relationship applied to both types of nucleophiles. In this sense these results strikingly parallel the attack of amines on acetylpyridinium ions.[39] For oxygen nucleophiles (H_2O and methanol) the increased selectivity for methanol with the phosphoramidates apparently is the result of achieving the transition state earlier along the reaction coordinate than with *O*-phosphate monoesters.

Acknowledgment. We would like to acknowledge the generous support of the National Institutes of Health (GM 13306) and the assistance of Mrs. Patricia A. Benkovic.

Synthesis and Base-Catalyzed Exchange of Dihydrobenzazocines[1a]

Robert M. Coates* and Edward F. Johnson[1b]

Contribution from the Department of Chemistry and Chemical Engineering, University of Illinois, Urbana, Illinois 61801. *Received August 3, 1970*

Abstract: Benzo[2,3]tropone oxime (**10**) undergoes Beckmann rearrangement to 2-benzazocin-1(2*H*)-one (**11a**) which upon methylation followed by hydride reduction affords 1-methyl-1,2-dihydro-1-benzazocine (**2**). In potassium *tert*-butoxide–dimethyl sulfoxide, **2** isomerizes to the dienamine, 1-methyl-1,6-dihydro-1-benzazocine (**3**). The relative rates of deprotonation (*i.e.*, sum of NCH_2 exchange and isomerization) in the amine series, **2**, *trans*-*N*-methyl-*N*-cinnamylaniline (**20**), *cis*-*N*-methyl-*N*-cinnamylaniline (**21**), 1-methyl-1,2-dihydroquinoline (**18**), are 1.0:8.4:7.6:0.012 in potassium *tert*-butoxide–dimethyl-d_6 sulfoxide–*tert*-butyl alcohol-*O*-*d*. In the enamine series, **3**, *trans*-*N*-methyl-*N*-(3-phenyl-1-propenyl)aniline (**22**), 1-methyl-1,4-dihydroquinoline (**19**), the relative exchange rates of the methylene groups are 1.0:0.59:0.035. In the dibenz series, 5-methyl-5,6-dihydrodibenz[*b*,*f*]azocine (**1**), 5-methyl-5,6,11,12-tetrahydrodibenz[*b*,*f*]azocine (**6**), *N*-methylphenanthridine (**7**), *N*-methyl-*N*-benzylaniline (**8**), the relative exchange rates in potassium *tert*-butoxide–dimethyl-d_6 sulfoxide are $1.0:0.13:0.51 \geq \sim 100$. Although no appreciable aromatic stabilization is detected in the kinetic data from the dibenz series, the moderately enhanced kinetic acidity of the benzazocines **2** and **3**, as compared to the dihydroquinoline models **18** and **19**, is attributed to a small degree of aromatic stabilization in the incipient 10π electron anion.

According to Huckel's $4n + 2$ rule, a fully conjugated, monocyclic orbital network containing 10π electrons should be "aromatic."[2-4] In recent years, molecules with 10π electrons in eight-,[5] nine-,[6-8] and ten-membered[4,9] carbocycles have been prepared, and in all cases except the cyclodecapentaenes, evidence demonstrating "aromatic" character has been obtained despite the severe angle strain associated with these medium-sized rings. The apparent stabilization of the cyclooctatetraene dianion[5] is especially striking, considering the additional electron repulsion present. On the other hand, the information available on the isoelectronic seven-,[10] eight-,[11,12] and nine-membered[13] heterocycles, in which the heteroatom contributes a lone pair to the formal count of 10π electrons, seems to indicate little of the special stability expected of an "aromatic" species.

We became interested in the properties of the potentially aromatic heterocyclic anologs of cyclooctatetraenide. Such molecules would contain the required 10π electron core but need carry only a single negative charge.[12,14] While the reduced net charge might confer an extra degree of stability compared to the cyclooctatetraene dianion, the chemical changes attending the heteroatom substitution would also open the way to reaction paths inaccessible to the hydrocarbon parent.

(1) (a) Taken in part from the Ph.D. Thesis of E. F. J., University of Illinois, Urbana, Ill., 1969; (b) National Institutes of Health Predoctoral Fellow, 1968–1969.

(2) (a) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961, Chapter 10; (b) M. E. Vol'pin, *Russ. Chem. Rev.*, **29**, 129 (1960).

(3) R. Breslow, *Chem. Eng. News*, 90 (June 28, 1965).

(4) (a) F. Sondheimer, *et al.*, *Chem. Soc. Spec. Publ.*, No. 21, 75 (1967); (b) E. Vogel, *ibid.*, No. 21, 113 (1967).

(5) (a) T. J. Katz and H. L. Strauss, *J. Chem. Phys.*, **32**, 1873 (1960); (b) T. J. Katz, *J. Amer. Chem. Soc.*, **82**, 3784, 3785 (1960); (c) T. J. Katz, W. H. Reinmuth, and D. E. Smith, *ibid.*, **84**, 802 (1962); (d) H. L. Strauss, T. J. Katz, and G. K. Fraenkel, *ibid.*, **85**, 2360 (1963).

(6) T. J. Katz and P. J. Garratt, *ibid.*, **86**, 5194 (1964); E. A. LaLancette and R. E. Benson, *ibid.*, **87**, 1941 (1965); P. J. Garratt and K. A. Knapp, *Chem. Commun.*, 1215 (1970).

(7) M. Ogliaruso, R. Rieke, and S. Winstein, *J. Amer. Chem. Soc.*, **88**, 4731 (1966).

(8) W. Grimme, M. Kaufhold, W. Dettmeier, and E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **5**, 604 (1966); P. Radlick and W. Rosen, *J. Amer. Chem. Soc.*, **88**, 3461 (1966).

(9) E. E. van Tamelen and T. L. Burkoth, *ibid.*, **89**, 151 (1967); S. Masamune, R. T. Seidner, H. Zenda, M. Wiesel, N. Nakatsuka, and G. Bigam, *ibid.*, **90**, 5286 (1968); S. Masamune and R. T. Seidner, *Chem. Commun.*, 542 (1969); T. L. Burkoth and E. E. van Tamelen in "Non-benzenoid Aromatics," Vol. I, J. P. Snyder, Ed., Academic Press, New York, N. Y., 1964, p 63.

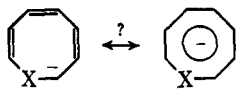
(10) N. L. Allinger and G. A. Youngdale, *J. Amer. Chem. Soc.*, **84**, 1020 (1962); R. Breslow and E. Mohacsi, *ibid.*, **85**, 431 (1963).

(11) (a) W. Schroth and B. Werner, *Angew. Chem., Int. Ed. Engl.*, **6**, 697 (1967); (b) N. L. Allinger and G. A. Youngdale, *J. Org. Chem.*, **25**, 1509 (1960); (c) W. W. Paudler and A. G. Zeiler, *ibid.*, **34**, 3237 (1969).

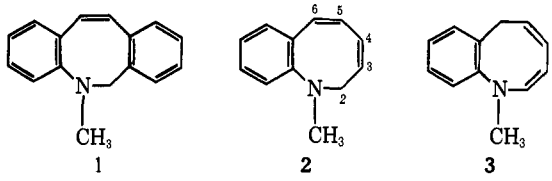
(12) H. S. Kasmai, *Diss. Abstr. B*, 30, 125 (1969).

(13) (a) A. P. Bindra, J. A. Elix, P. J. Garratt, and R. H. Mitchell, *J. Amer. Chem. Soc.*, **90**, 7372 (1968); P. J. Garratt, A. B. Holmes, F. Sondheimer, and K. D. C. Vollhardt, *ibid.*, **92**, 4492 (1970); (b) A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 903, 1521 (1969); J. M. Holovka, R. R. Grabbe, P. D. Gardner, C. B. Strow, M. L. Hill, and T. V. van Auken, *ibid.*, 1522 (1969); S. Masamune, S. Takada, and R. T. Seidner, *J. Amer. Chem. Soc.*, **91**, 7769 (1969); (c) S. Masamune, K. Hojo, and S. Takada, *Chem. Commun.*, 1204 (1969); A. G. Anastassiou and J. H. Gebrian, *J. Amer. Chem. Soc.*, **91**, 4011 (1969); *Tetrahedron Lett.*, 5239 (1969); (d) A. G. Anastassiou, S. W. Eachus, R. P. Cellura, and J. H. Gebrian, *Chem. Commun.*, 1133 (1970).

(14) (a) T. S. Cantrell and B. L. Harrison [*Tetrahedron Lett.*, 4477 (1967)] have recently called attention to such systems. (b) Azocinyl dianions, heterocyclic analogs of cyclooctatetraenide in which the nitrogen lone pair is orthogonal to the orbital network, have recently been prepared: L. A. Paquette, T. Kakihana, and J. F. Hansen, *ibid.*, 529 (1970); L. A. Paquette, J. F. Hansen, T. Kakihana, and L. B. Anderson, *ibid.*, 533 (1970).



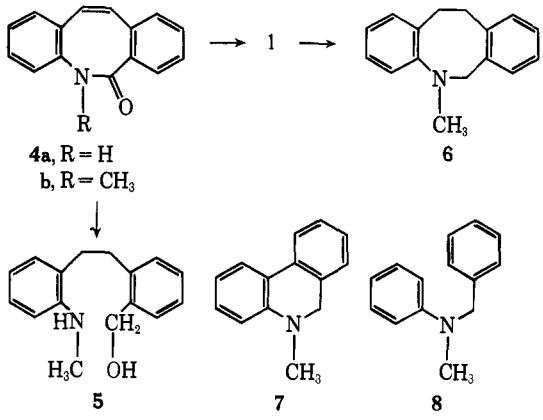
One possible route to such heterocyclooctatetraenide monoanions[14b] is deprotonation of the corresponding heterocyclooctatriene. In this paper we describe the synthesis of the three benz-annulated analogs of dihydroazocine, **1–3**, and a study of their base-catalyzed exchange and isomerization reactions as compared to various model compounds.[12]



1 2 3

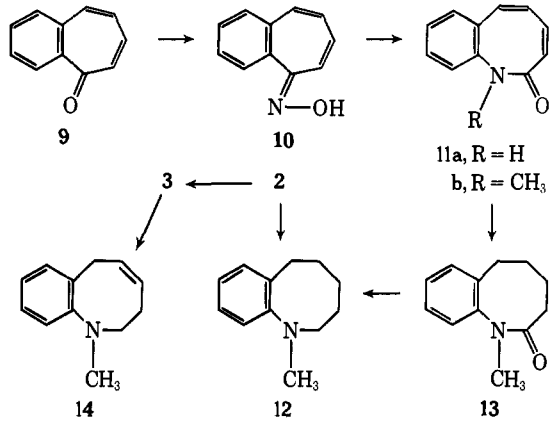
Syntheses and Structures

The known lactam **4a**[15] was converted to 5-methyl-5,6-dihydrodibenz[*b*,*f*]azocine (**1**) by methylation with methyl iodide and potassium hydroxide (94%) followed by reduction of **4b** with lithium aluminum hydride in ether (88%). If the reduction is carried out in refluxing tetrahydrofuran, ring cleavage and double bond reduction occur, giving mainly amino alcohol **5**. Catalytic hydrogenation of **1** furnished 5-methyl-5,6,11,12-tetrahydrodibenz[*b*,*f*]azocine (**6**) for use as a nonconjugated but structurally similar model compound. *N*-Methylphenanthridine (**7**) and *N*-methyl-*N*-benzylaniline (**8**) were also prepared for use as model compounds.



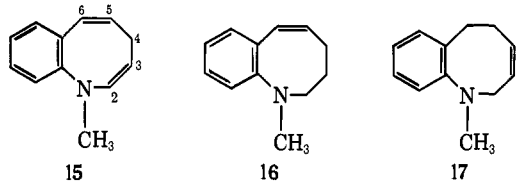
4a, R = H; b, R = CH_3 — **6** — **5** **7** **8**

The dihydrobenzazocine **2** was prepared in a similar fashion from benzo[2,3]tropone (**9**).[16] The oxime **10** was obtained in 42% yield by treatment with hydroxylamine in refluxing pyridine–ethanol.[17] Beckmann rearrangement of the corresponding benzene sulfonate was effected by prolonged heating (40 hr) in aqueous acetone.[18] The lactam so obtained (1-benzazocin-2-(1*H*)-one (**11a**)) was converted to the *N*-methyl derivative **11b** as before in 76% yield. Reduction of **11b** with either lithium aluminum hydride (72%) or aluminum hydride (81%)[19] afforded the desired 1-methyl-1,2-dihydro-1-benzazocine (**2**). The structure of **2** is supported by its spectral properties (see Experimental Section) and hydrogenation to the known[20] 1-methyl-1,2,3,4,5,6-hexahydro-1-benzazocine (**12**). The latter was also obtained by lithium aluminum hydride reduction of the tetrahydrolactam **13**.



