aqueous sodium bicarbonate and dichloromethane. The organic phase was washed with saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over 25 g of silica gel (chloroform–10% ammonium hydroxide in methanol, 40:1) to give 274 mg (90%) of aminoacetate **26a** as a colorless foam: IR ($CHCl_3$) 1726 cm^{-1}; NMR ($CHCl_3$) δ 1.11–2.91 (m, 12 H, CH_2), 2.08 (s, 3 H, CH_3COO), 3.14 (m, 1 H, NCH), 3.84 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3) 4.66 (dd, 1 H, J = 9, 4.5, ArCHN), 5.10 (qu, 1 H, J = 4.5, OCH), 6.97 (s, 1 H, Ar H), 7.01 (s, 1 H, Ar H); exact mass calcd for $C_{19}H_{26}BrNO_4$ m/e 411.1046, found m/e 411.1055.

***rel*-(2*R*,4*S*,10*R*)-2-Acetoxy-4-(3,4-dimethoxy-6-iodophenyl)octahydro-4*H*-quinolizine (26b).** Treatment of 0.5 g of **16b** as described above for **16a** gave 0.4 g (85%) of aminoacetate **26b** as a colorless foam: IR ($CHCl_3$) 1726 cm^{-1}; NMR ($CDCl_3$) δ 1.06–2.92 (m, 12 H, CH_2), 2.11 (s, 3 H, CH_3COO), 3.16 (m, 1 H, CHN), 3.86 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.43 (dd, 1 H, J = 9, 4.5, ArCHN), 5.10 (qu, 1 H, J = 4.5, OCH), 6.99 (s, 1 H, Ar H), 7.19 (s, 1 H, Ar H); exact mass calcd for $C_{19}H_{26}INO_4$ m/e 459.0908, found m/e 4259.0920.

Methyl 3-[4-[2-[*rel*-(2*R*,4*S*,10*R*)-2-Acetoxyoctahydro-4*H*-quinolizin-4-yl]-4,5-dimethoxyphenoxy]phenyl]propionate (28). To a solution of 348 mg (1.93 mmol) of methyl 3-(4-hydroxyphenyl)propionate[20] in 2 mL of pyridine, cooled in an ice bath, was added 72 mg (1.84 mmol) of sodium hydride (61.14% dispersion in mineral oil). The mixture was stirred for 15 min, 191 mg (1.93 mmol) of cuprous chloride was added at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. To the resulting brown solution was added 531 mg (1.29 mmol) of bromide **26a** in 3 mL of pyridine at room temperature. The mixture was warmed under reflux for 3 h followed by removal of the pyridine at room temperature in vacuo. The brown residue was partitioned between saturated aqueous ammonium chloride and dichloromethane. The organic phase was washed with 1.0 N aqueous sodium hydroxide and saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residual brown oil was chromatographed over alumina (ether–hexane, 1:1) to give a mixture of 33 mg (8%, based on NMR integration) of reduction product **27** and 201 mg (38%, based on NMR integration) of starting bromide **26a** in addition to 209 mg (32%) of pure diaryl ether **28**[19] as a colorless foam: IR ($CHCl_3$) 1727 cm^{-1}; NMR ($CDCl_3$) δ 1.10–3.23 (m, 17 H, CH_2 and NCH), 1.90 (s, 3 H, CH_3COO), 3.68 (s, 3 H, CO_2CH_3), 3.79 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 4.51 (t, 1 H, J = 6, ArCHN), 5.11 (qu, 1 H, J = 5, OCH), 6.49 (s, 1 H, Ar H), 6.73 (d, 2 H, J = 9, Ar H), 7.02 (s, 1 H, Ar H), 7.07 (d, 2 H, J = 9, Ar H); exact mass calcd for $C_{29}H_{37}NO_7$ m/e 511.2570, found m/e 511.2586.

Similar treatment of iodo amine **26b** gave **27**, recovered **26b**, and ether **28** in 12%, 18%, and 30% yields, respectively.

(±)-Vertaline (2). A solution of 126 mg (0.25 mmol) of diester **28** in 3.0 mL of 5% aqueous sodium hydroxide and 6.1 mL of methanol was warmed under reflux for 30 min. The solution was partially concentrated in vacuo, and the residual liquid was adjusted to pH 6 with 3 N aqueous hydrochloric acid by using bromthymol blue as an indicator. The solvent was removed in vacuo, and the residual solids were suspended in dichloromethane. The dichloromethane-soluble material was concentrated to afford 123 mg of crude hydroxy acid **29** as a pale green foam. This material gave spectral data (IR, ^1H NMR) in accord with those reported elsewhere[19] and was used directly in the next reaction.

