5 in ref 3a.

(10) Bates, R. B. In "Comprehensive Carbanion Chemistry"; Buncel, E.; Durst, T., Eds., Elsevier: Oxford, 1980; Part A, Chapter 1.

(11) An anionic rearrangement which might have proceeded via a [1,4]-sigmatropic proton shift[12a] has been shown not to involve such a process.[12b] Anionic [1,4]-sigmatropic shifts of silyl groups, however, are known.[12b]

(12) (a) Daney, M.; Labrande, B.; Lapouyade, R.; Bouas-Laurent, H. *J. Organomet. Chem.* **1978**, *159*, 385–399. (b) Daney, M.; Lapouyade, R.; Bouas-Laurent, H. *J. Org. Chem.* **1983**, *48*, 5055–5062.

Table III. Products from Deprotonation and Subsequent Methylation of 2-Butanone *N*-Benzylimine (7) in THF

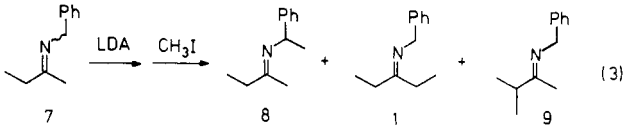
				% yield[b]		
[7][a]	[LDA][a]	temp, °C	time, h	8	1	9
0.24	0.27	−78	0.25	2	20	1
0.24	0.27	−78	2.25	6	82	2
0.76	0.87	−78	0.5	0	79	2
0.15	1.00	−78	0.66	4	72	2
0.07	0.10	−78	6.5	0	87	1
0.15	1.00	0	0.08	22	62	17
0.15	1.00	0	0.24	18	64	18
0.15	1.00	0	0.67	4	72	2
0.24	0.27	0	0.4	0	69	8
0.24	0.27	0	1.5	0	77	9
0.24	0.27	0	1.75	0	82	10

[a] Initial concentrations of reagents (±5%). [b] % yield relative to the total amount of imines 1, 7, 8, and 9.

we calculated the rate of isomerization of **2** to **3**. Relatively good first order kinetics were observed for the isomerizations over 1 to 3 half-lives. The results are collected in Table II. It can be seen that the 2-azaallyllithium reagent **2** isomerized to **3** slowly when it was generated in the presence of excess LDA, but more rapidly when an insufficient amount of base was used (entries 1 and 4). The rate of the isomerization of **2** to **3** at 0 °C was independent of base concentration (entries 1 and 2), but dependent on the total initial imine concentration and, thus, the final diisopropylamine concentration (entries 1 and 3). These results are best accommodated by the protonation–deprotonation sequence, pathway a in Scheme II.

The intermediacy of 2-azaallyllithium reagents like **2** in LDA deprotonations of *N*-benzyl ketimines has important consequences for the overall regioselectivity observed in the formation of 1-azaallyllithium reagents. Specifically, since C–N bond rotations in **2** are fast[13] relative to our observed lifetime of **2**, a benzylic deprotonation–protonation sequence could scramble the stereochemistry about the imine C=N double bond in an originally stereochemically pure imine, and regioselectivity in the ultimate formation of a 1-azaallyllithium reagent would thus be expected to be lowered as a function of the extent of 2-azaallyllithium reagent formation. We previously reported that (*Z*)-1-^{13}C-pentanone benzylimine was selectively deprotonated syn to the benzyl group by LDA at 25 °C;[6] in that study ^{13}C NMR peak areas uncorrected for NOE effects or differing relaxation times were measured to determine the product distribution. We have now repeated this regioselectivity study at 0 °C where the relative initial rates of formation of **2** and **3** from **1** are 3:2 (Table II). The alkylated products were purified by preparative GC, and corrected ^{13}C NMR peak areas were used; we observed low selectivity (syn:anti ca. 1:1) in the final product.