9 — **10** — **11a**, R = H; **b**, R = CH_3 — **3** — **2** — **14** **12** **13**

Treatment of **2** with potassium *tert*-butoxide in tetrahydrofuran or dimethyl sulfoxide effected isomerization[21] to the dienamine, 1-methyl-1,6-dihydro-1-benzazocine (**3**). The downfield shift of the *N*-methyl signal in the nmr spectrum of **3** (τ 6.87, compared to 7.18 for **2**) and the position (1615 cm^{-1}) and intensity of the C=C stretch in the infrared spectrum[22] are expected for the enamine structure. Furthermore, **3**



15 **16** **17**

could be reduced with sodium borohydride in methanol to the stable tetrahydroazocine **14**, a reaction characteristic of enamines.[23]

The 100-MHz nmr spectrum of the enamine provides additional evidence in favor of structure **3**, and in particular excludes the 1,4-dihydroazocine **15**. The enamine β hydrogen (H_3) is easily recognized as the high-field vinyl proton (τ 5.93) and appears as a pair of doublets with J = 11.0 and 6.3 Hz. The larger coupling arises from interaction with α hydrogen (H_2), which is seen as a clean doublet at τ 3.98, while the smaller constant results from coupling with one of the other vinyl protons (τ 4.66, H_4). The methylene group (H_6) appears as a clean doublet (J = 7.6 Hz) partially overlapping the four-line pattern from H-3. The doublet results from coupling with the vinyl proton at τ 4.27 (an overlapping doublet of triplets, H_5). These assignments are confirmed by decoupling experiments and the changes attending progressive deuterium exchange

(15) (a) C. van der Stelt, W. J. Heus, and W. Th. Nauta, *Arzneim. Forsch.*, 14, 116 (1964); (b) F. Sowinski and N. L. Yale, *ibid.*, 14, 117 (1964).

(16) E. W. Collington and G. Jones, *J. Chem. Soc. C*, 2656 (1969); *Chem. Commun.*, 958 (1968).

(17) T. Nozoe, T. Mukai, and K. Takase, *Sci. Rep. Tohoku Univ., Ser. I*, **39**, 164 (1956).

(18) M. Kröner, *Chem. Ber.*, 100, 3162 (1967).

(19) (a) M. J. Jorgenson, *Tetrahedron Lett.*, 559 (1962); (b) N. M. Yoon and H. C. Brown, *J. Amer. Chem. Soc.*, **90**, 2927 (1968).

(20) H. König and R. Huisgen, *Chem. Ber.*, **92**, 429 (1959).

(21) (a) C. C. Price and W. H. Snyder, *Tetrahedron Lett.*, 69 (1962); (b) J. Sauer and H. Prahl, *Chem. Ber.*, 102, 1917 (1969); (c) M. Rivière and A. Lattes, *Bull. Soc. Chim. Fr.*, 2539 (1967); 4430 (1968); (d) P. Caubere and M.-F. Hochu, *ibid.*, 459 (1968); (e) A. J. Hubert, *J. Chem. Soc. C*, 2048 (1968).

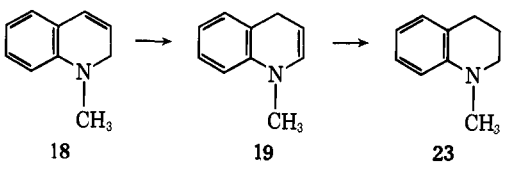
(22) (a) G. Stork, A. Brizzolara, H. Landesman, J. Szmuskovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963); (b) J. Szmuskovicz, *Advan. Org. Chem.*, 4, 1 (1963).

(23) J. Schmitt, J. J. Panouse, A. Hallot, P.-J. Cornu, P. Comoy, and H. Pluchet, *Bull. Soc. Chim. Fr.*, 807 (1963); J. A. Marshall and W. S. Johnson, *J. Org. Chem.*, **28**, 421 (1963).

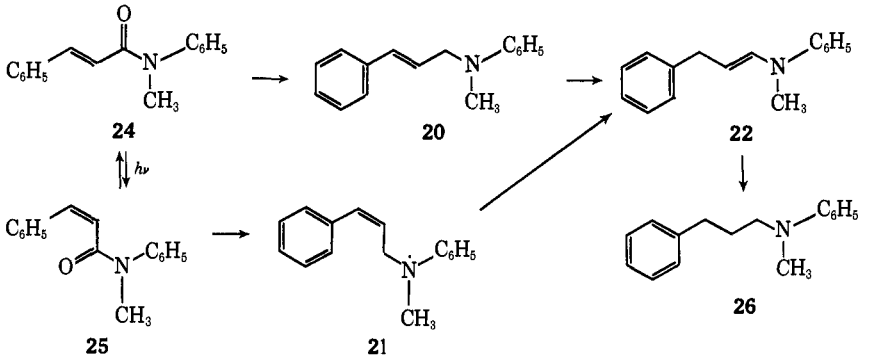
(see Experimental Section). To accommodate the alternative enamine structure **15** to these assignments, one would have to accept a five-bond coupling of 6.3 Hz between H-3 and H-6 and the ostensible absence of coupling between H-3 and the adjacent methylene protons.

The nonconjugated nature of the double bond in the borohydride reduction product **14** is also in agreement with this conclusion. In acidified ethanol the ultraviolet spectrum shows typical benzenoid absorption (λ_{sh} 207 mμ (log ε 3.96), λ_{min} 235 mμ (2.61), λ_{max} 257, 262, 270 mμ (2.79, 2.81, 2.70)), a pattern very similar to that of the hexahydroazocine **12**. In contrast, 3-methylbenzo-1,3-cyclooctadiene exhibits λ_{max} 235 mμ (3.855),[24] thus excluding the conjugated tetrahydroazocine **16**. The nmr spectrum of the trideuterated derivative, obtained by sodium borohydride reduction of **3**-*2,6,6-d*$_3$, clearly eliminates the other nonconjugated isomer **17**. The fact that the lowest field methylene absorption (d, τ 6.58) is cleanly erased is consistent only with deuteration of the benzylic–allylic methylene at C-6 in **14**.

The cyclic and acyclic compounds **18–22** were prepared for reference purposes. The known 1-methyl-1,2-dihydroquinoline (**18**)[25] isomerizes to the unstable enamine **19** upon exposure to potassium *tert*-butoxide in dimethyl sulfoxide. The spectral properties of **19** are appropriate for the enamine stucture, and in addition sodium borohydride reduction furnished the tetrahydroquinoline **23**.



18 19 23



24 20 22 25 21 26

The known *trans*-cinnamylamine (**20**)[26] was prepared in 56% yield by means of aluminum hydride reduction[19] of *N*-methyl-*trans*-cinnamanilide (**24**).[27] The use of lithium aluminum hydride with this[28] and other acyclic, unsaturated amides[29] can give reductive cleavage, polymerization, and double bond reduction. Photochemical isomerization of **24** gave rise to a stationary state with a trans–cis ratio of 47:53. Reduction of this mixture with aluminum hydride afforded a mixture of the corresponding amines from which *N*-methyl-*N*-*cis*-cinnamylaniline (**21**) was separated by preparative glpc. The magnitude of the coupling between the vinyl protons in the nmr spectra of the isomeric amides (**24**, J = 15.5 Hz; **25**, J = 12.5 Hz) and amines (**20**, J = 15.5 Hz; **21**, J = 11.6 Hz) confirms the geometrical assignments.[30]

Treatment of either the *cis*- or *trans*-cinnamylamines with potassium *tert*-butoxide effected isomerization to the *trans*-enamine **22**. It is worth noting that this synthetic approach to the preparation of enamines[21,31] provides a useful alternative to existing methods.[22] That the double bond geometry in **22** is trans is again clear from the magnitude of the vicinal coupling between the vinyl protons in the nmr spectrum (J = 13.5 Hz). Thus, the cyclic *cis*-enamine **19** has J = 7.8 Hz; for other acyclic enamines the ranges J_{cis} = 8.1–9.1 and J_{trans} = 13.4–13.9 Hz have been reported.[21b] Reduction of **22** with sodium borohydride produced *N*-methyl-*N*-3-phenylpropylaniline (**26**).

Kinetic Results

The rates of exchange of the heterocycles **1**, **6**, and **7** and the acyclic model **8** were determined in potassium *tert*-butoxide–dimethyl-d_6 sulfoxide at approximately 42° (probe temperature) by integration of the nmr spectrum as a function of time. The *N*-methyl absorption provided a convenient internal integration standard. The exchange process was followed through at least one and in most cases two half-lives, with good pseudo-first-order kinetics being observed. The data from a typical run are plotted in Figure 1. The rate of each model compound was measured either before or after a run with **1**, using the same base preparation and solvent batch in order to minimize uncertainties in the comparative rates. The results are summarized in Table I. The rate of exchange of **8** was too fast to determine with accuracy, since only two or three integrations could be obtained ($t_{1/2} \sim$ 30 sec) and these, being after the first half-life, are subject to considerable uncertainty. The relative rate of 100 is an estimate but should represent a lower limit. We also investigated the effect of varying the base concentration on the rate of exchange of **1** (Figure 2).

(24) H. Christol and F. Plenat, *Bull. Soc. Chim. Fr.*, 1325 (1962).
(25) K. Sutter-Kostič and P. Karrer, *Helv. Chim. Acta*, **39**, 677 (1956).
(26) R. F. Kleinschmidt and A. C. Cope, *J. Amer. Chem. Soc.*, **66**, 1929 (1944).
(27) N. Maxim and N. Ioanid, *Bull. Soc. Chim. Roum.*, **10**, 29 (1928); *Chem. Abstr.*, **22**, 4114 (1928).
(28) H. R. Snyder and R. E. Putnam, *J. Amer. Chem. Soc.*, **76**, 1893 (1954).
(29) V. M. Micovic and M. L. J. Mihailović, *J. Org. Chem.*, **18**, 1190 (1953); H. R. Snyder and R. E. Putnam, *J. Amer. Chem. Soc.*, **76**, 33 (1954); A. Uffer and E. Schlittler, *Helv. Chim. Acta*, **31**, 1397 (1948).
(30) F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York, N. Y., 1969, p 358.
(31) For reviews on base-catalyzed allylic rearrangements, see (a) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, Chapter 5; (b) C. D. Broaddus, *Accounts Chem. Res.*, **1**, 231 (1968); (c) A. J. Hubert and H. Reimlinger, *Synthesis*, 97 (1969).

Table I. Rates of *N*-Methylene Exchange for 5-Methyl-5,6-dihydro[*b*,*f*]azocine (**1**) Related Compounds in Potassium *tert*-Butoxide–Dimethyl-d_6 Sulfoxide

Compd	Runs	[KO-*tert*-Bu], *M*		$k_{obsd} \times 10^4$ sec^{-1}	k_{rel}[b]
1	4	0.36		21.2 ± 1.0	1.00
6	3	0.36	*C*-Benzyl[c]	5.66 ± 0.5	0.27
			N-Benzyl	2.85 ± 0.4	0.13
7	3	0.36		10.9 ± 1.0	0.51
1	1	0.026		3.59	1.00
6	1	0.026	*C*-Benzyl[c]	0.552	0.15
			N-Benzyl	0.617	0.17
8	2	0.026		~400[d]	~100[d]

[a] Slope of best-fit straight line by least-squares computer program; error is standard deviation from the average. [b] Rate relative to rate of **1** run on same day. [c] Rate based on exchange of two of the four *C*-benzyl protons. [d] Exchange too fast to measure accurately, rough estimate only.

The deuterated amines were recovered in high yield after 8–12-hr exposure (at least 10 half-lives) to potassium *tert*-butoxide in dimethyl-d_6 sulfoxide. The mass spectra, deuterium analyses, and nmr spectra confirmed the uncomplicated two-proton exchange of **1**, **7**, and **8**.

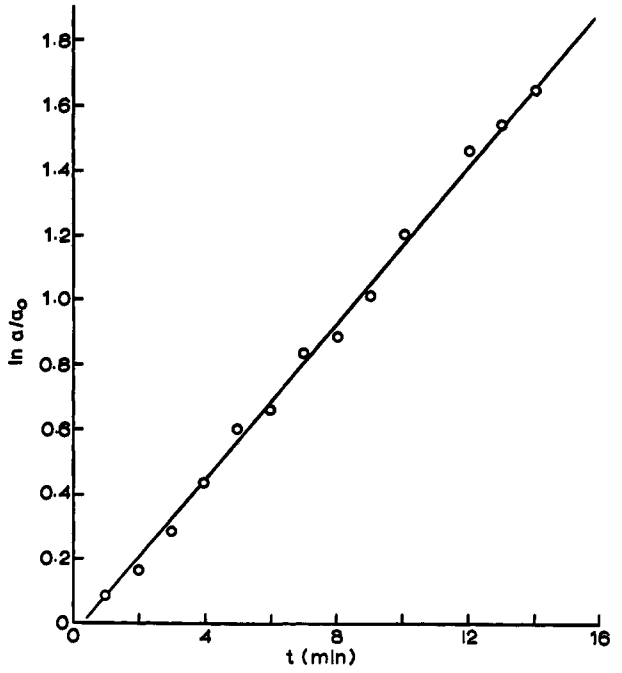


Figure 1. Plot of the proton exchange of 5-methyl-5,6-dihydrodibenz[*b*,*f*]azocine (**1**): 0.735 *M* in dimethyl-d_6 sulfoxide with 0.36 *M* potassium *tert*-butoxide.

The tetrahydroazocine **6**, however, undergoes exchange at the two *C*-benzyl positions (11 and 12) as well as the *N*-benzyl position (6). The nmr spectrum of recovered **6** (12 hr) indicated 0.17 H at position 6 and 1.75 H at positions 11 and 12 (not resolved). The mass spectrum showed the major deuterated species to be d_3 (16%), d_4 (51%), and d_5 (25%). Apparently one of the two *C*-benzyl positions exchanges rapidly ($t_{1/2}$ = 18 min) and the other about 180 times more slowly.