A solution of 123 mg (0.25 mmol) of hydroxy acid **29**, 87 mg (0.394 mmol) of 2,2′-dipyridyl disulfide,[27] and 103 mg (0.394 mmol) of triphenylphosphine in 2.0 mL of dichloromethane was stirred at room temperature for 50 min followed by removal of the solvent in vacuo. The residual pale green oil was dissolved in 500 mL of xylenes and heated under reflux for 20 h. The solvent was removed at 60 °C in vacuo over a 2-h period, and the residual pale brown oil was chromatographed over alumina (ether–hexane, 2:3) to give 57 mg (53%) of **2** as colorless prisms after recrystallization from methanol. This material was identical (TLC, IR, 300-MHz ^1H NMR) with an authentic sample of (−)-vertaline: mp 220–220.5 °C (lit[19] mp 224–225 °C); IR ($CHCl_3$) 1723 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.03–1.98 (m, 10 H), 2.22–2.32 (m, 1 H), 2.39 (br t, 1 H), 2.53–2.60 (m, 2 H), 2.84 (td, 1 H, J = 13, 5), 2.99–3.06 (m, 2 H), 3.41 (br d, 1 H, J = 10, ArCHN), 3.86 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.89 (br s, 1 H, OCH), 6.48 (dd, 1 H, J = 9, 3, Ar H), 6.76 (s, 1 H, Ar H), 6.85 (br s, 1 H, Ar H), 6.93 (dd, 1 H, J = 9, 3, Ar H), 7.22 (dd, 1 H, J = 8.5, 3, Ar H), 7.28 (dd, 1 H, J = 8.5, 3, Ar H).

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Registry No. (±)-**2**, 53494-86-3; (±)-**5**, 80735-94-0; (±)-**6**, 80696-76-0; **7**, 73157-68-3; (±)-**8**, 80696-77-1; (±)-**9**, 80696-78-2; (±)-**10**, 80696-79-3; (±)-**10** picrate, 80696-80-6; **11a**, 5392-10-9; **11b**, 61203-53-0; (±)-**12a**, 80696-81-7; (±)-**13a**, 80696-82-8; (±)-**13b**, 80696-83-9; (±)-**13c**, 80696-84-0; **14**, 23068-91-9; (±)-**15a**, 80718-98-5; (±)-**15b**, 80696-85-1; (±)-**16a**, 80696-86-2; (±)-**16b**, 80696-87-3; (±)-**17a**, 80696-88-4; (±)-**17b**, 80696-89-5; (±)-**18a** (isomer I), 80696-90-8; (±)-**18a** (isomer II), 80696-91-9; (±)-**18b** (isomer I), 80696-92-0; (±)-**18b** (isomer II), 80696-93-1; (±)-**21**, 80696-94-2; (±)-**22**, 80696-95-3; (±)-**23**, 80696-96-4; (±)-**24**, 80696-97-5; (±)-**25**, 80696-98-6; (±)-**26a**, 53425-27-7; (±)-**26b**, 80696-99-7; (±)-**27**, 60352-71-8; (±)-**28**, 53510-38-6; (±)-**29**, 53425-29-9; glutarimide, 1121-89-7; hexamethyldisilazane, 999-97-3; allyl bromide, 106-95-6; methyl 3-(4-hydroxyphenyl)propionate, 5597-50-2.

β-Substituted Organolithium Compounds. Reaction with Alkyl Halides, Dimethyl Disulfide, and Imines

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The reaction of β-substituted organolithium derivatives with several electrophiles leads to mono- as well as bifunctionalized organic compounds. Thus, by treatment of these dianions with alkyl halides a direct attack on the carbanionic carbon atom is performed, giving as a result substituted amines. When dimethyl disulfide is used, β-amino and β-hydroxy thioethers are obtained. Finally, on reaction with imines, 1-amino-3-hydroxy compounds and 1,3-diamines are obtained. Since these dianions are easily prepared by mercury–lithium transmetalation from β-substituted organomercurials resulting from the addition of mercury(II) salts to olefins, this whole process gives an appropriate way of functionalizing olefins.

The preparation of β-substituted organometallic compounds containing main-group metals has been a point of interest for two particular reasons: (a) a theoretical concern reflecting the difficulty of preparation and the instability of such compounds and (b) a practical concern since their reaction with electrophiles leads to bifunc-

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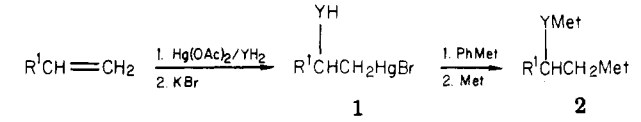
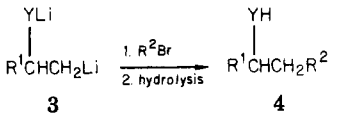
Scheme I[a]



[a] R¹ = H, alkyl, aryl; Y = O, PhN; Met = Li, Na, K.

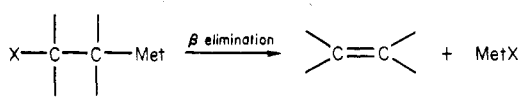
Scheme II[a]



[a] R¹ = H, Me, Ph; R² = Et, *n*-Pr, *n*-Bu; Y = PhN.

tionalized organic compounds.

The instability of these compounds is due to their easy decomposition to olefins through a β-elimination process which is strongly favored because of the different electronegativities of function X and the metal.[1] When the organometallic precursors are not obtained from a starting olefin, the β-elimination reaction has proved useful for synthetizing unsaturated compounds.[2]



X = Hal, OR, NR_2, SR; Met = Li, Na, K, MgHal, AlR_2

We have recently[3,4] reported on the preparation for the first time of organometallic compounds derived from lithium, sodium, and potassium bearing an amide or alkoxide function in the β-position with respect to the metal (**2**). The loss of electronegativity of the anionic heteroatom in these compounds inhibits their decomposition through β elimination. The above dianions are easily available by means of a mercury–metal transmetalation reaction from β-substituted organomercurials (**1**). These last compounds were prepared by the addition of mercury(II) salts to olefins in the presence of a protic substrate[5] (see Scheme I).

