Crystal Structure of 11d. Crystals of **11d** formed from 100% ethanol in the space group $P\bar{1}$ with a = 14.022 (4) Å, b = 15.719 (4) Å, c = 12.943 (3) Å, α = 97.90 (2)°, β = 115.39 (2)°, and γ = 104.91 (2)°. With Z = 4 the calculated density is 1.29 g/cm^3. Of the 6334 diffraction maxima measured with $2\theta \leq 114°$ by using Cu Kα radiation, 2996 (47%) were observed ($I \geq 3\sigma(I)$). Standard direct-method techniques[20] coupled with tangent-formula recycling[21] generated suitable starting positions. Full-matrix, least-squares refinements[22] minimizing $\sum w(|F_o| - |F_c|)^2$ with $w = (1/\sigma F_o)^2$ produced an unweighted R factor of 0.107. Because of the poor quality of the data, no attempt was made to find positions for the hydrogen atoms. The crystal lattice has two independent molecules; one is well-behaved while the naphthyl group in the second is disordered. This disordered region accounts for the small percentage of observed reflections. Bond distances and angles within this disordered naphthyl group show significant deviations from the naphthyl group on the first molecule. Table II (supplementary material) contains the final fractional coordinates and temperature parameters for **11d**.

Acknowledgment. We thank Dr. Jack Smith of Merck Sharp and Dohme Research Laboratories for obtaining the high-resolution mass spectra of compounds **8d** and **8e** and The Camille and Henry Dreyfus Foundation for financial support

Registry No. 8a, 75802-07-2; **8b**, 75802-08-3; **8c**, 75802-09-4; **8d**, 75802-10-7; **11a**, 75802-11-8; **11b**, 75802-12-9; **11c**, 75802-13-0; **11d**, 75802-14-1; **11e**, 75802-15-2; **11f**, 75802-16-3; 1-methyl-3,3-pentamethylenediaziridine, 26177-34-4; 1-ethyl-3,3-pentamethylenediaziridine, 52551-68-5; 1-isopropyl-3,3-pentamethylenediaziridine, 75802-17-4; phenyl isocyanate, 103-71-9; 1-naphthyl isocyanate, 86-84-0; benzoyl isocyanate, 4461-33-0.

Supplementary Material Available: Table II containing the final fractional coordinates and temperature parameters (2 pages). Ordering information is given on any current masthead page.

(20) Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J.-P.; Woolfson, M. M. "MULTAN 78, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data"; University of York: York, England, 1978.
(21) J. Karle, *Acta Crystallogr., Sect. B* **1978**, *B24*, 182.
(22) Stewart, J. M.; Kruger, G. J.; Ammon. H. L.; Dickinson, C.; Hall, S. R. "The X-Ray System, Version of June, 1972; No. TR-192"; Computer Science Center: University of Maryland, College Park, MD, 1972.

Synthesis of Hexahydro-3,3,5,5,7-pentaalkyl-2*H*-1,4-diazepin-2-ones from 1,3-Diamines and Ketones

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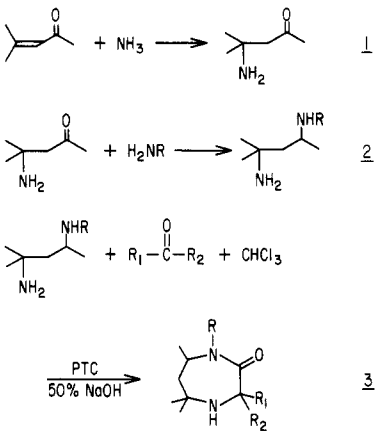
A new method for preparing mono- and bis(hexahydro-3,3,5,5,7-pentaalkyl-2*H*-1,4-diazepin-2-ones) is reported (Schemes I and II). The key step of this synthesis is the final one in which a 1,3-diamine is reacted with a ketone in the presence of sodium hydroxide, chloroform, and a phase-transfer catalyst (PTC). Bis(hexahydro-3,3,5,5,7-pentaalkyl-2*H*-1,4-diazepin-2-ones) are isolated as a mixture of diastereomers. Of these bis compounds, diastereomers of 1,1'-(1,2-ethanediyl)bis(hexahydro-3,3,5,5,7-pentamethyl-2*H*-1,4-diazepin-2-one) (**5a**) can be readily separated by a fractional recrystallization, or their diastereomeric distributions can be measured by ^{13}C NMR.