Since dihydrobenzazocine **2** as well as the model compounds **18**, **20**, and **21** underwent isomerization to the enamines, we measured both rates of exchange (where possible) and rates of isomerization. It was necessary to employ two mixed solvent systems (41.6 and 64.5% dimethyl-d_6 sulfoxide–*tert*-butyl alcohol-*O*-*d*) in order to obtain rates conveniently measurable by nmr integration. The rate of isomerization of **2** was determined in both solvent mixtures to permit relative rate comparisons among compounds run in both media.

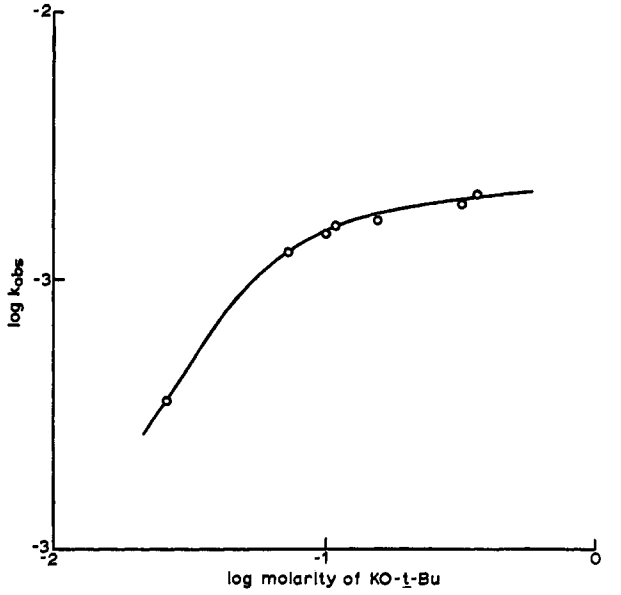


Figure 2. Rate of exchange (k_{obsd}) of 5-methyl-5,6-dihydrodibenz-[*b*,*f*]azocine (**1**) in dimethyl-d_6 sulfoxide at various concentrations of potassium *tert*-butoxide.

In most cases, the kinetics of exchange and/or isomerization were followed through one and usually two half-lives, the exceptions being the slow reactions with **18**, **19**, and **22**. A kinetic plot for the isomerization **2** → **3** is shown in Figure 3. In other runs the deviation of the individual points from the line was usually less than ±8% The kinetic data are summarized in Table II.

The rates of exchange refer only to exchange at the allylic methylene group. Since the methylene absorptions for **2** and **3** coincide, it was not possible to determine directly the exchange in **2**. However, this exchange rate must be much less than the isomerization rate of **2**, for the nmr spectrum of **3** after complete exchange of the methylene group shows no detectable decrease (exchange) in the H_2 doublet even at 72 hr (64.5% dimethyl-d_6 sulfoxide–*tert*-butyl alcohol-*O*-*d*). The other exchangeable proton, H_4, disappears slowly under these conditions ($t_{1/2} \sim 4.5$ hr, $k_{ex} \sim 2 \times 10^{-4}$ sec^{-1}). In potassium *tert*-butoxide–dimethyl-d_6 sulfoxide com-

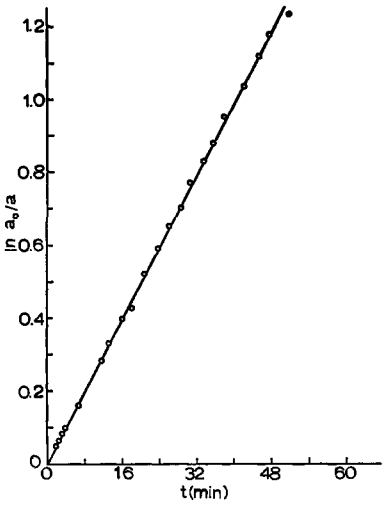


Figure 3. Plot of the isomerization of 1-methyl-1,2-dihydro-1-benzazocine (**2**) into 1-methyl-1,6-dihydro-1-benzazocine (**3**): 1.05 *M* in 64.5% dimethyl-d_6 sulfoxide–*tert*-butyl alcohol-*O*-*d* with 0.280 *M* potassium *tert*-butoxide.

plete exchange of H_2, H_4, and H_6 occurs after about 30 min.

The rate of isomerization reported for the *trans*-cinnamylamine **20** is an initial rate since curvature toward a steady state becomes evident at conversions greater than 50%. Examination of the spectrum at this time reveals the presence of a third component

Table II. Isomerization and Exchange Rate Constants for 1-Methyl-1,2-dihydrobenzazocine (**2**) and Related Compounds in Potassium *tert*-Butoxide–Dimethyl-d_6 Sulfoxide–*tert*-Butyl Alcohol-O-*d*

Compd	Runs	$k_{obsd} \times 10^4$ sec^{-1} [b]	k_{rel}
A. 0.147 *M* Potassium *tert*-Butoxide in 41.6% Dimethyl-d_6 Sulfoxide–*tert*-Butyl Alcohol-*O*-*d*[a]			
2	3	k_{iso} 3.64 ± 0.96 ($k_{ex} < 0.03$)	1.0
20	6	k_{iso} 11.5 ± 1.7[c]	3.2
		k_{ex} 9.3 ± 1.2	2.6
21	2	k_{iso} 15.0 ± 0.8[c]	4.1
		k_{ex} 6.6 ± 1.7	1.8
22	2	k_{ex} 0.86 ± 0.28	0.24
B. 0.280 *M* Potassium *tert*-Butoxide in 64.5% Dimethyl-d_6 Sulfoxide–*tert*-Butyl Alcohol-*O*-*d*[a]			
2	2	k_{iso} 40.3 ± 10.9	1.0
3	2	k_{ex} 16.1 ± 2.9	0.40
18	2	k_{iso} 0.49 ± 0.01 ($k_{ex} < 0.1$)	0.012
19	2	k_{ex} 0.58 ± 0.06	0.014

[a] Per cent means volume per cent before mixing. [b] Slope of best-fit straight line by least-squares computer program. k_{iso} = isomerization rate constant; k_{ex} = exchange rate constant (disappearance of allylic CH_2). Error is standard deviation from the average. [c] Initial rate.

(NCH_3, τ 6.86) in addition to the starting amine **20** (NCH_3, τ 7.04) and the final product, the *trans*-cinnamylenamine **22** (NCH_3, τ 6.92). This intermediate, which reaches a maximum relative concentration of 25–30%, also exhibits an apparent enamine β proton at about 0.3 ppm lower field than **22**, and therefore is very likely the *cis*-cinnamylenamine isomer **27**.[21b] The course of these isomerizations is illustrated in Figure 4.

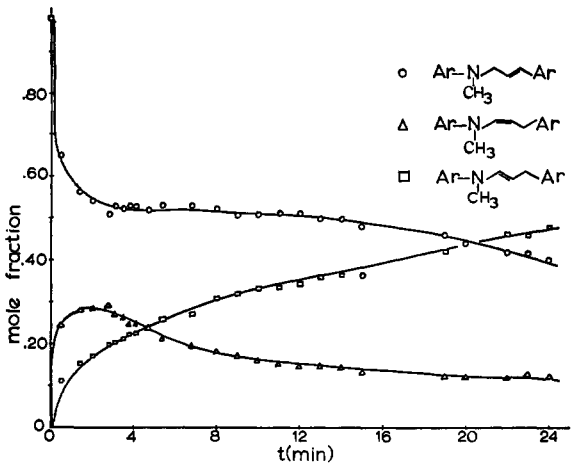


Figure 4. Plot of the isomerization of *trans*-*N*-methyl-*N*-cinnamylaniline (**20**): 0.843 *M* in 62.0% dimethyl-d_6 sulfoxide–*tert*-butyl alcohol-*O*-*d* with 0.155 *M* potassium *tert*-butoxide.

The *cis*-cinnamylamine, on the other hand, underwent direct isomerization to the trans enamine.[32]

Discussion

The interconversions of the various cinnamylamines and enamines can be interpreted in terms of the reaction scheme below. Evidently, the *trans*-amine **20** is deprotonated to the two isomeric allylic anions, **28** and **29**, the former leading to the *cis*-enamine **27**. There is precedent for the formation of cis isomers in allylic isomerizations.[21,31,33] The *cis*-cinnamylamine (**21**), on the other hand, affords only anion **30**, presumably owing to the severe steric interactions present in the alternative anion **31**; thus only the trans enamine is formed from **21**.

Before discussing the relative rates in Tables I and II, we must consider the kinetics of the exchange and isomerization processes. This is particularly important since the absence of a substantial kinetic isotope effect in the potassium *tert*-butoxide–dimethyl sulfoxide medium[34] has generated uncertainty regarding the significance of the observed exchange rates as an experimental measure of acidity.[35] A small or inverse isotope effect may indicate that the proton removal step (k_1 in eq 1) is not rate controlling, and is possibly due to

$$\mathrm{R{-}H + B^-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{[R{\cdots}H{-}B]^-} \xrightarrow{k_3} \mathrm{[R{\cdots}D{-}B]^-} \longrightarrow \mathrm{R{-}D + B^-} \quad (1)$$

a rapid reversal of this step (*i.e.*, $k_{-1} \gg k_3$).[34-36] The

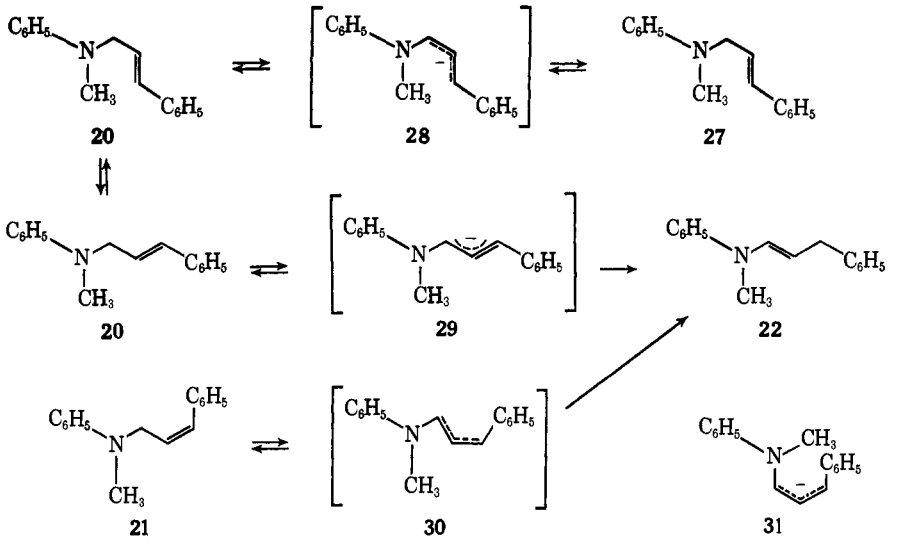
(32) Some curvature appears after about 70% conversion. This may indicate approach to a final enamine–amine equilibrium. In this case there could be as much as 10% of the two cinnamylamines present at equilibrium. For the other amine → enamine isomerizations (**2** → **3** and **18** → **19**) the amount of amine present at the final equilibrium is 6% or less.

(33) (a) H. Kloosterziel and J. A. A. van Drunen, *Recl. Trav. Chim. Pays-Bas*, **89**, 32, 37 (1970); (b) D. H. Hunter and R. W. Mair, *Can. J. Chem.*, **47**, 2361 (1969); (c) J. Elphimoff-Felkin and J. Huet, *C. R. Acad. Sci.*, **268**, 2210 (1969).

(34) J. E. Hofmann, A. Schriesheim, and R. E. Nickols, *Tetrahedron Lett.*, 1745 (1965).

(35) A. Streitwieser, Jr., and H. F. Koch, *J. Amer. Chem. Soc.*, **86**, 404 (1964).

(36) This interpretation was originally proposed by D. J. Cram: (a) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, **83**, 3696 (1961); (b) ref 31a, pp 27–31. For another interpretation, in which proton removal would still be rate determining, see J. R. Jones, *Chem. Commun.*, 710 (1967).

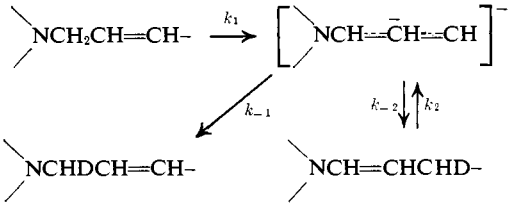


rate would then be determined by the second step (k_3), dissociation of the solvated carbanion intermediate. Since $k_1 \ll k_{-1}$ or k_3, the steady-state approximation holds[37] and the exchange rate $k_{obsd} = k_3k_1/k_{-1} = k_3K$, where K is in effect an equilibrium constant equal to k_1/k_{-1}.[36b]

If in a given series of compounds k_3 is invariant, then the observed rate of exchange will be determined by the magnitude of K, *i.e.* an equilibrium relation in which the acid RH and the conjugate base R^- are both involved. The thermodynamic stability of the anion should clearly be an important factor in determining the value of K and hence the rate of exchange. Furthermore, comparisons of relative rate data in dimethyl sulfoxide with similar data in other solvent systems show rather good agreement (usually within a factor of 2 or 3), with a few exceptions, as long as the structure of the substrate and exchanging position are kept reasonably constant.[36b,38] For these reasons, we feel that the relative exchange rates in Tables I and II are significant, if approximate, measures of relative anion stability.[39]

The curve in Figure 2 indicates that at higher base concentrations, the region in which most of the exchange rates in Table I were measured, the rate is essentially independent of the concentration of base. This leveling effect has been encountered previously, and attributed to aggregation of the basic species.[40] The relatively nonbasic higher aggregates are in equilibrium with a small and constant concentration of a catalytically active lower aggregate of the base. Since we found the relative exchange rates to be about the same (Table I) in either the level region (0.36 *M*) or the sloping region (0.026 *M*), this effect should not alter the significance of the data.