The stability of these organometallic compounds decreases in the Li > Na > K series in good agreement with the C–Met bond polarization.[6]

Some synthetic application of these new lithium derivative synthons (**3** = **2**, Met = Li) by reaction with oxygen, carbon dioxide, carbonyl compounds, and trimethylchlorosilane has been previously reported.[7] In the present paper the reactivity of compounds **3** is further investigated by studying their behavior toward different electrophiles such as alkyl halides, dimethyl disulfide, and imines.

Results and Discussion

Compounds **3** treated with different primary alkyl bromides at −78 °C, after hydrolyzation at a low temperature (−40 °C) with aqueous hydrochloric acid, led to the corresponding N-substituted arylamines **4** (see Scheme II and Table I). On the contrary, if secondary or tertiary alkyl bromides (R² = *i*-Pr, *i*-Bu, Cy, *t*-Bu) are used, generation of olefin by hydrogen bromide elimination takes place.[8] If any branching in the carbon chain is found at the β-carbon with respect to the halogen (R² = *sec*-Bu), a substitution reaction does not occur. In the case of using highly reactive alkyl bromides such as allyl and benzyl derivatives, the main reaction is a double decomposition process leading to diallyl or dibenzyl, resulting from the corresponding alkyl halide self-coupling.

Concerning the halogen, reaction with alkyl bromides provides good yields, on taking into account the abovementioned limitations (see Table I). With alkyl chlorides, yields are usually very low (<10%), and the reaction has no preparative interest. When alkyl iodides are employed, a double decomposition reaction between the organometallic compounds and the alkyl iodides has been ob-

Table I. Reaction of Dianions 3 (Y = PhN) with Alkyl Bromides. Obtention of *N*-Alkylarylamines (4)

compd	R¹	R²	% yield Hg⁰[a]	% yield 4[b]	bp, °C (mmHg)
4a	H	Et	85	62	59-60 (0.1)[c]
4b	H	*n*-Pr	85	56	66-68 (0.1)[d]
4c	H	*n*-Bu	88	54	84-86 (0.1)[e]
4d	Me	Et	70	60	65-67 (0.1)[f]
4e	Me	*n*-Pr	75	56	68-69 (0.1)
4f	Ph	Et	85	61	83-85 (0.001)
4g	Ph	*n*-Pr	73	52	92-94 (0.001)
4h	Ph	*n*-Bu	80	48	100-102 (0.001)

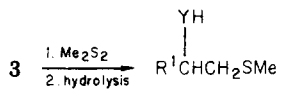
[a] Based on starting mercurial. [b] Based on Hg⁰ precipitated. [c] Lit.[9] bp 241–242 °C (752 mmHg). [d] Lit.[10] bp 130 °C (11 mmHg). [e] Lit.[11] bp 141–144 °C (13 mmHg). [f] Lit.[12] bp 242 °C (760 mmHg).

Table II. Reaction of 3 with Dimethyl Disulfide. Obtention of β-Hydroxy and β-Amino Thioethers 5

compd	Y	R¹	% yield Hg⁰[a]	% yield 5[b]	bp, °C (mmHg)
5a	O	Me	76	71	105-108 (160)[c]
5b	O	n-C_5H_{11}	81	82	53-55 (0.1)
5c	O	Ph	75	63	76-77 (0.001)[d]
5d	O	$PhCH_2$	80	65	84-86 (0.001)
5e	PhN	H	91	75	60-61 (0.001)
5f	PhN	Me	70	76	64-65 (0.001)
5g	PhN	Ph	73	63	96-98 (0.001)
5h	PhN	$PhCH_2$	52	62	130-135 (0.001)

[a] Based on starting mercurial. [b] Based on Hg⁰ precipitated. [c] Lit.[14] bp 67 °C (20 mmHg). [d] Lit.[15] bp 100 °C (0.5 mmHg).

Scheme III[a]



[a] R¹ = H, Me, n-C_5H_{11}, Ph, $PhCH_2$; Y = O, PhN.

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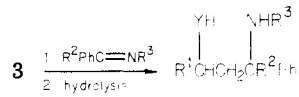
Table III. Reaction of 3 with Imines ($R^2PhC{=}NR^3$). Obtention of 1-Amino-3-hydroxy Compounds and 1,3-Diamines (6)

compd	Y	R^1	R^2	R^3	% yield Hg^0[a]	% yield 6[b]	mp, °C (solvent)
6a	O	Ph	H	Ph	75	60	124-127[c] (hexane/$CHCl_3$)
6b	O	Ph	H	4-ClC_6H_4	80	76	*d*
6c	O	Ph	H	4-$MeOC_6H_4$	65	71	*d*
6d	PhN	H	H	Ph	90	55	*d*
6e	PhN	H	Et	Ph	65	32	*d*
6f	PhN	H	H	4-ClC_6H_4	80	69	*d*
6g	PhN	H	H	4-$MeOC_6H_4$	83	59	*d*
6h	PhN	Me	H	Ph	69	79	*d*
6i	PhN	Ph	H	Ph	70	68	117-119 (hexane/$CHCl_3$)
6j	PhN	Ph	H	4-ClC_6H_4	75	68	*d*
6k	PhN	Ph	H	4-$MeOC_6H_4$	70	71	*d*

[a] Based on starting mercurial. [b] Based on Hg^0 precipitated. [c] Lit.[7] mp 124-127 °C. [d] Oil.