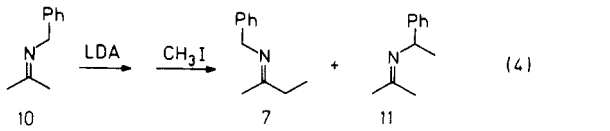
We had previously observed that 2-butanone imines exhibit substantially higher kinetic acidity at the methyl position than at the methylene position in deprotonations at −78 °C.[3a] Thus, we studied the deprotonation of the N-benzylimine of 2-butanone (**7**) to determine if a 2-azaallyllithium reagent could be formed. Treatment of an 80:20 mixture of the *E* and *Z* isomers of **7** with LDA at −78 °C or 0 °C followed by methylation gave the *N*-phenethylimine of 2-butanone (**8**) resulting from benzylic C–H deprotonation and the products (**1**, **9**) from alkylation of the 1-azaallyllithium reagents formed by deprotonations at the α-positions to the imine carbon (eq 3). In these studies, the results of which are collected in Table III, we



7 8 1 9 (3)

never observed a large amount of the phenethylimine product **8**. Also, in ^{13}C NMR experiments similar to that described above for **1**, we did not observe the formation of an intermediate benzyl anion species in high yield. It is known that (*Z*)-2-butanone imines are deprotonated at the methyl position much faster than (*E*)-2-butanone imines are deprotonated,[3a] thus it is most likely that products **8** and **9** arose almost exclusively from deprotonation of (*E*)-**7**. This result implies that the kinetic acidity of the benzylic and methylene protons in (*E*)-**7** are roughly comparable.

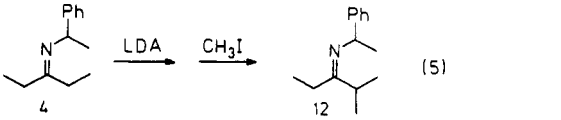
From the results with the 2-butanone *N*-benzylimine **7**, it should be expected that the *N*-benzylimine of acetone (**10**) would be deprotonated by LDA almost entirely at the α-methyl positions rather than at the benzylic position. Treatment of **10** with LDA in THF at various temperatures followed by methylation, in fact, gave almost entirely the 2-butanone product **7** with only traces (<0.5%) of the *N*-phenethyl imine **11** (eq 4). In one experiment, iodomethane was mixed with substrate **10** before the reagents were added to LDA at −78 °C so that any short-lived benzylic anion might be trapped. Under these conditions substantial methylation of LDA occurred, and again only traces of **11** were observed.



10 7 11 (4)

If the kinetic acidities of the methyl and benzylic positions of **10** were close to one another, the deuterated compound **10**-d_6 (derived from acetone-d_6) might exhibit a kinetic isotope effect in the α deprotonation reaction which would be manifested in increased benzylic anion formation. When **10**-d_6 was treated with LDA in a ^{2}H NMR experiment, we observed rapid formation of the 1-azaallyllithium reagent. Deuterium was incorporated into the benzylic position at a rate orders of magnitude less rapid than that of anion formation which is inconsistent with the formation of a 2-azaallyllithium reagent in any appreciable concentration as an intermediate in the formation of the 1-azaallyllithium reagent.

We briefly explored the possibility that phenethyl imines may be deprotonated at the benzylic position in competition with deprotonation at an α-position. When the *N*-phenethylimine of 3-pentanone (**4**) was treated with LDA and the resulting mixture was alkylated, the only product observed by GC was the *N*-phenethylimine of 2-methyl-3-pentanone (**12**) (eq 5). The addition of a methyl group at the benzylic position thus diminishes the kinetic acidity of the remaining proton.