For the amines which undergo isomerization to enamines, the kinetic scheme below indicates that the desired rate of deprotonation (k_1) for the amines is a composite of both isomerization and exchange.[41] A steady-state derivation,[37] with the assumption that the equilibrium constant is much greater than one ($K = k_1k_{-2}/k_2k_{-1} \gg 1$, gives the relationships expressed in eq 2 and 3, the factor of two being the statistical correction required in the isomerization. For the cases in which this assumption does not hold (cinnamylamines **20** and **21**[32]), eq 2 and 3 are valid for the initial rates of isomerization and exchange. For the enamine products, the rates of exchange directly measure the rates of deprotonation.



$$k_{iso} = 2k_1\left(\frac{k_{-2}}{k_{-1} + k_{-2}}\right)$$

$$k_{ex} = k_1\left(\frac{k_{-1}}{k_{-1} + k_{-2}}\right) \quad (2)$$

$$k_1 = k_{iso}/2 + k_{ex} \quad (3)$$

Here again, there could be an undetected internal return preceding the observable exchange reaction in both the amines and enamines (see above discussion); if so, the measured values for the deprotonation rates (k_1) would represent a lower limit of the true rates of proton

(37) The steady-state approximation should be valid since in no case did we observe nmr signals which could be attributed to the accumulation of an anion intermediate.

(38) (a) A. I. Shatenshtein, I. O. Shapiro, I. A. Romanskii, G. G. Isaeva, and E. A. Yakovleva, *Org. Reactiv.* (*USSR*), 3, 246 (1966); *Reakts. Sposobnost. Org. Soedin.*, 3, 98 (1966); A. I. Shatenshtein and I. O. Shapiro, *Russ. Chem. Rev.*, 37, 845 (1968); Yu. I. Shapiro, L. I. Belen'kii, I. A. Romanskii, F. M. Stoyanovich, Ya. L. Gol'dfarb, and A. I. Shatenstein, *J. Gen. Chem. USSR*, 38, 1938 (1968); (b) A. Streitwieser, Jr., J. A. Hudson, and F. Mares [*J. Amer. Chem. Soc.*, 90, 648 (1968)] have found that the relative exchange rates of a series of fluorobenzenes in sodium methoxide–methanol are remarkably similar to the relative rates in lithium cyclohexylamide–cyclohexylamine despite the absence of a primary isotope effect in the former medium.

(39) For other recent uses of the potassium *tert*-butoxide–dimethyl-d_6 sulfoxide medium for estimating relative acidities see: S. W. Staley and D. W. Reichard, *ibid.*, 91, 3998 (1969); J. M. Brown and J. L. Occolowitz, *J. Chem. Soc. B*, 411 (1968).

(40) J. E. Hofmann, R. J. Muller, and A. Schriesheim, *J. Amer. Chem. Soc.*, 85, 3000, 3002 (1963); A. Schriesheim and C. A. Rowe, Jr., *ibid.*, 84, 3160 (1962); D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, *ibid.*, 83, 3678 (1961).

(41) (a) We have assumed that deprotonation of the amines and enamines directly produces a common anion intermediate. (b) This scheme neglects the very real possibility that the amine → enamine isomerizations proceed in part by way of an intramolecular pathway, *i.e.*, isomerization without exchange.[31a,b,42] Although the existence of such an intramolecular mechanism would not, of course, affect the measured rate of isomerization, the extent of intramolecularity would be a reflection of the degree of internal return involved in the exchange of the enamines.

(42) (a) S. Bank, C. A. Rowe, Jr., and A. Schriesheim, *J. Amer. Chem. Soc.*, 85, 2115 (1963); (b) J. Klein and S. Brenner, *Chem. Commun.*, 1020 (1969).

transfer.[43] The relative rates of ionization, calculated from the data in Table II and eq 3, are collected in Table III.

Table III. Relative Rates of Deprotonation of 1-Methyl-1,2-dihydro-1-benzazocine (**2**), 1-Methyl-1,6-dihydro-1-benzazocine (**3**), and Related Compounds in Potassium *tert*-Butoxide–Dimethyl-d_6 Sulfoxide–*tert*-Butyl Alcohol-*O*-*d*

Amines	$(k_1)_{rel}$	Enamines	$(k_{ex})_{rel}$
2	1.0	**3**	1.0
20	8.4	**22**	0.59
21	7.6	**19**	0.035
18	0.012		

The relative exchange rates in Table I do not reflect any special stabilization for the potentially aromatic dibenzazocinyl anion, which must intervene in the exchange of **1**. Although the tetrahydroazocine model **6** does in fact exchange more slowly (0.13 or 0.17), the acyclic model **8** is much faster.[44] Furthermore, *N*-methylphenanthridine (**7**) undergoes exchange at a rate of about one-half (0.51) that of **1**, despite the fact that the conjugate base of **7** possesses 8π electrons and is therefore formally antiaromatic.[45,46]

While the relative rates of deprotonation for the dihydrobenzazocines and the corresponding model compounds (Table III) show a comparable spread, the relative position of the dihydrobenzazocines **2** and **3** has moved closer to the acyclic analogs. Thus, **2** exhibits a kinetic acidity about 83 times that of 1,2-dihydroquinoline (**18**) and about one-eighth that of the two cinnamylamines (**20** and **21**).[48] The 1,6-dihydroazocine (**3**) actually exchanges more readily than the acyclic enamine **22** and about 30 times faster than *N*-methyl-1,4-dihydroquinoline (**19**). Although the rate differences are not large, it seems likely that the enhanced relative acidity of **2** and **3**, compared to **18** and **19**, has its origin in the different electronic configuration of the incipient heterocyclic carbanions.

The unstrained dihydroquinoline anion would be expected to permit more effective charge delocalization, yet it actually appears to be less stable. Although the greater stability of the azocinyl anion might be attributed to the extra conjugation afforded by the additional double bond, models indicate that none of the nonplanar conformations available to the anion (assuming either trigonal or tetrahedral hybridization) will permit effective overlap among all of the p orbitals simultaneously.

That the aromatic stabilization, if such it is, has become evident in the dihydrobenzazocinyl anion as compared to the dihydrodibenzazocinyl anion, is consistent with the previously observed dampening of aromaticity effects by benzannulation.[49] In addition, the fusion of the extra benzene ring in the dihydrodibenzazocinyl anion would be expected to increase the angle strain in the planar configuration necessary for optimal electron delocalization.[50,51] It should be noted, however, that *sym*-dibenzcyclooctatetraene dianion apparently exhibits "aromatic" character despite the presence of two flanking benzene rings.[52]

It is clear from the data in Tables I and III that any enhanced kinetic acidity of the dihydrobenzazocines **1–3** due to aromatic stabilization is relatively small. It is, of course, possible that the geometry of the transition state for deprotonation does not actually resemble the anion intermediate; thus, a large aromatic stabilization could have gone undetected in such kinetic measurements (see above). Nevertheless, the relatively small effects we have observed would seem to be consistent with currently available information on 10π electron heterocycles in which the heteroatom contributes an electron pair to the orbital system. Although a few[11c,12,13d] of the presently known heterocycles of this type[10–13] have given some evidence of aromaticity, the effects in these cases were also rather small. The bicyclic 4-azapentalenyl anion, although not strictly comparable owing to the additional 4–8 overlap, is considerably less stable than expected.[53] One factor which must seriously offset any aromatic stabilization of the azocinyl anions is the considerable angle strain associated with flattening the eight-membered ring.[2a,5c,54]

The faster relative rates of the acyclic amines **8**, **20**, and **21** may be a reflection of the conformational freedom in the intermediate anion.[44] In the absence of ring constraints, the respective acyclic carbanions are free to adopt a conformation in which conjugative stabilization is maximized and electronic repulsion with

(43) It is worth pointing out that the positional selectivity observed in the exchange of the 1,6-dihydrobenzazocine (see above) requires that there be no internal return in the deprotonation of the 1,2-dihydrobenzazocine (**2**). Since exchange at the 2 position of **3** is much slower than exchange at the 6 position, the collapse ratio[31a,b] in this case must be much greater than one, *i.e.*, $k_{-2}/k_{-1} \gg 1$. Thus, the rate of isomerization of **2** directly measures the true rate of deprotonation.

(44) It is possible that the structural differences between the cyclic and acyclic compounds are sufficient to alter external factors (*e.g.*, solvation) and hence invalidate interpretations of the data based on internal, structural factors.

(45) Antiaromaticity is defined as conjugative destabilization as opposed to conjugative stabilization predicted for acyclic structures: R. Breslow, J. Brown, and J. J. Gajewski, *J. Amer. Chem. Soc.*, **89**, 4383 (1967).

(46) A number of cyclic compounds with 8π electrons have been prepared including the cycloheptatrienyl anion[47a] and its pentaphenyl derivative,[47b] the seven-membered ring heterocycles azepin[47c] and oxepin,[47d] and various six-membered ring diheterocycles.[2,47e]

(47) (a) H. J. Dauben, Jr., and M. R. Rifi, *J. Amer. Chem. Soc.*, **85**, 3041 (1963); W. von E. Doering and P. P. Gaspar, *ibid.*, **85**, 3043 (1963); (b) R. Breslow and H. W. Chang, *ibid.*, **87**, 2200 (1965); (c) J. A. Moore and E. Mitchell, *Heterocycl. Compounds*, **9**, 224 (1967); L. A. Paquette in "Nonbenzenoid Aromatics," Vol. I, J. P. Snyder, Ed., Academic Press, New York, N. Y., 1969, p 250; (d) E. Vogel and H. Günther, *Angew. Chem., Int. Ed. Engl.*, **6**, 385 (1967); (e) W. Schroth, B. Streckenbach, and B. Werner, *Z. Chem.*, 7, 152 (1967); W. Schroth, F. Billig, and G. Reinhold, *Angew. Chem., Int. Ed. Engl.*, **6**, 698 (1967); M. Mazharuddin and G. Thyagarajan, *Tetrahedron*, **25**, 517 (1969).

(48) Although a careful study was not performed, the rate of exchange of *N*-methyl-*N*-benzylaniline (**8**) under the same conditions appeared to be less then 1/300th the rate of exchange of the *trans*-cinnamylamine (**20**).

(49) (a) Reference 31a, pp 65–66; (b) D. Meuche, H. Strauss, and E. Heilbronner, *Helv. Chim. Acta*, **41**, 57 (1958); G. Naville, H. Strauss, and E. Heilbronner, *ibid.*, **43**, 1221 (1960).

(50) K. Mislow and H. D. Perlmutter, *J. Amer. Chem. Soc.*, **84**, 3591 (1962).

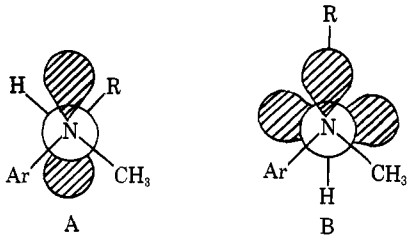
(51) The nmr spectrum (and in particular the singlet nature of the NCH_2 grouping) of **1** remained unchanged down to $-100°$. Thus, either the inversion barrier of **1** is low, or the chemical shifts of the potentially nonequivalent methylene protons are identical by coincidence. It should be noted that ring inversion with Dreiding models of **1** can be effected without actually proceeding through a planar transition state.

(52) T. J. Katz, M. Yoshida, and L. C. Siew, *J. Amer. Chem. Soc.*, **87**, 4516 (1965).

(53) W. H. Okamura and T. J. Katz, *Tetrahedron*, **23**, 2941 (1967); see also T. S. Cantrell and B. L. Harrison, *Tetrahedron Lett.*, 1299 (1969); H. Volz and B. Messner, *ibid.*, 4111 (1969); H. Volz, U. Zirngibl, and B. Messner, *ibid.*, 3593 (1970).

(54) F. A. L. Anet and L. A. Bock, *J. Amer. Chem. Soc.*, **90**, 7130 (1968).

the nitrogen lone pair is minimized (*e.g.*, A or B). Recent studies on the inversion and rotation rates in the



isoelectronic hydrazines have demonstrated barriers larger than the corresponding amines.[55] The electron repulsion between the adjacent filled p orbitals is evidently one important factor which increases the barrier to inversion and/or rotation.[56]

Experimental Section[57]

Materials. Tetrahydrofuran was distilled from lithium aluminum hydride and stored over sodium wire prior to use. Dimethyl-d_6 sulfoxide (DMSO-d_6, 99.6%, Stohler Isotope Chemicals or Merck Sharp and Dohme of Canada, Ltd) was used without further purification. *tert*-Butyl alcohol-*O*-*d* was prepared by the method of Cram and Rickborn[58] and shown to be 93% deuterated (Calcd for C_4H_9DO: D, 10.0 atom %. Found: D, 9.30 atom %). Potassium *tert*-butoxide (MSA Corporation) was sublimed once immediately prior to use.