Scheme IV[a]



6

[a] R^1 = H, Me, Ph, R^2 = H, Et; R^3 = Ph, 4-ClC_6H_4, 4-$MeOC_6H_4$; Y = O, PhN.

served, leading thus to the corresponding coupling products.

When the starting material is an oxymercurial (1, Y = O; Scheme I), compound 3 (Y = O), which is more unstable than the nitrogen derivative,[3,4] is obtained. The reaction of these compounds 3 with different alkyl halides does not lead in any case to the expected substitution products under the tested reaction conditions (−78 to 0 °C). In its place, either the corresponding compounds resulting from a decomposition of 3 through a β-elimination process (that is, the starting olefin; see Scheme I) or the corresponding compound originated by abstracting a proton from the reaction media, were obtained (4; Y = O, R^2 = H).

The interest in the above reaction is due to its total regioselectivity. Even with an excess of alkyl bromide (1:4 molar ratio) and a temperatures ranging from −78 to −40 °C, the product resulting from an attack on carbanionic carbon is exclusively obtained. It is necessary to keep the reaction for several hours at a higher temperature (−40 to +20 °C) in order to notice contamination of products 4 with variable amounts of dialkylated products.

When β-functionallized organolithium compounds 3 were allowed to react at −78 °C with dimethyl disulfide and after hydrolyzation with water,[13] the corresponding β-hydroxy and β-amino thioethers 5 were obtained (see Scheme III and Table II).

The reaction of β-substituted organolithium compounds 3 with several imines at −78 °C, followed by 2 N sulfuric acid hydrolysis, leads to the corresponding 1-amino-3-hydroxy compounds and 1,3-diamines (6; see Scheme IV and Table III). These results supplement the reactivity study of compounds 3 with carbonyl compounds already reported by us.[7] Thus, 1-amino-3-hydroxy compounds have been prepared in two ways; e.g., compound 6a is similar to the one previously obtained by reacting 3 with benzaldehyde. Among all the systems described above we outline the method for 1,3-diamines containing different groups on both nitrogen atoms because of their preparative difficulty by other synthetic methods.

Finally, we have studied the reactivity of 3 with other electrophiles. In the reaction with aliphatic and aromatic nitriles, the expected reaction product, i.e., the corresponding imine or the carbonyl compound resulting from its hydrolysis, was not isolated in any case. In its place nitrile cyclotrimerization product was obtained together with products from hydrolysis of organolithium compounds 3. In the same way the reaction with other acid derivatives such as acid chlorides or esters leads to product mixtures of difficult separation and so it lacks any preparative interest.

Experimental Section

General Methods. Melting points were determined with a Büchi melting point apparatus and are uncorrected. Infrared spectra (IR) were run on a Pye-Unicam SP-1000 spectrometer. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Varian EM-390 spectrometer. The purity of volatile distilled products was determined in a GLC Varian Aerograph 2800 instrument equipped with a OV-101 Chromosorb column. Elemental analyses were carried out with a Perkin-Elmer 240 elemental analyzer.

The chemical shifts are in δ relative to Me_4Si, and coupling constants (*J* values) are in hertz. Assignments were made by double resonance experiments. The broad singlets assigned to OH and NH groups disappeared on addition of a drop of deuterium oxide to the NMR sample.

Starting mercurials (1) were prepared according to literature methods.[5,16] The lithium powder used in the transmetalation process was commercially available. The reactants were of the best commercial grade available and were used without further purification. THF was dried by reflux with potassium metal and stored under argon. All reactions were run under argon, and all glassware was dried before use.

Reaction of the β-Substituted Organolithium Compounds 3 with Alkyl Bromides. General Procedure. To a previously evacuated 250-mL two-necked flask containing dry THF (125 mL) was added mercurial 1 (20 mmol) under argon atmosphere. The solution was cooled at −78 °C, an ether solution of phenyllithium[17] (20 mmol) was added dropwise in 10 min, lithium powder (120 mmol) was added, and the mixture was mechanically stirred for 8 h. The reaction mixture was filtered (G-3 funnel) at −78 °C, the collected mercury weighed, and the corresponding alkyl bromide (20 mmol) added to the resulting clear solution of 3. The temperature was allowed to rise to −40 °C in 12 h. The reaction mixture was hydrolyzed with water and neutralized with aqueous hydrochloric acid. The resulting mixture was extracted with ether, and the ether layer was washed with water and dried over anhydrous sodium sulfate. Solvents were removed under reduced

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pressure (15 mmHg), and the residue was distilled (see Table I).

***N*-Butylaniline (4a)**:[9] IR (film) 3400 (NH) cm^{-1}; NMR (CCl_4) δ 0.9 (t, 3, J = 6 Hz, CH_3), 1.35–1.65 [m, 4, $(CH_2)_2$], 3.0 (t, 2, J = 6 Hz, CH_2N), 3.3 (br s, 1, NH), 6.35–7.2 (m, 5, Ph).