Recently we disclosed the facile preparation of hindered piperazinones.[2] The UV stabilization properties of these piperazinones and hexahydro-1,4-diazepin-2-ones which we describe in this paper are excellent in various plastics, especially in polypropylene. The synthesis of mono- and bis(hexahydro-3,3,5,5,7-pentaalkyl-2*H*-1,4-diazepin-2-ones) is presented in this paper. Emphasis is placed on the final step of the three-step synthesis as shown in Schemes I and II.

Results and Discussion

The synthesis of hexahydro-3,3,5,5,7-pentaalkyl-2*H*-1,4-diazepin-2-ones (**3**) begins with diacetonamine **1** obtained from mesityl oxide and concentrated ammonium hydroxide. This is followed by the reductive amination of **1** with an appropriate amine to give a 1,3-alkanediamine (**2**). Finally, the reaction of **2** with a ketone and trichloromethyl anion yields the desired hexahydro-3,3,5,5,7-pentaalkyl-2*H*-1,4-diazepin-2-ones (**3**). This three-step reaction is summarized in Scheme I.

Scheme I

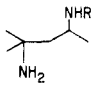


The first step was carried out by a modified literature method.[3] When mesityl oxide and concentrated ammonium hydroxide are simply heated to 45–50 °C, the reaction time can be shortened from 3 days to several hours.

(1) Lai, J. T.; Son, P. N.; Westfahl, J. C. Presented in part at the 179th National Meeting of the American Chemical Society, Houston, TX, Mar 23–28, 1980.
(2) J. T. Lai, "Abstracts of Papers", 178th National Meeting of the American Chemical Society, Washington, DC, Sept 9–14, 1979; American Chemical Society: Washington, DC, 1979; ORGN 250. Also see: *J. Org. Chem.* **1980**, *45*, 754–755.
(3) Haeseler, P. R. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. 1, p 196.

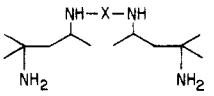
0022-3263/81/1946-0323$01.00/0

Table I. Yields of Mono- and Bis(1,3-alkanediamines)

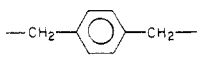
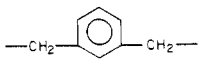


2

amine	R	yield, %	bp, °C (kPa)
2a	Bu	91.1	74-78 (0.93)
2b	$C_{12}H_{25}$	53.0	132-134 (0.053)
2c	CH_2CH_2OH	59.9	67-74 (0.013)



4

amine	X	yield, %	bp, °C (kPa)
4a	$-(CH_2)_2-$	48.8	119-124 (0.053)
4b	$-(CH_2)_3-$	7.8	118-123 (0.026)
4c	$-(CH_2)_6-$	52.4	144-145 (0.020)
4d	$-(CH_2)_3N(CH_3)(CH_2)_3-$	7.3	155-170 (0.013)
4e		14.7	158-171 (0.017)
4f		20.8	166-180 (0.040)

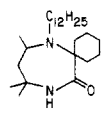
After removal of excess ammonia, the resulting diacetonamine solution (about 30% solution) can be used for the subsequent step. Since the diacetonamine solution is thermally unstable, it is desirable to use it immediately or store it in a refrigerator until it is used.

The second step involves a reductive amination of diacetonamine with a desired amine in the presence of amalgamated aluminum. Strangely enough, a drop- or portion-wise addition of the amines caused an exothermic reaction which sometimes was hard to control. The reaction is practically complete after 4–5 h. Bis(1,3-alkanediamines) (4) can be prepared in a similar way, except for the excess diacetonamine required for the reaction. The yields, ranging from 7.3% to 91.1%, depend on the solubility of the amine in aqueous solution. The average yield is 50–60% as shown in Table I.

The final step involves the reaction of 1,3-alkanediamine with a ketone and trichloromethyl anion which is generated in situ by the reaction of chloroform with 50% aqueous sodium hydroxide solution in the presence of a phase-transfer catalyst.