5-Methyldibenz[*b*,*f*]azocin-6-one (46). Methyl iodide (25.7 g, 181 mmol) was added over a 30-min period to a refluxing solution of 4.0 g (18.1 mmol) of dibenz[*b*,*f*]azocin-6-(5*H*)-one (**4a**)[15b] and 6.0 g of potassium hydroxide in 200 ml of acetone. The acetone was removed under reduced pressure and the resulting residue was dissolved in ether. The ether solution was extracted with 10% hydrochloric acid, water, and saturated salt solution, dried (Na_2SO_4), and evaporated. The solid residue (4.0 g, 94%, mp 123–127°) was recrystallized from hexane–ethyl acetate to give pure **4b**: mp 127–129°; $\nu_{max}^{CCl_4}$ 3000, 1650, 1495, 1380, 1310, 1100 cm^{-1}; $\lambda_{max}^{ethanol}$ 265 mμ (log ε 4.20); τ 2.92 (m, 10 H), 6.67 (s, 3 H).

Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.57; H, 5.47; N, 5.84.

5-Methyl-5,6-dihydrodibenz[*b*,*f*]azocine (1). Lactam **4b** (2.9 g, 12.3 mmol) was added to a suspension of lithium aluminum hydride (2.3 g, 60.6 mmol) in 250 ml of refluxing ether by means of a Soxhlet extraction apparatus. The mixture was heated under reflux for 6.5 hr. The reduction complex was decomposed by the successive addition of 2.3 ml of water in tetrahydrofuran, 2.3 ml of 15% sodium hydroxide, and 6.9 ml of water. The resulting granular precipitate was filtered and washed with hot ether. The filtrate was dried (Na_2SO_4) and evaporated to give 2.9 g of a yellow oil. The oil was chromatographed on 120 g of silica gel by elution with 10–50% benzene in petroleum ether (bp 30–60°). Fractions containing **1** were combined and concentrated to give a yellow oil which crystallized upon storage in the cold. Recrystallization from petroleum ether (bp 30–60°) gave 2.4 g (88%) of **1** as yellow crystals: mp 63.5–65.0°; $\nu_{max}^{CCl_4}$ 3020, 2850, 1595, 1495, 1435, 1355, 1185, 1095, and 935 cm^{-1}; $\lambda_{max}^{ethanol}$ 264, 299 (sh), 375 mμ (log ε 4.23, 3.65, 3.36); $\lambda_{max}^{acid\ soln}$ 257 mμ (log ε 3.31); τ 3.03 (m, 8 H), 3.58 (s, 2 H), 5.84 (s, 2 H), and 7.27 (s, 3 H); mass spectrum, *m/e* 221 (M^+).

Anal. Calcd for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.92; H, 6.97; N, 6.37.

1-Methylamine-1′-hydroxymethyldibenzyl (5). A solution of **4b** (4.0 g, 17 mmol in 50 ml of tetrahydrofuran) was added dropwise over a 30-min period to a stirred suspension of lithium aluminum hydride (2.58 g, 68 mmol in 300 ml of tetrahydrofuran). The suspension was heated at reflux for 16 hr; then the product was isolated as described above. The oily product was dissolved in ether and extracted into 10% hydrochloric acid. The aqueous phase was neutralized with aqueous ammonium hydroxide and extracted with ether. The combined ether extracts were washed with water and brine, dried (Na_2SO_4), and evaporated. The solid residue was chromatographed on 120 g of silica gel eluting with petroleum ether (bp 30–60°)–benzene and benzene–ether mixtures. Combination of appropriate fractions afforded (in elution order) **1** (726 mg after recrystallization, 19%), an oil, and crystalline amino alcohol **5** (2.3 g, 56%). Recrystallization from ether–petroleum ether (bp 30–60°) gave pure **5**: mp 102–104°; $\nu_{max}^{CHCl_3}$ 3590, 3400, 2980, 1603, 1585, 1510, 1470, 1310, 1170, 995 cm^{-1}; $\lambda_{max}^{ethanol}$ 247, 298 mμ (log ε 4.01, 3.52); τ 3.08 (m, 8 H), 5.40 (s, 2 H, $-CH_2OH$), 6.85 (s, 2 H, OH, NH), 7.18 (m, 4 H, $-CH_2CH_2-$), 7.22 (s, 3 H); mass spectrum, *m/e* 241 (M^+, 53%), 120 (100%); diacetyl derivative (acetic anhydride, pyridine), ν_{max} 1740, 1665 cm^{-1}; τ 6.87 (s, 3 H, NCH_3), 7.92 (s, 3 H, CH_3CON), 8.27 (s, 3 H, CH_3CO_2).

Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.39; H, 7.84; N, 5.73.

5-Methyl-5,6,11,12-tetrahydrodibenz[*b*,*f*]azocine (6). Platinum oxide (100 mg) in 15 ml of ethyl acetate containing 832 mg (3.76 mmol) of **1** was stirred under hydrogen at atmospheric pressure. After 5.5 hr, more than the theoretical amount of hydrogen had been absorbed and the yellow solution had become clear. The solution was filtered, the solvent removed under reduced pressure, and the residue crystallized from petroleum ether (bp 30–60°), affording 681 mg (81%) of **6**: mp 56–57°; $\nu_{max}^{CCl_4}$ 3025, 2920, 1595, 1490, 1440, 1350, 1235, 1200, 1095, 1050, and 950 cm^{-1}; $\lambda_{max}^{ethanol}$ mμ (log ε), 260 (3.90); in acid solution, 263 (2.89); τ 3.04 (m, 8 H), 5.80 (s, 2 H), 6.83 (s, 4 H), 7.12 (s, 3 H); mass spectrum, *m/e* 223 (M^+).

Anal. Calcd for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 85.83; H, 7.50; N, 6.02.

5-Methyl-5,6-dihydrophenanthridine (7). The following procedure is a modification of that described by Sugasawa and Matsuo.[59] A solution of phenanthridine methiodide (19.2 g, 59.8 mmol),[60] silver nitrate (41.2 g, 242 mmol), and concentrated hydrochloric acid (35 ml) in 300 ml of ethanol was heated under reflux for 5 hr. The resulting precipitate was filtered while hot and the ethanol was evaporated under reduced pressure. The residue was dried and used without further purification.

A suspension of lithium aluminum hydride (1.5 g, 39 mmol) in 200 ml of tetrahydrofuran was heated to reflux in a Soxhlet extractor containing 2.0 g of the solid residue. After 11 hr (1.1 g had been extracted), the excess hydride was destroyed and the mixture acidified with hydrochloric acid. The tetrahydrofuran was removed under reduced pressure, and the aqueous solution was neutralized with ammonium hydroxide, and then extracted with ether. The combined ether solutions were washed with water and saturated salt solution, dried (Na_2SO_4), and evaporated. The slightly yellow oil so obtained solidified on cooling. Recrystallization from petroleum ether (bp 30–60°) gave 600 mg (66%): mp 44.5–46.0° (lit.[60] mp 46–48°); τ DMSO-d_6 2.82 (m, 8 H), 5.86 (s, 2 H), 7.14 (s, 3 H).

***N*-Methyl-*N*-benzylaniline (8).** This amine was prepared by the reaction of *N*-methylaniline and benzyl chloride in the presence of sodium bicarbonate at 100°.[61] The aniline was purified by distillation prior to use: bp 112° (0.5 mm) (lit.[62] bp 158–160° (8 mm)); τ^{CCl_4} 3.15 (m, 10 H, aromatic), 5.55 (s, 2 H, NCH_2), 7.06 (s, 3 H, NCH_3).

(55) S. J. Brois, *Tetrahedron Lett.*, 5997 (1968); J. E. Anderson, D. L. Griffith, and J. D. Roberts, *J. Amer. Chem. Soc.*, **91**, 6371 (1969); J. E. Anderson, *ibid.*, **91**, 6374 (1969); M. J. S. Dewar and W. B. Jennings, *Tetrahedron Lett.*, 339 (1970); J. R. Fletcher and I. O. Sutherland, *Chem. Commun.*, 687 (1970), and pertinent references cited.

(56) D. L. Griffith and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 4089 (1965); F. A. L. Anet, R. D. Trepka, and D. J. Cram, *ibid.*, **89**, 357 (1967); A. Rauk, L. C. Allen, and K. Mislow, *Angew. Chem., Int. Ed. Engl.*, **9**, 400 (1970).

(57) Infrared spectra were obtained in 10% carbon tetrachloride solutions with a Perkin-Elmer Infracord Model 137. Nmr spectra were recorded with a Varian A60A or A56/60 spectrometer, in deuteriochloroform solution with tetramethylsilane as an internal standard, unless otherwise noted. Ultraviolet spectra were obtained in absolute ethanol with a Cary 14 spectrometer. Mass spectra were determined by Mr. J. Wrona on an Atlas CH_4 mass spectrometer. Microanalyses were carried out in the University of Illinois microanalysis laboratory by Mr. J. Nemeth and associates. All melting points were taken in open capillary tubes using a Thomas Hoover apparatus and are uncorrected.

(58) D. J. Cram and B. Rickborn, *J. Amer. Chem. Soc.*, **83**, 2178 (1961).

(59) S. Sugasawa and H. Matsuo, *Chem. Pharm. Bull.*, **6**, 601 (1958).

(60) P. Karrer, L. Szabo, H. J. V. Krishna, and R. Schwyzer, *Helv. Chim. Acta*, **33**, 294 (1950).

(61) H. Gilman and A. H. Blatt, Ed., "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 102.

(62) V. L. Tweedie and J. C. Allabashi, *J. Org. Chem.*, **26**, 3676 (1961).

Benzo[2,3]tropone Oxime (10). A solution of 12.1 g (174 mmol) of hydroxylamine hydrochloride was prepared by dissolving the hydrochloride in a hot mixture of 90 ml of absolute ethanol and 70 ml of pyridine. Benzo[2,3]tropone[16] (8.9 g, 55.7 mmol) was added along with a wash solution of 20 ml of pyridine. The resulting solution was heated at reflux for 3 hr. The cooled pyridine–ethanol solution was evaporated under reduced pressure and the residue was recrystallized from hexane (bp 60–68°), yielding 4.1 g of **10** (42%) in 2 crops of crystals: first crop, 3.3 g (mp 103–105°); second crop, 0.8 g (mp 99–105°). Smaller runs were purified by column chromatography on alumina, then recrystallized several times from hexane: mp 105.5–106.5°; $\nu_{max}^{CHCl_3}$ 3580, 3240, 3000, 1640, 1595, 1490, 1455, 1325, 1290, 1080, 968, 925 cm^{-1}; τ 0.08 (br s, $H_{1/2}$ = 12 Hz, 1 H, O*H*), 2.20–2.86 (m, 4 H), 3.03–3.38 (m, 2 H), 3.52–3.98 (m, 2 H); *m/e* 171 (M^+, 88%), 154 (M − OH, 25%), 128 (M − NOH, 100%); benzene sulfonate derivative of **10** (see below): mp 116–117° (recrystallized from hexane–ethyl acetate); $\nu_{max}^{CHCl_3}$ 3030, 1640, 1590, 1570, 1480, 1445, 1370, 1185, 1090 cm^{-1}; τ 1.82–2.06 (m, 2 H), 2.20–2.75 (m, 7 H), 2.92–3.85 (m, 4 H).

Anal. Calcd for $C_{17}H_{13}NO_3S$: C, 65.57; H, 4.22; N, 4.50. Found: C, 65.43; H, 4.30; N, 4.27.

1-Benzazocin-2(1*H*)-one (11a). A solution of 4.0 g (23.4 mmol) of oxime **10** was dissolved in 100 ml of pyridine at 0°. After 4.7 g of benzenesulfonyl chloride (26.6 mmol) was added dropwise, the reaction solution was stirred for 30 min at 0° and then for 60 min at room temperature. The reaction was diluted with ether, filtered, and evaporated under reduced pressure without further purification. The residue (for properties and purification, see above) was dissolved in 100 ml of acetone and 80 ml of water, and then heated at reflux for 40 hr. The acetone was evaporated under reduced pressure and the remaining aqueous solution was extracted three times with ether. The combined ether phases were washed with water and brine, dried (Na_2SO_4), and evaporated. The residue was then recrystallized from methylene chloride–hexane (bp 60–68°) to afford 2.7 g (68% from **10**) of **11a**. An analytical sample was recrystallized from petroleum ether (bp 90–110°)–ethyl acetate: mp 170.5–171.5°; $\nu_{max}^{CHCl_3}$ 3400, 3170, 2950, 1655, 1570, 1485, 1450, 1415, 1395, 1335, 1225, 1105 cm^{-1}; τ^{DMSO-d_6} 0.56 (br s, $H_{1/2}$ = 6 Hz, 1 H, –N*H*), 2.57–3.37 (m, 5 H), 3.55–4.02 (m, 3 H).

Anal. Calcd for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.26; H, 5.30; N, 7.91.