***N*-Pentylaniline (4b)**:[10] IR (film) 3420 (NH) cm^{-1}; NMR (CCl_4) δ 0.9 (t, 3, J = 6 Hz, CH_3), 1.2–1.75 [m, 6, $(CH_2)_3$], 3.0 (t, 2, J = 6 Hz, CH_2N), 3.45 (br s, 1, NH), 6.35–7.25 (m, 5, Ph).

***N*-Hexylaniline (4c)**:[11] IR (film) 3420 (NH) cm^{-1}; NMR (CCl_4) δ 0.9 (t, 3, J = 6 Hz, CH_3), 1.15–1.65 [m, 8, $(CH_2)_4$], 3.0 (t, 2, J = 6 Hz, CH_2N), 3.55 (br s, 1, NH), 6.35–7.2 (m, 5, Ph).

***N*-(1-Methylbutyl)aniline (4d)**:[12] IR (film) 3400 (NH) cm^{-1}; NMR (CCl_4) δ 0.95 (t, 3, J = 6 Hz, CH_3CH_2), 1.15 (d, 3, J = 6 Hz, CH_3CH), 1.3–1.55 [m, 4, $(CH_2)_2$], 3.2 (br s, 1, NH), 3.3–3.6 (m, 1, CH), 6.35–7.15 (m, 5, Ph).

***N*-(1-Methylpentyl)aniline (4e)**: IR (film) 3400 (NH) cm^{-1}; NMR (CCl_4) δ 0.95 (t, 3, J = 6 Hz, CH_3CH_2), 1.15 (d, 3, J = 6 Hz, CH_3CH), 1.3–1.5 [m, 6, $(CH_2)_3$], 3.15 (br s, 1, NH), 3.25–3.6 (m, 1, CH), 6.35–7.2 (m, 5, Ph).

Anal. Calcd for $C_{12}H_{19}N$: C, 81.29; H, 10.80; N, 7.90. Found: C, 81.17; H, 10.66; N, 7.84.

***N*-(1-Phenylbutyl)aniline (4f)**: IR (film) 3460 (NH) cm^{-1}; NMR (CCl_4) δ 0.85 (t, 3, J = 6 Hz, CH_3), 1.2–1.45 (m, 2, CH_2CH_3), 1.55–1.85 (m, 2, CH_2CH), 3.65 (br s, 1, NH), 4.2 (t, 1, J = 6 Hz, CH), 6.3–7.3 (m, 10, aromatic H).

Anal. Calcd for $C_{16}H_{19}N$: C, 85.30; H, 8.50; N, 6.22. Found: C, 85.41; H, 8.34; N, 6.12.

***N*-(1-Phenylpentyl)aniline (4g)**: IR (film) 3420 (NH) cm^{-1}; NMR (CCl_4) δ 0.9 (t, 3, J = 6 Hz, CH_3), 1.15–1.45 [m, 4, $(CH_2)_2$], 1.55–1.9 (m, 2, CH_2CH), 3.5 (br s, 1, NH), 4.2 (t, 1, J = 6 Hz, CH), 6.3–7.3 (m, 10, aromatic H).

Anal. Calcd for $C_{17}H_{21}N$: C, 85.29; H, 8.84; N, 5.85. Found: C, 85.30; H, 8.89; N, 5.90.

***N*-(1-Phenylhexyl)aniline (4h)**: IR (film) 3400 (NH) cm^{-1}; NMR (CCl_4) δ 0.85 (t, 3, J = 6 Hz, CH_3), 1.1–1.45 [m, 6, $(CH_2)_3$], 1.55–1.85 (m, 2, CH_2CH), 3.7 (br s, 1, NH), 4.2 (t, 1, J = 6 Hz, CH), 6.3–7.3 (m, 10, aromatic H).

Anal. Calcd for $C_{18}H_{23}N$: C, 85.32; H, 9.15; N, 5.53. Found: C, 85.50; H, 9.08; N, 5.54.

Reaction of 3 with Dimethyl Disulfide. General Procedure. To a previously evacuated 250-mL two-necked flask containing dry THF (125 mL) was added mercurial 1 (20 mmol) under an argon atmosphere. The solution was cooled at −78 °C, an ether solution of phenyllithium[17] (20 mmol) was added dropwise in 10 min, lithium powder (120 mmol) was added, and the mixture was mechanically stirred for 8 h. The reaction mixture was filtered (G-3 funnel) at −78 °C, the collected mercury weighed, and dimethyl disulfide (20 mmol) added to the resulting clear solution of **3**. The temperature was allowed to rise to 20 °C in 12 h. The reaction mixture was hydrolyzed with water. The resulting mixture was extracted with ether, and the ether layer was washed with water and dried over anhydrous sodium sulfate. Solvents were removed under reduced pressure (15 mmHg), and the residue was distilled (see Table II).

2-Hydroxypropyl methyl sulfide (5a):[14] IR (film) 3360 (OH), 1060 (CO) cm^{-1}; NMR ($CDCl_3$) δ 1.2 (d, 3, J = 6 Hz, CH_3C), 2.1 (s, 3, CH_3S), 2.2–2.7 (br s, 1, OH), 2.5–2.65 (m, 2, CH_2), 3.6–4.0 (m, 1, CH).