Initially acetone cyanohydrin[4] was used instead of acetone, but the yields were poor, as shown by **3a** and **3b** in Table II. By replacing acetone cyanohydrin with acetone, **3b** can be prepared in 66% yield rather than 32%. Subsequently, all the reactions were carried out with acetone. The poor yield for compound **3d** is due to the tendency of the compound to decompose during distillation.

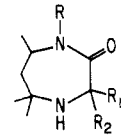
Cyclohexanone also gave a poor yield (24%) as shown by compound **3c**. An interesting aspect of this reaction is that this is the only reaction from which we were able to isolate a structural isomer **3c'** (7-dodecyl-8,10,10-trimethyl-7,11-diazaspiro[5.6]dodecan-12-one).



3c'

(4) Acetone cyanohydrin gave higher yields of the desired piperazainones than acetone (see ref 1). For this reason acetone cyanohydrin was initially used in the synthesis of 1,4-diazepin-2-ones also.

Table II. Synthesis of 1-Alkyl-hexahydro-3,3,5,5,7-pentasubstituted-2*H*-1,4-diazepin-2-ones

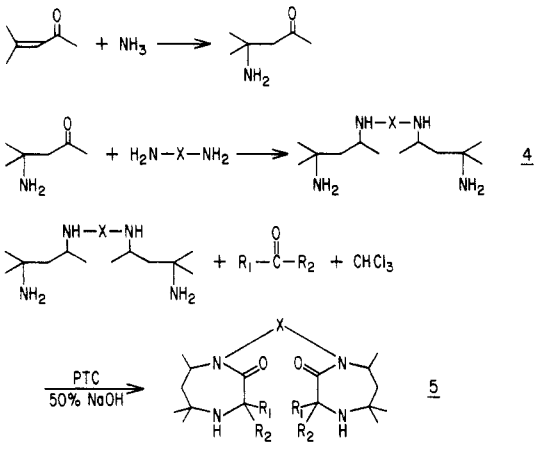


3

compd	R	R_1	R_2	yield, %	bp, °C (kPa)
3a	Bu	CH_3	CH_3	11.3[a]	70-76 (0.026)
3b	$C_{12}H_{25}$	CH_3	CH_3	66.5 (31.9)[a]	180-185 (0.047)
3c	$C_{12}H_{25}$	$-(CH_2)_5-$		23.9[b]	200-206 (0.026)
3d	CH_2CH_2OH	CH_3	CH_3	18.5	72-74[c]

[a] Acetone cyanohydrin (rather than acetone) was used in the reaction. [b] A 10.2% yield of **3c'** is not included. [c] Melting point.

Scheme II

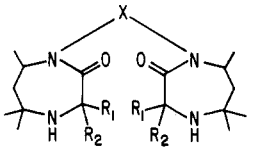


Following the same reaction scheme described for the synthesis of hexahydro-1,4-diazepin-2-ones, bis(hexahydro-1,4-diazepin-2-ones) can be readily made from bis(1,3-alkanediamines) (4), a ketone, and trichloromethyl anion. This reaction scheme is shown as Scheme II, and the yields of various bis(hexahydro-1,4-diazepin-2-ones) are listed in Table III.

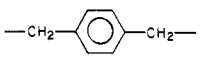
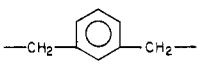
As observed with hexahydro-1,4-diazepin-2-one derivatives, both acetone cyanohydrin and cyclohexanone gave poor yields. For example, when acetone cyanohydrin was replaced with acetone, more than a 20-fold increase was obtained for **5a** and **5c**.