1-Methyl-1-benzazocin-2-one (11b). A solution of 1.175 g (6.90 mmol) of **11a** and 1.5 g (26.8 mmol) of potassium hydroxide in 30 ml of acetone was heated to reflux. A second solution containing 4.3 ml (69.0 mmol) of methyl iodide in 10 ml of acetone was added dropwise over a 30-min period. After 60 min of additional refluxing, the cooled acetone solution was evaporated under reduced pressure. The residue was dissolved in ether, and the ether solution was extracted twice with 5% hydrochloric acid, twice with water, and once with brine, dried (Na_2SO_4), and evaporated to dryness under reduced pressure. The residue (1.1 g) was recrystallized from hexane (bp 30–60°) to afford 971 mg (76.5%) of **11b**: mp 111–115°; analytical sample was recrystallized twice more from hexane; mp 115.5–116.5°; $\nu_{max}^{CHCl_3}$ 3010, 1647, 1610, 1573, 1496, 1445, 1395 cm^{-1}; τ 2.55–2.92 (m, 4 H, aromatic), 3.05–4.04 (m, 4 H, vinyl), 6.78 (s, 3 H, –NC*H*$_3$).

Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.80; H, 6.18; N, 7.58.

1-Methyl-1,2-dihydro-1-benzazocine (2). A suspension of aluminum hydride [prepared by the method of Jorgenson[19a] from 590 mg (4.42 mmol) of aluminum chloride and 604 mg (15.9 mmol) of lithium aluminum hydride] in 30 ml of ether was cooled to 0°. Amide **11b** (1.0 g, 5.41 mmol) was added, followed by 20 ml of ether, to increase the solubility of **11b**. The ether solution was stirred for 75 min at 0° and the hydride quenched as previously described. The resulting yellow solution was filtered, evaporated, and chromatographed on 40 g of silica gel eluting with increasing proportions of ether in petroleum ether (bp 30–60°). After removing the solvent under reduced pressure, 750 mg (81%) of a yellow oil was recovered. Reduction of **11b** with lithium aluminum hydride (45 min, 0°) afforded a 72% yield of **2**: bp ~85° (0.1 mm) (short-path distillation); ν_{max}^{neat} 2990, 2830, 2770, 1595, 1495, 1445, 1370, 1295, 1190, 1090, 950 cm^{-1}; $\lambda_{max}^{ethanol}$ 225, 398 mμ (log ε 4.27, 2.89); $\tau_{100\ MHz}^{CCl_4}$ 2.80–3.25 (m, 4 H, aromatic), 3.67 (d, $J_{5,6}$ = 12 Hz, 1 H, ArC*H*=), 3.88–4.28 (m, 3 H, vinyl), 6.18 (d, $J_{2,3}$ = 4.5 Hz, 2 H, NCH_2, three-line pattern at 60 MHz), 7.18 (s, 3 H, NCH_3); *m/e* 171 (M^+, 80%), 144 (100%).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.08; H, 7.70; N, 8.18.

1-Methyl-1,2,3,4,5,6-hexahydro-1-benzazocine (12). A solution of 199 mg (1.16 mmol) of **2** and 30 mg of platinum oxide in 5.0 ml of ethyl acetate was stirred under an atmosphere of hydrogen at room temperature. After 3 hr, more than the theoretical amount of hydrogen had been absorbed, and the solution had become almost colorless. The solution was filtered, dried (Na_2SO_4), and evaporated under reduced pressure. Chromatography on 12 g of silica gel eluting with 1–4% ether in petroleum ether (bp 30–60°) gave 180 mg (88.5%) of **12**, which was purified further by preparative glc (5 ft, 20% SE column, 127°) to afford a colorless liquid: ν_{max}^{neat} 2900, 2770, 1605, 1580, 1495, 1380, 1290, 1110 cm^{-1}; τ^{CCl_4} 2.85–3.10 (m, 4 H, aromatic), 7.12–7.38 (m, including NCH_3 singlet at 7.27, 7 H, NCH_3, ArCH_2, NCH_2), 8.25–8.47 (m, 4 H, H_3 and H_5), 8.62–9.00 (m, 2 H, H_4).

Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.32; H, 9.77; N, 8.29.

1-Methyl-3,4,5,6-tetrahydro-1-benzazocin-2-one (13). A solution of 150 mg (0.812 mmol) of **11b** and 34 mg of platinum oxide in 5.0 ml of ethyl acetate was stirred under an atmosphere of hydrogen. After 3 hr at room temperature, the reaction appeared to be complete (glpc, 5 ft, 3% SE 30, 170°). The solution was filtered and evaporated under reduced pressure. Chromatography on 3.5 g of silica gel eluting with increasing proportions of ether in petroleum ether (bp 30–60°) gave 140 mg (91.5%) of **13**: mp 57–60°; analytical sample recrystallized twice from petroleum ether (bp 30–60°); mp 60–61.5°; $\nu_{max}^{CHCl_3}$ 2900, 1625, 1485, 1445, 1380, 1135, 1105 cm^{-1}; τ 2.65–2.90 (m, 4 H, aromatic), 6.70 (s, 3 H, NCH_3), 7.0–8.9 (br m, 8 H, –$(CH_2)_4$–).

Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.31; H, 7.98; N, 7.14.

Lithium Aluminum Hydride Reduction of 13. A solution of 63 mg (0.334 mmol) of **13** in 10 ml of ether was added dropwise to a suspension of 50 mg (1.32 mmol) of lithium aluminum hydride in 10 ml of ether at 0°. The combined mixture was stirred at 0° for 40 min and at room temperature for 20 min. After the reduction complex was destroyed as described previously, the ether solution was filtered, washed with water and then with brine, dried (Na_2SO_4), and evaporated under reduced pressure. The nmr spectrum of the resulting crude material was identical with that of **12** (with the exception of an impurity peak at τ 2.0). Preparative glc (5 ft, 20% SE 30, 127°) afforded 40 mg (68.5%) of pure amine. The infrared spectrum of the reduction product is identical with the spectrum of **12**; *m/e* 175 (M^+, 100%), 144 (56%), 132 (62%); picrate (recrystallized from 95% alcohol), mp 171.5–172.5° dec (lit. mp[20] 171–172° dec).

1-Methyl-1,6-dihydro-1-benzazocine (3). A solution of 365 mg (2.14 mmol) of **2** and 1.95 ml of 1.11 *M* potassium *tert*-butoxide (2.14 mmol, not sublimed) in 4.0 ml of tetrahydrofuran was stirred for 15 hr at room temperature. The reaction solution was poured into 20 ml of 10% ether–petroleum ether (bp 30–60°) and extracted with a 5% solution of sodium bicarbonate (20 ml). The aqueous phase was washed with ether, and the ether phases combined, washed with 5% sodium bicarbonate, dried (Na_2SO_4), and evaporated. Short-path distillation (0.1 mm, oil bath at 190°) afforded 150 mg (41%) of **3** and a polymeric residue: ν_{max}^{neat} 3000, 2900, 1615, 1485, 1365, 1260, 1185, 1095 cm^{-1}; $\tau_{100\ MHz}^{DMSO-d_6}$ 2.65–3.10 (m, 4 H, aromatic), 3.98 (d, $J_{2,3}$ = 11.0 Hz, 1 H, H_2), 4.27 (d t, $J_{4,5}$ = 10.2 Hz, $J_{5,6}$ = 7.6 Hz, 1 H, H_5), 4.66 (dd, $J_{3,4}$ = 6.3 Hz, $J_{4,5}$ = 10.2 Hz, 1 H, H_4), 5.93 (2d, J = 11, 6.3 Hz, 1 H, H_3), 6.02 (d, $J_{5,6}$ = 7.6 Hz, 2 H, H_6) 6.87 (s, 3 H, NCH_3); decoupling experiments, irradiate at τ 4.01 ($H_3 \rightarrow$ d), 4.26 ($H_6 \rightarrow$ s), 4.68 ($H_3 \rightarrow$ d), 5.95 ($H_2 \rightarrow$ s, $H_5 \rightarrow$ d, $H_4 \rightarrow$ d); *m/e* 171 (M^+, 100%), 144 (62%).

1-Methyl-1,2,3,6-tetrahydro-1-benzazocine (14). A solution of 155 mg (0.907 mmol) of **2** in 5 ml of tetrahydrofuran was treated with 1.2 ml (1.80 mmol) of 1.5 *M* potassium *tert*-butoxide in tetrahydrofuran. The solution was stirred for 2 hr at room temperature and then the solvent was evaporated under a stream of nitrogen. The resulting residue was dissolved in a 50:50 mixture of hexane (bp 60–68°)–benzene; this solution was then decanted and evaporated. After a portion (23 mg) was removed for spectral studies, the remaining oil was dissolved in 5.0 ml of methanol; then excess sodium borohydride was added in small portions. After stirring the reaction at room temperature for 90 min and then heating to reflux for 3 hr, the reduction appeared to be complete according to glpc (5 ft, 3% SE 30, 137°). Ether and water were added and the aqueous phase, after separation, was reextracted with ether. The combined ether solutions were extracted twice with water and once with brine, dried (Na_2SO_4), and evap-

orated to dryness. The resulting oil was chromatographed on 10 g of silica gel eluting with increasing proportions of ether in petroleum ether (bp 30–60°). Fractions containing **14** were combined to afford 52 mg (39% from **2**). An analytical sample was obtained by preparative glpc (5 ft, 20% SE 30, 161°): ν_{max} 3000, 2900, 2770, 1595, 1490, 1450, 1285, 1090, 1040 cm^{-1}; $\lambda_{max}^{cyclohexane}$ 263 mμ (log ε 3.66); λ_{sh}^{EtOH,H^+} 207 (3.96), λ_{min} 235 (2.61), λ_{max} 257, 262, 270 (2.79, 2.81, 2.70);[63] τ^{CCl_4} 2.82–3.17 (m, 4 H, aromatic), 4.25–4.48 (m, 2 H, vinyl), 6.58 (d, $J_{5,6}$ = 4.5 Hz, 2 H, H_6), 6.98 (t, $J_{2,3}$ = 5.5 Hz, 2 H, H_2), 7.15 (NCH_3), 7.92 (q, J = 6 Hz, 2 H, H_3); *m/e* 173 (M^+, 100%), 144 (64%).

Anal. Calcd for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.08. Found: C, 83.10; H, 8.80; N, 7.87.

1-Methyl-1,2-dihydroquinoline (18). Amine **18** was prepared by the method of Sutter-Kostic and Karrer;[25] however, simple distillation did not remove the impurity (**19**): bp 65° (0.15 mm) (lit.[25] bp 80° (0.08 mm)); $\lambda_{max}^{cyclohexane}$ 232.5, 288, 348 (log ε 4.67, 3.56, 3.55) (lit.[25] λ_{max}^{EtOH} 230, 290, 345 (log ε 4.41, 3.42, 3.31)); ν_{max}^{neat} 3010, 2770, 1660, 1640, 1595, 1495, 1550, 1305, 1210, 1095, 1045 cm^{-1}; τ (DMSO-d_6–*tert*-BuOD) (DMSO-d_5 τ 7.48, internal standard) 2.72–3.75 (m, 5 H, aromatic), 4.28 (dt, $J_{3,4}$ = 9.8 Hz, $J_{2,3}$ = 4.0 Hz, 1 H, =C*H*CH_2), 5.98 (dd, $J_{2,4}$ = 1.8 Hz, 2 H, NCH_2), 7.32 (s, 3 H, NCH_3).

1-Methyl-1,4-dihydroquinoline (19). A solution of 2.85 g (19.7 mmol) of **18** in 15 ml of dimethyl sulfoxide was treated with 1.88 g (16.8 mmol) of potassium *tert*-butoxide (not sublimed). The black solution was left at room temperature for 4.5 hr, and then the products were isolated by the same procedure used for **3**. Vacuum distillation (67° (0.3 mm)) afforded 1.63 g (59%) of **19**. Pure 1,4-dihydro compound was extremely heat and air sensitive, but appeared to be stable at −78°, or in solution, for periods up to 12 hr: ν_{max}^{neat} 3040, 2880, 2790, 1655, 1595, 1490, 1350, 1290, 1230, 1090, 1043, 1010 cm^{-1}; $\tau^{DMSO\text{-}d_6}$ (DMSO-d_5 τ 7.48, internal standard) 2.72–3.68 (m, 4 H, aromatic), 3.93 (dt, $J_{2,3}$ = 7.8 Hz, $J_{2,4}$ = 1.5 Hz, 1 H, H_2), 5.52 (quintet, $J_{3,4}$ = 3.8 Hz, 1 H, H_3), 6.48 (d, 2 H, H_4), 6.99 (s, 3 H, NCH_3).

1-Methyl-1,2,3,4-tetrahydroquinoline (23). A solution of 312 mg (2.15 mmol) of **19** in 10 ml of methanol was treated with excess sodium borohydride in several portions. The methanol solution was heated to reflux, while continuing to add sodium borohydride, for 5 hr. After isolation by the same procedure used for compound **26** (see below), 205 mg (65%) of **23** was recovered, and then purified by preparative glc (5 ft, 20% SE 30, 118°): ν_{max}^{neat} 2925, 1600, 1500, 1345, 1093, 1057, 1002, 740 cm^{-1}; τ 2.80–3.63 (m, 4 H, aromatic), 6.85 (t, $J_{3,4}$ = 5.5 Hz, 2 H, H_2), 7.18 (s, NCH_3, lit.[64a] 7.18), 7.27 (t, $J_{2,3}$ = 6.5 Hz (5 H (includes NCH_3), H_4), 8.18 (quintet, 2 H, H_3); *m/e* 147 (M^+, 87%), 146 (M − 1, 100%).