2-Hydroxyheptyl methyl sulfide (5b): IR (film) 3370 (OH), 1050 (CO) cm^{-1}; NMR ($CDCl_3$) δ 0.9 (t, 3, J = 6 Hz, CH_3C), 1.1–1.65 [m, 8, $(CH_2)_4$], 2.1 (s, 3, CH_3S), 2.5–2.6 (m, 2, CH_2S), 2.6–2.8 (br s, 1, OH), 3.5–3.85 (m, 1, CH).

Anal. Calcd for $C_8H_{18}OS$: C, 59.21; H, 11.18. Found: C, 59.42; H, 11.22.

2-Hydroxy-2-phenylethyl methyl sulfide (5c):[15] IR (film) 3380 (OH), 1060 (CO) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (s, 3, CH_3), 2.65–2.8 (m, 2, CH_2), 2.8–2.95 (br s, 1, OH), 4.6–4.8 (m, 1, CH), 7.0–7.4 (m, 5, Ph).

2-Hydroxy-3-phenylpropyl methyl sulfide (5d): IR (film) 3400 (OH), 1070 (CO) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (s, 3, CH_3), 2.5–2.65 (m, 2, CH_2S), 2.8 (d, 2, J = 6 Hz, CH_2C), 2.3–2.9 (br s, 1, OH), 3.7–4.05 (m, 1, CH), 7.0–7.4 (m, 5, Ph).

Anal. Calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74. Found: C, 65.93; H, 7.72.

Methyl 2-(phenylamino)ethyl sulfide (5e): IR (film) 3360 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (s, 3 CH_3), 2.7 (t, 2, J = 6 Hz, CH_2S), 3.3 (t, 2, J = 6 Hz, CH_2N), 4.0 (br s, 1, NH), 6.5–7.3 (m, 5, Ph).

Anal. Calcd for $C_9H_{13}NS$: C, 64.62; H, 7.83; N, 8.37. Found: C, 64.71; H, 7.78; N, 8.50.

Methyl 2-(phenylamino)propyl sulfide (5f): IR (film) 3350 (NH) cm^{-1}; NMR ($CDCl_3$) δ 1.3 (d, 3, J = 6 Hz, CH_3C), 2.1 (s, 3, CH_3S), 2.5–2.8 (m, 2, CH_2), 3.7–3.9 (m, 2, NH and CH), 6.4–7.3 (m, 5, Ph).

Anal. Calcd for $C_{10}H_{15}NS$: C, 66.25; H, 8.34; N, 7.72. Found: C, 66.41; H, 8.26; N, 7.80.

Methyl 2-phenyl-2-(phenylamino)ethyl sulfide (5g): IR (film) 3390 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.05 (s, 3, CH_3), 2.75–2.95 (m, 2, CH_2), 4.2–4.6 (m, 2, NH and CH), 6.35–7.5 (m, 10, aromatic H).

Anal. Calcd for $C_{15}H_{17}NS$: C, 74.03; H, 7.04; N, 5.75. Found: C, 73.98; H, 7.10; N, 5.78.

Methyl 3-phenyl-2-(phenylamino)propyl sulfide (5h): IR (film) 3360 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (s, 3, CH_3), 2.65 (d, 2, J = 6 Hz, CH_2S), 2.95 (d, 2, J = 6 Hz, CH_2C), 3.5–4.0 (m, 2, NH and CH), 6.4–7.5 (m, 10, aromatic H).

Anal. Calcd for $C_{16}H_{19}NS$: C, 74.66; H, 7.44; N, 5.44. Found: C, 74.52; H, 7.35; N, 5.51.

Reaction of 3 with Imines. General Procedure. To a previously evacuated 250-mL two-necked flask containing dry THF (125 mL) was added mercurial 1 (20 mmol) under an argon atmosphere. The solution was cooled at −78 °C, an ether solution of phenylithium[17] (20 mmol) was added dropwise in 10 min, lithium powder (120 mmol) was added, and the mixture was mechanically stirred for 8 h. The reaction mixture was filtered (G-3 funnel) at −78 °C, the collected mercury weighed, and the corresponding imine (20 mmol) added t the resulting clear solution of **3**. The temperature was allowed to rise to 20 °C in 12 h. The reaction mixture was hydrolyzed with 2 N sulfuric acid, and the aqueous layer was alkalinized with 3 N potassium hydroxide. The resulting mixture was extracted with ether, and the ether layer was washed with water and dried over anhydrous sodium sulfate. Solvents were removed under reduced pressure (0.001 mmHg), and the residue was recrystallized (see Table III).

1,3-Diphenyl-3-(phenylamino)-1-propanol (6a):[7] IR (Nujol) 3320 (OH), 3300 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.05–2.25 (m, 2, CH_2), 3.9 (br s, 2, OH and NH), 4.5–4.7 (m, 1, CHN), 4.75–4.95 (m, 1, CHO), 6.9–7.5 (m, 15, aromatic H).

1,3-Diphenyl-3-[(4-chlorophenyl)amino]-1-propanol (6b): IR ($CHCl_3$) 3480 (OH), 3460 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.0–2.2 (m, 2, CH_2), 3.5 (br s, 2, OH and NH), 4.4–4.6 (m, 1, CHN), 4.7–4.9 (m, 1, CHO), 6.9–7.5 (m, 14, aromatic H).