The crude products **5a** and **5c** melted over a wide range, suggesting mixtures of diastereoisomers. The isomers of **5c** were separated by extraction into high- and low-melting isomers in a 49:51 ratio. Although the isomers were not distinguishable by GC or TLC, differences between the two diastereomers can be found in the IR and NMR spectra data. In the IR spectrum the major difference between the two isomers lies in a 22-cm^{-1} shift in the carbonyl band (1617 cm^{-1} for the high-melting isomer vs. 1595 cm^{-1} for the low-melting isomer). Since these bands are so close together, they cannot be used to estimate the ratio of the two isomers. Similarly, ^1H NMR spectra are not useful for the same purpose, for only a slight difference in the chemical shifts for the eight methyl groups at carbons 3, 3', 5, and 5' are detectable (four singlets at δ 1.35, 1.33, 1.13 and 1.12 for the low-melting isomer vs. singlets at δ 1.15 and 1.45 for the other isomer). However, the presence of four singlets for the methyl protons suggests that the low-melting isomer may have the *RS* configuration.[5]

Table III. Yields of Bis(hexahydro-3,3,5,5,7-pentasubstituted-2*H*-1,4-diazepin-2-ones)



5

compd	X	R_1	R_2	yield, %	mp, °C
5a	$-(CH_2)_2-$	CH_3	CH_3	62.4 (3.4)[a]	132-182
5b	$-(CH_2)_3-$	CH_3	CH_3	2.1[a]	126-129
5c	$-(CH_2)_6-$	CH_3	CH_3	52.1 (5.3)[a]	122-192
5d	$-(CH_2)_6-$	$-(CH_2)_5-$		11.0	167-169
5e	$-(CH_2)_3N(CH_3)(CH_2)_3-$	CH_3	CH_3	20.2[a]	231-233[b]
5f		CH_3	CH_3	23.1	200-207
5g		CH_3	CH_3	12.2	144-150

[a] Rather than acetone, acetone cyanohydrin was used in the reaction. [b] Boiling point at 0.026 kPa.

Table IV. Effect of Various Catalysts on the Yield and Diastereomeric Distribution of 1,1′-(1,2-Ethanediyl)bis(hexahydro-3,3,5,5,7-pentamethyl-2*H*-1,4-diazepin-2-one) (5a)

			ratio of diastereomers,[b] %	
expt	type and amt of catalyst[a]	yield, %	high melting	low melting
A	3.9% $CH_3OCH_2CH_2OCH_3$	36.3		
B	3.9% BTEAC[c]	62.4	(48.6)[d]	(51.4)[d]
C	3.9% $(CH_3OCH_2CH_2OCH_2CH_2)_2O$	60.3	38.9	61.1
D	10.8% $CH_3(OCH_2CH_2)_nOH$ (av mol wt 350)	67.0	40.0 (40.7)[d]	60.0 (59.3)[d]
E	3.9% $CH_3(OCH_2CH_2)_nOH$ (av mol wt 350)	67.3	42.6	57.3
F	10.8% $CH_3(OCH_2CH_2)_nOH$ (av mol wt 5000)	67.9	46.3	53.7
G	3.9% $(-CH_2CH_2O-)_n$ (av mol wt 200 000)	56.7	40.8	59.2
H	none	63.1[e]	49.3	50.7

[a] Weight percent of *N,N′*-bis(3-amino-1,3-dimethylbutyl)-1,2-ethanediamine used. [b] Measured by ^{13}C NMR unless specified otherwise. [c] Benzyltriethylammonium chloride. [d] Values in parentheses for separation by fractional crystallization. [e] Methylene chloride was used as the solvent.

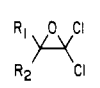
On the other hand, ^{13}C NMR spectra are very useful in determining semiquantitatively the ratio of two diastereomers. Thus by measuring the peak heights due to the methylene carbon atom attached to the amide group (δ 47.55 for the high-melting isomer and δ 48.46 for the low-melting one) in the broad-band, decoupled ^{13}C NMR, one can determine the ratio of the two diastereomers. An excellent agreement between the result obtained from ^{13}C NMR and from the fractional recrystallization can be seen in Table IV (see experiment D).

The facile separation of diastereomers and estimation of the diastereomeric distribution of **5a** by ^{13}C NMR prompted us to investigate the effect of the reaction conditions on the yield and diastereomeric distribution of **5a**. The results are summarized in Table IV.

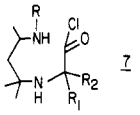
Initially, benzyltriethylammonium chloride (BTEAC) was used as a phase-transfer catalyst, and we were able to make **5a** in 62.4% yield (see experiment B in Table IV). Acyclic ethers were found to be slightly better than BTEAC, and up to a 67% yield of **5a** could be isolated provided the ether had a molecular weight of between 350 and 5000 (see experiments D–F in Table IV). The amount of the catalyst used appears to have no significant effect on the yield of **5a**, but lesser amounts of the catalyst increase the high-melting isomer content (see experiment D and E).