4 12 (5)

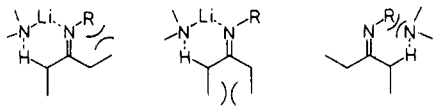
Discussion

As noted in the introduction, the benzylic protons of *N*-benzylimines which do not contain α-protons were known to be relatively acidic.[7] Our results show that the kinetic acidity of the benzylic position is so high that

(13) C–C bond rotations in 1-azaallyllithium reagents derived from aldehyde imines have been observed by NMR spectroscopy ($\Delta G^{\ddagger}$'s of 17–23 kcal/mol); C–N bond rotations have lower activation energies.[14]

predominant benzylic deprotonation can be obtained even in ketone imines which contain α-protons. Presumably the rate of LDA deprotonation at the benzylic positions in various benzylimines is relatively constant, and the amount of 2-azaallyllithium reagent vs. 1-azaallyllithium reagent formed reflects primarily the kinetic acidity at the α-positions. This conclusion is consistent with the observation that the amount of 2-azaallyllithium reagent increases as the steric demands about the α-positions increase in the series acetone, 2-butanone, and 3-pentanone *N*-benzylimines. It is also consistent with our previous observations that simple 3-pentanone imines are deprotonated by LDA less rapidly than their 2-butanone imine counterparts[3a,6] and our report that (*Z*)-2-butanone imines are deprotonated more rapidly at methyl than (*E*)-2-butanone imines are deprotonated at methylene.[3a]

The steric effects on the rates of α-deprotonations of imines of LDA in THF are readily rationalized by *closed* transition states for these deprotonations. For example, steric interactions in **13–15** are expected to slow the syn

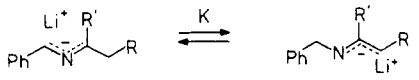


13 14 15

and anti α-deprotonations of a 3-pentanone imine in the relatively poor solvent THF. Similar transition states successfully account for the stereoselectivity seen in LDA deprotonations of various carbonyl compounds and their nitrogen analogs.[14,15,17] We have also used *closed* transition states to explain the regioselectivity of deprotonations of 2-butanone imines.[3a]

The kinetic acidities we observed in deprotonations of 3-pentanone *N*-benzylimine (**1**) and 2-butanone *N*-benzylimine (**2**) are in the order methyl > benzylic > methylene. The kinetic acidities of the α-protons in **1**, **7**, and **10** appear to parallel the thermodynamic acidities measured by Fraser, Houk, et al.[18] The relative pK_a's in THF determined in that study were 0 (CH_3 in **10**), 0.3 (CH_3 in **7**), 2.0 (CH_2 in **7**), and 2.4 (CH_2 in **1**).[18]

The 1-phenyl-2-azaallyllithium reagents **2** and **16** studied



2 (R = Me, R' = Et; K > 100) 3

16 (R = R' = Me; K > 100) 17

18 (R = H, R' = Ph; K < 10) 19

in this work are unstable with respect to their corresponding 1-benzyl-1-azaallyllithium reagent counterparts **3** and **17**, respectively. However the 1,3-diphenyl-2-azaallyllithium reagent **18** does not isomerize to its 1-azaallyl isomer **19**.[7a] Thus, the replacement of the destabilizing alkyl group at R' in **2** and **16** with the stabilizing phenyl group in **18** more than offsets the heteroatom stabilization available in **19** but not in **18**. Since the pK_a of 1,1,3-triphenyl-2-azapropene is ca. 24–25 in dimethyl sulfoxide and *N*-methylpyrrolidin-2-one[19] and the pK_a's of simple imines in THF are in the low 30's,[18] this result might have been predicted.

The formation of a 2-azaallyllithium reagent could be a complicating factor in synthetic sequences where stereochemical control in an imine deprotonation is desired. Highly regioselective deprotonations of imines have been reported, but in some cases the high regioselectivity results from the stereochemistry about the C=N double bond.[3] Since the stereochemical purity of the imine would be lost in formation of the 2-azaallyllithium reagent, one would be advised to avoid using *N*-benzylimines as equivalents of ketones for regiochemically controlled "enolate" formation. Overall diastereoselectivity in deprotonations and subsequent alkylations of imines employing chiral benzylic amine auxiliaries also would be lowered by deprotonation at the benzylic site resulting in racemization of the chiral auxiliary. However, our brief study of the reaction of phenethylimine **4** with LDA suggested that no benzylic deprotonation occurred in this case.