Anal. Calcd for $C_{21}H_{20}ClNO$: C, 74.66; H, 5.97; N, 4.14. Found: C, 74.73; H, 6.06; N, 4.20.

1,3-Diphenyl-3-[(4-methoxyphenyl)amino]-1-propanol (6c): IR ($CHCl_3$) 3480 (OH), 3460 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.15–2.35 (m, 2, CH_2), 3.6 (s, 3, CH_3), 3.7 (br s, 2, OH and NH), 4.4–4.6 (m, 1, CHN), 4.7–4.9 (m, 1, CHO), 7.0–7.5 (m, 14, aromatic H).

Anal. Calcd for $C_{22}H_{23}NO_2$: C, 79.25; H, 6.95; N, 4.20. Found: C, 79.33; H, 7.07; N, 4.27.

***N*-[1-Phenyl-3-(phenylamino)propyl]aniline (6d)**: IR ($CHCl_3$) 3400 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (q, 2, J = 6 Hz, CH_2C), 3.15 (t, 2, J = 6 Hz, CH_2N), 4.0 [br s, 2, $(CNH)_2$], 4.5 (t, 1, J = 6 Hz, CH), 6.45–7.35 (m, 15, aromatic H).

Anal. Calcd for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33; N, 9.26. Found: C, 83.49; H, 7.25; N, 9.32.

***N*-[3-Phenyl-3-(phenylamino)pentyl]aniline (6e)**: IR ($CHCl_3$) 3460 (NH) cm^{-1}; NMR ($CDCl_3$) δ 0.8 (t, 3. J = 6 Hz, CH_3), 2.05 (t, 2, J = 6 Hz, CH_2C), 2.3 (q, 2, J = 6 Hz, CH_2CH_3), 3.1 (t, 2, J = 6 Hz, CH_2N), 3.7 [br s, 2, $(CNH)_2$], 6.25–7.55 (m, 15 aromatic H).

Anal. Calcd for $C_{23}H_{26}N_2$: C, 83.59; H, 7.93; N, 8.48. Found: C, 83.67; H, 8.02; N, 8.55.

4-Chloro-*N*-[1-phenyl-3-(phenylamino)propyl]aniline (6f): IR ($CHCl_3$) 3400 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (q, 2, J = 6 Hz, CH_2C), 3.2 (t, 2, J = 6 Hz, CH_2N), 3.85 [br s, 2, $(CNH)_2$], 4.45 (t, 1, J = 6 Hz, CH), 6.3–7.5 (m, 14 aromatic H).

Anal. Calcd for $C_{21}H_{21}ClN_2$: C, 74.88; H, 6.28; N, 8.32. Found: C, 74.96; H, 6.39; N, 8.38.

4-Methoxy-*N*-[1-phenyl-3-(phenylamino)propyl]aniline (6g): IR ($CHCl_3$) 3420 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.05 (q, 2, J = 6 Hz, CH_2C), 3.2 (t, 2, J = 6 Hz, CH_2N), 3.7 (s, 3, CH_3), 3.75 [br s, 2, $(CNH)_2$], 4.45 (t, 1, J = 6 Hz, CH), 6.4-7.35 (m, 14, aromatic H).

Anal. Calcd for $C_{22}H_{24}N_2O$: C, 79.48; H, 7.28; N, 8.43. Found: C, 79.59; H, 7.16; N, 8.49.

***N*-[1-Phenyl-3-(phenylamino)butyl]aniline (6h)**: IR ($CHCl_3$) 3420 (NH) cm^{-1}; NMR ($CDCl_3$) δ 1.15 (d, 3, J = 6 Hz, CH_3), 1.95 (t, 2, J = 6 Hz, CH_2), 3.4-3.65 (m, 1, $CHCH_3$), 3.95 [br s, 2, $(CNH)_2$], 4.6 (t, 1, J = 6 Hz, CHPh), 6.45-7.4 (m, 15, aromatic H).

Anal. Calcd for $C_{22}H_{24}N_2$: C, 83.50; H, 7.64; N, 8.85. Found: C, 83.59; H, 7.53; N, 8.91.

***N*-[1,3-Diphenyl-3-(phenylamino)propyl]aniline (6i)**: IR (Nujol) 3380 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.3 (t, 2, J = 6 Hz, CH_2), 3.9 [br s, 2, $(CNH)_2$], 4.45 [t, 2, J = 6 Hz, $(CH)_2$], 6.25-7.35 (m, 20, aromatic H).

Anal. Calcd for $C_{27}H_{26}N_2$: C, 85.67; H, 6.92; N, 7.40. Found: C, 85.72; H, 6.88; N, 7.46.

4-Chloro-*N*-[1,3-diphenyl-3-(phenylamino)propyl]aniline (6j): IR ($CHCl_3$) 3400 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.3 (t, 2, J = 6 Hz, CH_2), 3.7 [br s, 2, $(CNH)_2$], 4.45 [t, 2, J = 6 Hz, $(CH)_2$], 6.25-7.35 (m, 19, aromatic H).

Anal. Calcd for $C_{27}H_{25}ClN_2$: C, 78.53; H, 6.10; N, 6.78. Found: C, 78.62; H, 6.01; N, 6.86.