The nmr and ir spectra of **23** are identical with spectra of the product obtained from hydrogenation of **18** (PtO_2, 1 atm of H_2, room temperature, 6.5 hr); picrate (recrystallized from ethanol) mp 121–122° (lit. mp 121,[64b] 125°[64a]).

***N*-Methyl-*trans*-cinnamanilide (24).** A solution of *trans*-cinnamoyl chloride (25.8 g, 155 mmol) in 150 ml of benzene was added dropwise to a stirred solution of freshly distilled *N*-methylaniline (15.0 g, 140 mmol) in 150 ml of benzene and 150 ml of pyridine. The combined solution was stirred for 2 hr at room temperature, and then poured into water. The organic phase was washed with 5% sodium hydroxide, 10% hydrochloric acid, water, and finally with brine, and then dried (Na_2SO_4) and evaporated to dryness. The solid residue (mp 70–72°) was recrystallized from ethyl acetate–hexane (bp 60–68°) affording 32.8 g (98.7%) of **24**: mp 71.5–72.5° (lit.[27] mp 70°); $\nu_{max}^{CHCl_3}$ 2995, 1650, 1613, 1595, 1495, 1450, 1420, 1380, 1125 cm^{-1}; τ 2.32 (d, $J_{2,3}$ = 15.5 Hz, 1 H, Ar-C*H*=), 2.52–2.92 (m, 10 H, phenyl), 3.65 (d, 1 H, COC*H*=), 6.60 (s, 3 H, NCH_3).

***N*-Methyl-*N*-*trans*-cinnamylaniline (20).** A solution of **24** (12.0 g, 50.7 mmol) and 75 ml of tetrahydrofuran was added dropwise to a solution of aluminum hydride (56.0 mmol) in 130 ml of tetrahydrofuran at 0°. The aluminum hydride was prepared[19a] from lithium aluminum hydride (1.65 g, 43.4 mmol) and aluminum chloride (1.87 g, 14.0 mmol). After addition of **24**, the resulting solution was stirred at 0° for 30 min. The reduction complex was decomposed as described above. The filtered tetrahydrofuran solution was combined with an earlier run prepared in the same manner using 4.0 g (16.9 mmol) of **24**. The combined solutions were dried (Na_2SO_4) and evaporated to dryness. Distillation of the resulting oil (15.4 g) gave 8.6 g (56.5%): bp 142–152° (0.4 mm) (lit.[26] 153° (0.33 mm)); ν_{max}^{neat} 3025, 1598, 1503, 1448, 1350, 1115, 963, 741, 683 cm^{-1}; τ 2.62–3.02 (m, 7 H, phenyl), 3.15–3.47 (m, 3 H, phenyl), 3.50, 3.88 (ABX_2, pattern, $J_{2,3}$ = 15.5 Hz, $J_{1,2}$ = 4.5 Hz, 2 H, $-CH_2CH{=}CH-$), 6.04 (d, 2 H, NCH_2), 7.10 (s, 3 H, NCH_3); picrate (recrystallized from alcohol), mp 126–127° dec (lit.[26] 127–128° dec).

***N*-Methyl-*cis*-cinnamanilide (25).** A solution of **24** (2.0 g, 5.94 mmol) in 200 ml of absolute ethanol was irradiated (Pyrex filter, Hanovia 450-W medium-pressure mercury lamp) for 5.5 hr. The mixture at equilibrium contained 53% cis compound as determined by glc (5 ft, 5% SE 30, 203°). Two such runs were combined and then chromatographed on 90 g of silica gel eluting with increasing proportions of ether in petroleum ether (bp 30–60°). The fractions eluted with 50 and 100% ether contained 3.85 g (96.5%) of the cis and trans amides. Compound **25** was separated from **24** by preparative glc (5 ft, 20% SE 30, 219°); the analytical sample was prepared by a second pass through the preparative glc column: mp 48.5–49.5°; $\nu_{max}^{CHCl_3}$ 3005, 1642, 1590, 1490, 1427, 1356, 1295, 1125 cm^{-1}; τ 2.54–3.20 (m, 10 H, phenyl), 3.61, 4.17 (AB dd, $J_{2,3}$ = 12.5 Hz, 2 H, vinyl), 6.72 (s, 3 H, NCH_3).

Anal. Calcd for $C_{16}H_{15}NO$: C, 80.96; H, 6.37; N, 5.90. Found: C, 80.70; H, 6.59; N, 5.91.

***N*-Methyl-*N*-*cis*-cinnamylaniline (21).** The mixture of cis and trans amides (3.5 g, 14.8 mmol) obtained from photolysis of **24** was dissolved in 20 ml of tetrahydrofuran and reduced with aluminum hydride by the same procedure used for the reduction of **24**. The solution was stirred for 45 min at 0° and quenched as described above. The resulting oil was chromatographed on 90 g of silica gel eluting with increasing proportions of ether in petroleum ether (bp 30–60°). The 2 and 4% ether fractions contained 2.5 g (76%) of cis and trans anilines. The cis aniline was separated by preparative glpc (5 ft, 20% SE 30, 180°): ν_{max} 3022, 1598, 1503, 1445, 1365, 1245, 1200, 1110, 1033, 992 cm^{-1}; τ^{CCl_4} 2.70–3.10 (m, 7 H, phenyl), 3.28–3.60 (m, 4 H, phenyl + Ar-C*H*=), 4.36 (quintet, $J_{1,2}$ = 5.8 Hz, $J_{2,3}$ = 11.6 Hz, 1 H, $-CH_2CH{=}$), 5.86 (dd, $J_{1,3}$ = 1.5 Hz, 2 H, NCH_2), 7.15 (s, 3 H, NCH_3).

Anal. Calcd for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 86.02; H, 7.67; N, 6.28.

***N*-Methyl-*N*-(3-phenyl-1-propenyl)aniline (22).** (a) A solution of 3.0 g (13.5 mmol) of freshly distilled **20** was dissolved in 20 ml of dry tetrahydrofuran under a nitrogen atmosphere. Potassium *tert*-butoxide (3.0 g, 26.8 mmol, not sublimed) was added, and the reaction was stirred at room temperature for 30 min. After approximately half the solvent was evaporated under reduced pressure, 30 ml of a 1:1 mixture of benzene–hexane (bp 60–68°) was added. The resulting solution was extracted twice with water and once with brine dried (Na_2SO_4), and evaporated under reduced pressure. The residue was distilled at 126–129° (0.1 mm) to afford 2.17 g (77.5%) of **22**: ν_{max}^{neat} 3020, 2880, 1648, 1595, 1500, 1324, 742, 688 cm^{-1}; λ_{max} 250, 281.5 mμ (log ε 4.01, 4.25); $\tau^{benzene}$ 5.30 (quintet, $J_{1,2}$ = 13.5 Hz, $J_{2,3}$ = 7.0 Hz, 1 H, $CH_2CH{=}$), 6.65 (d, 2 H, NCH_2), 7.30 (s, 3 H, NCH_3).

Anal. Calcd for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 85.86; H, 7.87; N, 6.30.

(b) A solution of 8.50 mg (0.381 mmol) of **21** was dissolved in 0.30 ml of dimethyl sulfoxide in an nmr tube. An aliquot (0.070 ml, 0.109 mmol) of 1.53 *M* potassium *tert*-butoxide was added. The resulting nmr spectrum was identical with the nmr spectrum (in dimethyl sulfoxide) of **22** prepared from **20**.

***N*-Methyl-*N*-3-phenylpropylaniline (26).** A solution of 190 mg (0.855 mmol) of **22** was dissolved in 10 ml of methanol. Sodium borohydride was added, and the methanol solution was heated to reflux. More sodium borohydride was added in several portions until the reaction was complete (6 hr, followed by glpc, 5% SE 30, 180°). Water (20 ml) and ether (20 ml) were used to extract the methanol solution, while the aqueous phase was extracted with fresh ether. The combined organic phases were extracted three times with 10 ml of 10% hydrochloric acid. The acidic solutions were neutralized with concentrated ammonium hydroxide, and then extracted three times with ether. The combined ether phases were extracted twice with water and once with brine, dried (Na_2SO_4), and evaporated. The resulting oil was chromatographed on 10 g of silica gel eluting with increasing proportions of ether in petroleum ether (bp 30–60°). Evaporation of 2, 4, and 8% ether fractions afforded 105 mg (54.5%) of **26**. Further purification was accomplished by preparative glpc (5 ft, 20% SE 30, 183°): ν_{max}^{neat} 3005, 2900, 1600, 1500, 1450, 1370, 1300, 1045, 1002 cm^{-1}; τ 2.65–

(63) The log ε values for **14** in acidified ethanol were calculated with respect to λ_{max}^{EtOH} 264, and assuming that $\epsilon_{264}^{EtOH} = \epsilon_{263}^{cyclohexane}$.

(64) (a) T. Kametani and K. Kigasawa, *Chem. Pharm. Bull.*, **14**, 566 (1966); (b) P. J. Scheuer, W. I. Kimoto, and K. Ohinata, *J. Amer. Chem. Soc.*, **75**, 3029 (1953).

2.98 (m, 7 H, phenyl), 3.22–3.48 (m, 3 H, phenyl), 6.68 (t, $J_{1,2}$ = 7.2 Hz, 2 H, H_1), 7.12 (s, 3 H, NCH_3), 7.35 (t, $J_{2,3}$ = 7.5 Hz, 2 H, H_3), 8.10 (m, 2 H, H_2); *m/e* 225 (M^+, 19.5%), 120 (100%); picrate (recrystallized from ethanol) mp 132–133° (lit.[65] mp 133–134°).

General Method for Exchange Kinetics of 1 and 6–8. In a given series of kinetic runs, all compounds whose relative rates were to be compared were studied one after the other in as short a time period as possible. The same base solution was used throughout the run. The potassium *tert*-butoxide solution was prepared for each series of runs immediately prior to use by dissolving in DMSO-d_6 to 1.5 *M*. The base was handled and weighed in an argon atmosphere.

The molarity of the base solution was determined by titration with 0.01 *M* (or 0.1 *M*) hydrochloric acid solution using phenolphthalein as an indicator. After the kinetic run was complete (except for the runs at 0.026 *M* base concentration) one or more aliquots of the reaction mixture were withdrawn, quenched with water, and titrated as above. In all reported runs the base concentration of the reaction mixture was the same as the initial base concentration within ±10%. All glassware used in the kinetics was dried at 140° for at least 8 hr. All compounds used were dried under reduced pressure in a drying pistol for at least 8 hr.

A typical kinetic run proceeds as follows: 65.0 mg (0.292 mmol) of **1** was transferred to an nmr tube and covered (under nitrogen) with a 5-mm serum cap. Shortly before the kinetics were performed, 0.300 ml of DMSO-d_6 was added by means of a syringe. The base solution was prepared immediately prior to use by dissolving 370.2 mg of 3.30 mmol of potassium *tert*-butoxide in 2.20 ml of DMSO-d_6 under an argon atmosphere.

After the azocine had dissolved, the nmr tube was placed in the nmr probe and equilibrated for 15–20 min at the probe temperature (~42°). An aliquot (0.100 ml) of the stock base solution was injected into the azocine solution, and the tube was shaken for 30 sec before being placed back into the probe. The integrals of the vinyl (τ 3.54), *N*-methylene (τ 5.88), and *N*-methyl (τ 7.34) positions were scanned every minute for 15 min. For all compounds the *N*-methyl position was used as a standard of three hydrogens. For **1**, the use of the vinyl protons as a standard gave the same rate constant within experimental error.

A plot of the natural logarithm of the number of hydrogens at the *N*-methylene position at a given time over the number of hydrogens at time zero (2) *vs.* time gave a good straight line (see Figure 1). A least-squares program run on the IBM 1800 computer gave the slope and intercept for the best straight line. The rate constants are reported in Table I.

General Method for Isomerization and Exchange Kinetics of 2, 3, and 18–22. In general, the procedure previously given was followed; however, the following differences should be noted. The solvent used in these runs was either a 41.6 or a 64.5% (volume per cent) dimethyl-d_6 sulfoxide–*tert*-butyl alcohol-*O*-*d* mixture. The cosolvents were mixed and sealed in a glass ampoule before use. Solvent from the same batch was used for all runs requiring that solvent percentage.

The potassium *tert*-butoxide solution was prepared in dimethyl-d_6 sulfoxide as described previously. For runs using the 64.5% dimethyl-d_6 sulfoxide, a 0.100-ml aliquot of the prepared base solution was injected into the sample. For runs at the 41.6% dimethyl-d_6 sulfoxide, a 0.05-ml aliquot of base was injected into the nmr tube. The base concentration was determined by titration before injection into the solution of the compound to be studied.

All compounds used were either distilled before use or distilled and sealed in ampoules under a nitrogen atmosphere and stored at 0°. It was necessary to store **18** and **19** at −78°. In all cases, 0.420 mmol of a given compound was weighed into an nmr tube. It was necessary to store the dimethyl-d_6 sulfoxide solutions of the enamines **3**, **19**, and **22** at −78° prior to use in a kinetic run.

The rate of exchange at the methylene group of the enamines was determined as described above, *i.e.*, integration of the methylene and *N*-methyl absorptions at various times. For the amines, the rate of exchange was obtained by integration of the *N*-methylene with respect to the *N*-methyl bands for both the amine starting material and the enamine product. The rate of isomerization is then determined from the ratio of the two *N*-methyl integrations. A least-squares computer program was used to convert the integration data into exchange and isomerization rates. Graphical plots of the data gave in most cases good straight lines (for exceptions see Discussion and ref 32) with individual points deviating less than ±8%. A kinetic plot for the **2** → **3** isomerization is shown in Figure 3; the observed rate constants and relative rates are collected in Table II.