The conversion of a 2-azaallyllithium reagent to a 1-azaallyllithium reagent followed by an alkylation reaction may have some synthetic utility. For example, as shown in eq 2, we were able to effect an oxidation and an α-alkylation of an amine in one reaction sequence from the readily available *N*-benzylidene precursor. Related procedures have been reported for the oxidation of a primary amine to a ketone.[20] However, the slow deprotonation rate and the low yield of desired product that we obtained from imine **6** suggest severe limitations for this sequence; under the conditions we used, it is likely that condensation of the imine occurred as a side reaction. We have not investigated the viability of using other, more reactive bases for this sequence. Kauffmann also has noted difficulties in attempting to prepare 1-phenyl-2-azaallyllithium reagents,[7a] presumably from *N*-benzylidene derivatives of primary alkyl amines.

Experimental Section

General. All reactions involving organometallic species were run under an inert atmosphere of nitrogen or argon using routine procedures. ^{1}H NMR spectra were recorded on a Varian T-60 or EM-390 spectrometer. ^{2}H NMR spectra were recorded on a Varian XL-200 spectrometer using benzene-d_6 as an internal standard. ^{1}H-decoupled ^{13}C NMR spectra were recorded at 25 MHz on a JEOL PFT-100 spectrometer equipped with a low temperature apparatus using benzene-d_6 for a lock signal; chemical shifts were measured relative to the upfield signal of THF which we defined as δ 25.0. GC analyses were performed on a Hewlett-Packard Model 5880 or 5790 or Varian Model 2440 chromatograph using capillary columns (38-m Carbowax 20M or 25-m SE-30). Ketones and amines used in the imine preparations and *n*-butyllithium in hexane were obtained from Aldrich Chemical Co. THF was distilled from potassium–benzophenone immediately before use. Diisopropylamine (Aldrich Chemical Co.) was distilled from CaH_2 and stored over molecular sieves.

Imine Syntheses. Most of the imines used in this work were synthesized from ketones and amines in benzene with azeotropic distillation of water. The preparations of **1**, **7**, **9**, and **10** have been reported.[3a] The *N*-phenethylimines of 3-pentanone (**4**), 2-butanone (**8**), and acetone (**11**) and *N*-benzylidene-1-ethylpropylamine (**6**) were prepared from the amines and ketones in 55–73% isolated yield after distillation. Imine **4** had bp 61–64 °C (0.01 torr) (lit.[21]

(14) Lee, Y. Y.; Lynch, T. J.; Mao, D. T.; Bergbreiter, D. E.; Newcomb, M. *J. Am. Chem. Soc.* **1981**, *103*, 6215–6217.

(15) This effect was first reported by Ireland's group.[16a] There have been several subsequent studies of stereoselectivity in formation of enolates and azaallylmetal reagents; see ref 16b for a discussion.

(16) (a) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868–2877. (b) Davenport, K. G.; Newcomb, M.; Bergbreiter, D. E. *J. Org. Chem.* **1981**, *46*, 3143–3144.

(17) Ahlbrecht, H.; Düber, E. O.; Enders, D.; Eichenauer, H.; Weuster, P. *Tetrahedron Lett.* **1978**, 3691–3694. Knorr, R.; Löw, P. *J. Am. Chem. Soc.* **1980**, *102*, 3241–3242. Knorr, R.; Weiss, A.; Löw, P.; Räpple, E. *Chem. Ber.* **1980**, *113*, 2462–2489. Meyers, A. I.; Williams, D. R.; White, S.; Erickson, G. W. *J. Am. Chem. Soc.* **1981**, *103*, 3088–3093.

(18) Fraser, R. R.; Breese, M.; Chuaqui-Offermanns, N.; Houk, K. N.; Rondan, N. G. *Can. J. Chem.* **1983**, *61*, 2729–2734.

(19) Bordwell, F. G.; Branca, J. C.; Hughes, D. L.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3305–3313.