4-Methoxy-*N*-[1,3-diphenyl-3-(phenylamino)propyl]aniline (6k): IR ($CHCl_3$) 3370 (NH) cm^{-1}; NMR ($CDCl_3$) δ 2.1-2.35 (m, 2, CH_2), 3.65 (s, 3, CH_3), 4.15 [br s, 2, $(CNH)_2$], 4.3-4.6 [m, 2, $(CH)_2$], 6.35-7.35 (m, 19, aromatic H).

Anal. Calcd for $C_{28}H_{28}N_2O$: C, 82.32; H, 6.91; N, 6.86. Found: C, 82.41; H, 7.02; N, 6.94.

Registry No. 1 (R' = Ph; Y = O), 67931-44-6; 1 (R', = Ph; Y = PhN), 55552-57-3; 1 (R = Me; Y = PhN), 52969-24-1; 1 (R' = H; Y = PhN), 52969-23-0; **3** (R' = Ph; Y = O), 68090-83-5; **3** (R' = H; Y = PhN), 68110-48-5; **3** (R' = Me; Y = PhN), 71912-91-9; **3** (R' = Ph; Y = PhN), 68090-82-4; **4a**, 1126-78-9; **4b**, 2655-27-8; **4c**, 4746-32-1; **4d**, 2716-62-3; **4e**, 80865-89-0; **4f**, 80865-90-3; **4g**, 62740-72-1; **4h**, 80865-91-4; **5a**, 6943-87-9; **5b**, 80865-92-5; **5c**, 7714-93-4; **5d**, 80865-93-6; **5e**, 80865-94-7; **5f**, 80865-95-8; **5g**, 80865-96-9; **5h**, 80865-97-0; **6a**, 4566-58-9; **6b**, 4293-32-7; **6c**, 4274-54-8; **6d**, 80865-98-1; **6e**, 80865-99-2; **6f**, 80866-00-8; **6g**, 80866-01-9; **6h**, 80866-02-0; **6i**, 80866-03-1; **6j**, 80866-04-2; **6k**, 80866-05-3; ethyl bromide, 74-96-4; propyl bromide, 106-94-5; butyl bromide, 109-65-9; PhCH=NPh, 1013-88-3; $PhCH{=}NC_6H_4Cl$-4, 41839-60-5; $PhCH{=}NC_6H_4OMe$-4, 5291-46-3; EtCPh=NPh, 14752-72-8.

Conformational Behavior of 1-Alkyl-1,2,3,4-tetrahydroazocin-2-ones

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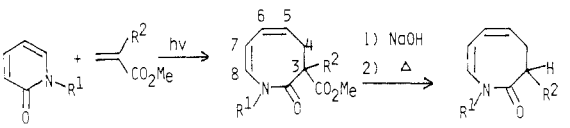
Several of the title compounds were synthesized, and their ^1H NMR spectra were studied at various temperatures. When the temperatures were lowered, simple patterns due to 3-CH_2 and N-CH_2 geminal protons and the N-β-$(CH_3)_2$ group on 1-mehyl- (**1**), 1-ethyl- (**2**), and 1-isobutyl-1,2,3,4-tetrahydroazocin-2-ones (**3**) became sharp multiplets after passing through the coalescence points. The T_c (-60 to -40 °C) and ΔG_c^* (10.3-10.9 kcal/mol) values were reasonably explained as being due to the ring inversion associated with rotation of the N-C(α) bond. ^1H NMR spectra of **2** with a large 3-substituent were also temperature dependent. The temperature-dependent chemical shifts were concluded to be due to population changes in the chiral azocinone ring systems, where steric hindrance due to the 3-substituent plays a major role.

Conformational processes of medium-ring compounds are rather complex, since a number of relatively weak interactions are involved. Several eight-membered rings compounds have been studied, and the roles of pseudorotation as well as the ring inversions have been elucidated.[1] From this aspect, eight-membered unsaturated lactams (azocinones) and the irhomologues are also expected to afford valuable information on conformational processes. In the previous paper, the present authors have reported that several geminal protons of N-alkyl groups in 3-substituted 1-alkyl-1,2,3,4-tetrahydroazocin-2-ones are in nonequivalent magnetic environments as detected by ^1H NMR spectra.[2] N-α-geminal protons of the 1-ethyl group of the corresponding azocinone without a 3-substituent, however, are located in an equivalent environment.[2] The temperature-dependent ^1H NMR spectra were suggested to be due to the restricted rotation around N(1)-C(α) bond in combination with ring inversion. As to the experimental observation, however, Anet has given a new interpretation: the temperature-dependent chemical shift is explained by the population changes between the rapidly equilibrating rotamers associated with the tetrahydroazocinone ring interconversion between two nonplanar forms.[3]

Scheme I



R^1	R^2
Me	H
Et	Me
i-Bu	

	R^1	R^2
4:	Me	H
5:	Et	H
6:	i-Bu	H
7:	Et	Me

	R^1	R^2
1:	Me	H
2:	Et	H
3:	i-Bu	H
8:	Et	Me

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(2) K. Somekawa, S. Kumamoto, T. Matsuo, and I. Ueda, *Tetrahedron*, **36**, 81 (1980).
(3) F. A. L. Anet, *Tetrahedron Lett.*, 2133 (1980).

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