5-Methyl-5,6-dihydrodibenz[*b*,*f*]azocine-d_2 (1-d_2). After at least 12 hr in potassium *tert*-butoxide–DMSO-d_6, the completed kinetic runs were quenched with D_2O, combined (three runs—theoretical yield of 146 mg), and the starting material was recovered. As much solvent as possible was evaporated under a stream of nitrogen. Chromatography of the resulting oil on 10 g of silica gel eluting with 1–50% benzene in petroleum ether (bp 30–60°) gave 130 mg of pure **1**-d_2 (89%): mp 63.0–64.5°; mmp with **1**, 62.5–64.5°; $\nu_{max}^{CCl_4}$ 2130, 2060 cm^{-1}. The nmr spectrum was identical with **1** except for the disappearance of the singlet at τ 5.84. The deuterium distribution was 10.0% d_1, 85.2% d_2, 4.9% d_3 (mass spectrum).

Anal. Calcd for $C_{16}H_{13}D_2N$: D, 13.33 atom %. Found: D, 13.05 atom %.

5-Methyl-5,6,11,12-tetrahydrodibenz[*b*,*f*]azocine-d_4 (6-d_4). Using the procedure described for **1**-d_2, 121 mg (82.5%) of crystalline **6**-d_4 was recovered from the kinetic runs. Recrystallization from petroleum ether (bp 30–60°) gave pure **6**-d_4; mp 55–57°; mmp with **6**, 55–57°; $\nu_{max}^{CCl_4}$ 2200, 2160, 2070 cm^{-1}.

The nmr spectra shows the peaks at τ 3.04 and 7.12 unchanged. However, the singlets at τ 5.80 and 6.83 show a considerable decrease in intensity (relative areas compared to the methyl singlet at τ 7.12 are 0.17:1.75:3.00). On this basis, the recovered material contains 4.08 deuterium atoms. The mass spectrum shows the parent peak at 10 eV to have an *m/e* of 227 and gives the following isotope ratio: 4.8% d_6, 24.8% d_5, 51.3% d_4, 16.4% d_3, and 2.7% d_2 or a total of 4.13 deuteriums/molecule.

5-Methyl-5,6-dihydrophenanthridine-d_2 (7-d_2). A sample of 112 mg (0.575 mmol) of **7** was added to 62 mg (0.44 mmol) of potassium *tert*-butoxide in an erlenmeyer flask under an argon atmosphere. DMSO-d_6 (0.80 ml) was injected through the serum cap stopper and the resulting solution was stirred for 5.5 hr. The reaction was quenched with D_2O and the solvent was evaporated under a stream of nitrogen. The resulting oil crystallized upon standing overnight at −20° (103 mg, 91%). Recrystallization from petroleum ether (bp 30–60°) gave pure **7**-d_2; mp 43–44.5°; mmp with **7**, 43–45°.

The nmr spectra shows the peaks at τ 2.82 and 7.14 unchanged. However, the singlet at τ 5.86 has decreased by approximately 90%. The mass spectrum at 10 eV shows the parent peak to have a *m/e* of 197 and shows an isotope ratio of 82.8% d_2, 9.0% d_1, and 8.1% d_0 or at least 1.74 deuteriums/molecule.

***N*-Methyl-*N*-benzylaniline-d_2 (8-d_2).** A solution of 0.23 ml (~1.27 mmol) of **8** and 165 mg (1.46 mmol) of potassium *tert*-butoxide in 1.6 ml of dimethyl-d_6 sulfoxide was stirred at room temperature for 30 min, and then quenched with deuterium oxide. After the solvent had been partially evaporated under a stream of nitrogen, water and ether were added. The ether solution was extracted with water, dried (Na_2SO_4), and evaporated under reduced pressure. Chromatography on 10 g of silica gel eluting with 1–50% benzene in petroleum ether (bp 30–60°) gave relatively pure **8**-d_2. Two passes through a preparative glpc column (5 ft, 20% SE 30, 200°) furnished an almost colorless analytical sample; $\nu_{max}^{CCl_4}$ 2120, 2080 cm^{-1}. The nmr spectrum shows the complete disappearance of the singlet at τ 5.55.

Anal. Calcd for $C_{14}H_{13}D_2N$: D, 13.33 atom %. Found: D, 12.40 atom %.

Deuteration of 3. The continued deuterium incorporation into **3** was followed by nmr after the initial methylene exchange (64.6% dimethyl-d_6 sulfoxide–*tert*-butyl alcohol-*O*-*d*). The following peak changes were noted (the aromatic and *N*-methyl protons were unchanged): after 4.5 hr (~1:1, **3**-*6,6*-d_2:**3**-*6,6,4*-d_3), τ 3.99 (d, $J_{2,3}$ = 11 Hz, H_2), 4.27 (br d, J_{obsd} ~ 4 Hz, H_5), 4.64 (AB dd, J = 6, 10 Hz, H_4 in **3**-d_2), 5.86 (d, $J_{2,3}$ = 11 Hz, H_3 in **3**-d_3), 5.86 (dd, $J_{2,3}$ = 11 Hz, $J_{3,4}$ = 6 Hz, H_3 in **3**-d_2); after 72 hr (**3**-*6,6,4*-d_3), τ 3.99 (d, $J_{2,3}$ = 11 Hz, H_2), 4.27 (br s, H_5), 5.86 (d, $J_{2,3}$ = 11 Hz, H_3).

Treatment of **2** with potassium *tert*-butoxide (1.5 *M*) in dimethyl-d_6 sulfoxide for 30 min at ±42° gave the following nmr data as expected for **3**-*6,6,4,2*-d_4: τ 4.27 (br s, H_5), 5.86 (br s, H_3).

1-Methyl-1,2,3,5-tetrahydro-1-benzazocine-d_3 (14-*4,6,6*-d_3). After 72 hr at room temperature, deuterated **3** was recovered by extracting the contents of four kinetic runs (two runs of **2** and two runs of **3** in 64.6% dimethyl-d_6 sulfoxide/0.100 ml of 1.2 *M* potassium *tert*-butoxide, 282 mg, 1.65 mmol) with 10% ether–petroleum ether (bp 30–60°) and 5% sodium bicarbonate. The aqueous layer was extracted once more with the same solvent mixture. The combined organic phases were extracted twice with 5% sodium

(65) D. A. Archer and H. Booth, *J. Chem. Soc.*, 322 (1963).

bicarbonate and once with brine, dried (Na_2SO_4), and evaporated. The resulting oil was dissolved in methanol and treated with sodium borohydride as described earlier for the preparation of **14**. Chromatography on 10 g of silica gel eluting with 4% ether–petroleum ether (bp 30–60°) afforded 114 mg (38%) of **14**-d_3. Further purification was accomplished by preparative glc (5 ft, 20% SE 30, 125°): deuterium distribution (ms); 7.4% d_0, 12.0% d_1, 23.8% d_2, 49.3% d_3, 8.0% d_4, average of 2.4 deuterium atoms; τ 2.82–3.17 (m, 4 ArH), 4.39 (br s, $H_{1/2}$ = 6.0 Hz, 1.34 H, mainly H_5), 6.98 (t, J = 5.5 Hz, 2 H, H_2), 7.15 (NCH_3, 3 H), 7.94 (br t, $J \sim$ 5.5 Hz, 1.7 H, H_3), average of 2.6 deuterium atoms.

N-**Methyl-1,2,3,4-tetrahydroquinoline-**d_x (**23-2,4,4-**d_3). A solution of 243 mg (1.67 mmol) of **18** in 1.0 ml of dimethyl-d_6 sulfoxide was treated with 0.20 ml (0.24 mmol) of 1.2 *M* potassium *tert*-butoxide (in dimethyl-d_6 sulfoxide). After 82 hr at room temperature, the product was isolated and reduced using the above procedure for the preparation of **14**-d_3 yielding 198 mg (79%) of **23**-d_3. This product was purified further by preparative glpc (5 ft, 20% SE 30, 115°): deuterium distribution (ms) 15.0% d_2, 84.7% d_3, 0.4% d_4, average of 3.0 deuterium atoms; τ 2.80–3.63 (m, 4 H), 6.85 (tt, J_{HD} = 1.5 Hz, 1.1 H), 7.18 (s, 3 H), 8.18 (br d, $J_{2,3}$ = 6.0 Hz, 2 H); average of 2.8 deuterium atoms.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. We are grateful to the National Science Foundation for the funds to purchase the Varian 100-MHz nmr spectrometer, to W. T. Ford and J. I. Brauman for helpful discussions, and to the National Institutes of Health for financial assistance.

N,N-Disubstituted Aminomethyllithium Compounds

Donald J. Peterson

Contribution from The Procter & Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45239. *Received December 12, 1970*

Abstract: Five members of a novel class of heteroatom-substituted organometallic compounds, $RR'NCH_2Li$, have been conveniently prepared by a transmetalation reaction between the appropriate (N,N-disubstituted aminomethyl)tributyltin and *n*-butyllithium. The stabilities of these organolithium compounds varied with substitution at nitrogen. For example, in mixed tetrahydrofuran–hexane solvent, *N,N*-dimethylaminomethyllithium (**1′**) decomposed *ca.* 50% during 18 hr at 45°, while *N*-methyl-*N*-phenylaminomethyllithium decomposed completely within 4 hr at 25°. **1′** was found to be significantly less reactive than *n*-butyllithium as a metalating agent which thereby demonstrates that the *N,N*-dimethylamino substituent, relative to an alkyl group, has an overall stabilizing effect on a carbon–lithium bond. In addition to its obvious synthetic utility, **1′** proved useful as an intermediate for the conversion of benzophenone to $(CH_3)_2NCH{=}C(C_6H_5)_2$ and $(C_6H_5)_2CHCHO$.

Within the past few years several new types of heteroatom-substituted organometallic compounds have been prepared in which the heteroatom bears no formal charge. Included in this list of useful synthetic intermediates are sulfur-, phosphorus-, silicon-, and oxygen-substituted methyllithium compounds. The first two organometallic compounds are

$$ZCH_2Li$$

$$Z = RS, R_2P, R_3Si, RO$$

readily obtained by metalation of the corresponding weakly acidic methanes,[1–3] while the last compound has been realized in acceptable yield from the reaction of an α-halomethyl ether with lithium.[4] Silylmethyllithium compounds have been obtained by both types of reactions.[5–7] As reported in a recent preliminary communication,[8] this series of heteroatom-substituted organometallic compounds has been extended to include the parent nitrogen carbanion, *N,N*-dimethylaminomethyllithium, by yet a third method, *i.e.*, a transmetalation reaction between *n*-butyllithium·TMEDA (*N,N,N′,N′*-tetramethylethylenediamine) and (*N,N*-dimethylaminomethyl)tributyltin. The transmetalation route is far superior to the direct metalation method[9] for preparing the aminomethyllithium compound in that the former is rapid and essentially quantitative in contrast to the latter reaction which is very slow and affords the desired compound in low yield.

We now report the synthesis of some additional nitrogen-substituted methyllithium compounds by the transmetalation reaction, variations of the method, and initial findings pertaining to the chemical behavior of these novel organolithium compounds.

Transmetalation reactions between *n*-butyllithium and (N,N-disubstituted aminomethyl)tributyltin compounds, **1–3**, occurred quantitatively within a few minutes in hexane at 0°, while the presence of a small amount of tetrahydrofuran was required to achieve similar results with **4** and **5**. Ether was intermediate to

$$\underset{\mathbf{1\text{–}5}}{RR'NCH_2Sn(C_4H_9\text{-}n)_3} + n\text{-}C_4H_9Li \xrightarrow{0^\circ} RR'NCH_2Li + (n\text{-}C_4H_9)_4Sn$$

$$\mathbf{1'\text{–}5'}$$

1, **1′**, R,R′ = CH_3
2, **2′**, R,R′ = $(-CH_2-)_5$
3, **3′**, R,R′ = $-H_2CCH_2OCH_2CH_2-$
4, **4′**, R = CH_3; R′ = C_6H_5
5, **5′**, R,R′ = C_6H_5

tetrahydrofuran and hexane in its ability to facilitate the reaction. TMEDA, as used in the initial[8] generation of

(1) D. J. Peterson, *J. Org. Chem.*, **32**, 1717 (1967).
(2) E. J. Corey and D. Seebach, *ibid.*, **31**, 4097 (1966).
(3) D. J. Peterson, *J. Organometal. Chem.*, **8**, 199 (1967).
(4) U. Schöllkopf, H. Küpers, H.-J. Traencker, and W. Pitteroff, *Justus Liebigs Ann. Chem.*, **704**, 120 (1967).
(5) J. W. Connolly and G. Urry, *Inorg. Chem.*, **2**, 645 (1963).
(6) D. J. Peterson, *J. Organometal. Chem.*, **9**, 373 (1967).
(7) D. J. Peterson, *J. Org. Chem.*, **33**, 780 (1968).
(8) D. J. Peterson, *J. Organometal. Chem.*, 21, P63 (1970).
(9) D. J. Peterson and H. R. Hays, *J. Org. Chem.*, **30**, 1939 (1965).