(20) Corey, E. J.; Achiwa, K. *J. Am. Chem. Soc.* **1969**, *91*, 1429–1432.

bp 75–82 °C (0.001 torr)); imine **6** had bp 49–51 °C (0.01 torr) (the compound has been reported without a bp, but the ^{1}H NMR spectrum reported[22] was the same as that of our sample), imine **8** had bp 54–55 °C (0.01 torr) (lit.[21] bp 90–96 °C (0.1 torr)), and imine **11** had bp 75–76 °C (0.15 torr) (lit.[21] bp 75–80 °C (0.2 torr)).

Samples of 2-methyl-3-pentanone *N*-benzylimine (**5**) and *N*-phenylethylimine (**12**) for GC analysis were prepared by deprotonation and subsequent methylation of the corresponding 3-pentanone imines **1** and **4**. The preparation of **12** is representative. Imine **4**, 0.47 g (2.5 mmol), was added dropwise to a solution of 3 mmol of LDA in 10 mL of THF at 0 °C. After 1.5 h, the reaction mixture was cooled to −78 °C and 3.2 mmol of iodomethane was added dropwise. After 0.5 h, the solution was quenched with brine, and 10 mL of ether was added to the reaction mixture. After phase separation, the organic phase was washed with brine and then dried over $MgSO_4$. Analytical GC indicated a 96% conversion of **4** to **12**. The solvent was removed in vacuo, and the residue was purified by preparative GC (SE-30 on 80/100 Chromosorb G). The major isomer of imine **12** had the following ^{1}H NMR spectrum: ($CDCl_3$) δ 7.1–7.5 (m, 5 H), 4.6–4.9 (q, 1 H), 2.7–3.3 (m, 1 H), 2.25 (q, 2 H), 1.4 (d, 3 H), 1.0 (d, 6 H), 0.9 (t, 3 H). The major isomer of imine **5** had the following ^{1}H NMR spectrum: ($CDCl_3$) δ 7.2–7.3 (s, 5 H), 4.56 (s, 2 H), 2.3–2.4 (m, 1 H), 2.3 (q, 2 H), 1.1 (d, 6 H), 1.05 (t, 3 H).

Acetone-d_6 Benzylimine (10-d_6). Benzylamine (10 g) in CH_2Cl_2 was washed thrice with 10-mL portions of D_2O. The solution containing the deuterated amine was distilled (bp 180 °C) after drying over K_2CO_3. The ^{1}H NMR spectrum indicated >93% deuterium incorporation at nitrogen. A dry 100-mL flask, fitted with a universal water separator with a reflux condenser and a magnetic stirring bar, was charged with 50 mL of CH_2Cl_2, 5.5 g of benzylamine-*N*-d_2 (0.05 mol), and 8 g of acetone-d_6 (0.11 mol). The solution was heated at reflux until 1.0 mL of water was removed azeotropically. The solvent was removed at reduced pressure, and the resulting oil was flash distilled (oil bath temperature at 120 °C) under a 0.01 torr vacuum to yield 4 g (52%) of **10**-d_6; bp 70–74 °C (0.15 torr). An ^{1}H NMR spectrum indicated >93% deuterium content at the α positions by comparison of the α signals' integral with that of the benzylic position. Use of *N*-protiobenzylamine in this synthesis led to lower deuterium levels in the final product.

^{13}C NMR studies were performed in a manner similar to that previously reported.[3a] A "clean" LDA solution was prepared (1 M), and 2 mL of the solution was added to a dry, Ar-flushed 10-mm NMR tube fitted with a serum cap. After cooling the base solution to −78 °C, 260 mg of **1** (1.5 mmol) was added dropwise with shaking. The NMR tube was placed into the temperature equilibrated probe of the spectrometer. Spectra were obtained at 1, 11, 21, and 31 min and 1, 2, 4, and 8 h.

^{1}H NMR studies were performed in a manner similar to the ^{13}NMR studies. "Clean" LDA solution (0.5 mL, 1 M) was added to a dry, Ar-flushed 5-mm NMR tube. The base solution was cooled to −78 °C, and 70 mg (0.4 mmol) of **1** was added. The sample was inserted in the cooled probe of the spectrometer. Spectra were obtained as the probe temperature was raised.

^{2}H NMR studies were performed in a manner similar to the ^{13}C NMR studies. A solution of LDA (0.2 mol) in THF was prepared, and 2 mL of this solution was transferred by syringe into an Ar-flushed, 10-mm NMR tube fitted with a serum cap. Benzene-d_6 (20 μL) was added as an internal standard. The solution was cooled to −78 °C, and a solution of **10**-d_6 in THF (0.23 M, 1.0 mL) was added. The tube was placed in the −80 °C probe of the spectrometer. Spectra obtained within 5 min and after 1.5 h showed no benzyl-*d* signal. After several h at 25 °C, the ^{2}H NMR spectrum contained a signal for the benzylic position.

Regioselectivity and kinetic studies were performed in a manner similar to that previously reported.[3a] Thus, LDA solutions (10 mL) of the desired concentration were prepared in a 40-mL flask. After cooling the solutions to the desired temperatures (−78 °C or 0 °C), the appropriate amount of imine was added dropwise with stirring. At various times, 0.5 mL aliquots of the reaction mixtures were removed by syringe and added to tubes containing excess iodomethane in THF which had been cooled to −78 °C. Product ratios were determined by analytical GC.

Acknowledgment. This work was supported by grants from the National Institutes of Health (GM 26268) and the Robert A. Welch Foundation.

Registry No. **1**, 31776-82-6; **2**, 98611-97-3; **3**, 88101-29-5; **4**, 18805-17-9; **5**, 98611-95-1; **6**, 27845-52-9; (*E*)-**7**, 72037-48-0; (*Z*)-**7**, 77390-49-9; **8**, 77449-24-2; **9**, 98611-98-4; **10**, 1197-48-4; **10**-d_6, 98611-96-2; **11**, 18805-14-6; **12**, 98611-94-0; $PhCH_2NH_2$, 100-46-9; $PhCH_2ND_2$, 45579-94-0; $CD_3C(O)CD_3$, 666-52-4.

(21) Wurmb-Gerlich, D.; Vögtle, F.; Mannschreck, A.; Staab, H. A. *Liebigs Ann. Chem.* **1967**, *708*, 36–50.
(22) Parry, K. A. W.; Robinson, P. J.; Sainsbury, P. J.; Waller, M. J. *J. Chem. Soc. B* **1970**, 700–703.

Mechanisms of the Thermal Isomerization about the C=N$^+$ Bond of Some Iminium Salts[1]

Marianne Pankratz and Ronald F. Childs*

Department of Chemistry, McMaster University, Hamilton, Ontario, L8S 4M1 Canada

Received April 17, 1985

The thermal stereomutations of a series of *N*-aryl 3-arylpropenylidene iminium perchlorate salts have been examined. These salts crystallize as *E,E* isomers but isomerize thermally about the C=N bond in solution. The rates of isomerization (**8** → **9**) were measured at 100 °C in trifluoroacetic acid. A Hammett correlation of the rate constants indicated that two mechanisms operate in the system. The iminium salts with electron-withdrawing substituents react by a nucleophile-catalyzed mechanism, while those with electron-donating substituents isomerize by a protonation mechanism. This latter process was shown to involve protonation on nitrogen.

Iminium ions are implicated in several important natural processes. For example, it has been proposed that chlorophyll, the light-absorbing pigment of the photosynthesis process, forms an iminium ion in the natural system.[2] Another important iminium linkage is that between the light-absorbing retinal molecule and the protein opsin in rhodopsin, the visual pigment.[3]

A key feature of the chemistry of the visual pigments is the stereomutations which can occur about the multiple bonds in the retinal-derived chromophore. Photochemically and thermally induced isomerizations about several of the C=C bonds have been reported. In addition, recent

(1) This work was supported by a grant from the Natural Science and Engineering Research Council of Canada.
(2) Ward, B.; Chang, C. K.; Young, R. *J. Am. Chem. Soc.* **1984**, *106*, 3943–3950.
(3) Uhl, R.; Abrahamson, E. W. *Chem. Rev.* **1981**, *81*, 291–312.

0022-3263/85/1950-4553$01.50/0