Compound **5a** was also prepared in 63% yield without the use of any PTC (see experiment H in Table IV). The reaction takes about 40% longer than the one which uses the catalyst. However, the advantages of not using any PTC are twofold: (a) elimination of the use and recovery of the catalyst and (b) the easier control of the exothermic reaction which takes place during the addition of a base.

Regardless of whether one uses PTC or not, an involvement of 1,1-dichloro-1,2-epoxyalkane (**6**) in the formation of a hexahydro-1,4-diazepin-2-one from the 1,3-diamine and trichloromethyl anion is speculated (a similar intermediate was invoked by others[6,7]). An attack on epoxide **6** by the primary amino group of a 1,3-diamine (**2**) followed by that on the ensuing acyl chloride (**7**) by another amino group would result in the formation of a hexahydro-1,4-diazepin-2-one (**3**).



6



7

In conclusion, hexahydro-1,4-diazepin-2-ones can be prepared in good yields by reacting 1,3-alkanediamines

(5) The proton NMR work carried out with an optically active shift reagent gave an inconclusive result from which a definite assignment of configuration was not possible.

(6) Compere, Edward L., Jr.; Weinstein, David A. *Synthesis* **1977**, 852.
(7) Lind, Hanns; Winkler, Tamma *Tetrahedron Lett.* **1980**, *21*, 119.

with acetone (rather than acetone cyanohydrin) and trichloromethyl anion in the presence of a catalyst such as poly(ethylene glycol methyl ether). The diastereomeric distribution of compound **5a** can be readily determined by either a fractional recrystallization or by ^{13}C NMR.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 467 spectrometer. All ^1H NMR spectra were determined on a Varian A-60 spectrometer and chemical shifts are reported in δ units relative to Me_4Si. ^{13}C NMR spectra were obtained by using a Bruker Model HX-90E. The mass spectra were determined on a Varian MAT 311A. Melting points were taken on a Mel-Temp apparatus and are uncorrected.

Diacetonamine (1). In a 3-L, three-necked flask were placed 937.5 g (9.6 mol) of mesityl oxide and 1225 mL of concentrated ammonium hydroxide. The mixture was heated to 45–50 °C for about 4 h and then stirred overnight at room temperature. The following morning the excess ammonia was stripped off at reduced pressure (water aspirator). The resulting yellow solution showed 27.4% diacetonamine content. It was kept in a refrigerator until it was ready to be used in the subsequent reaction.

General Procedure for the Preparation of 1,3-Diamines 2a–c and 4a–f. For a 1-mol-scale reaction in the preparation of 1,3-diamines **2a–c**, 30 g of 20-mesh aluminum granules, 130 mL of water, and 1.0 g of mercuric chloride are placed in a 1-L, three-necked flask. To the above cooled mixture (about 0 °C) is added dropwise a solution of **1** (1 mol) and an alkylamine (1 mol). By adjusting the addition rate, the reaction temperature is maintained at 20–35 °C. The addition takes about 30 min. After reacting overnight at room temperature, the reaction mixture is heated to 90 °C for 1 h, cooled, and filtered. The filtrate is stirred with about 15 g of sodium hydroxide pellets, forming two layers. The aqueous layer is extracted twice with 100 mL of ether. The ether extracts are combined with the above organic layer, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue is then fractionated at reduced pressure to isolate the desired 1,3-diamines **2a–c**.

Bis(1,3-diamines) **4a–f** are prepared by following the same procedure as for **2a–c** with a 2:1 molar ratio of diacetonamine and a diamine.

Representative examples are supplied below. Spectral data and elemental analyses for other 1,3-diamines listed in Table I are given in the supplementary material.

***N*^{2}-Butyl-4-methyl-2,4-pentanediamine (2a).** In a 1-L, three-necked flask were placed 150 mL of water, 1.0 g of mercuric chloride, and 30 g of granular aluminum while the flask was kept near 0 °C with an acetone–dry ice bath. When a vigorous evolution of hydrogen started, a premixed mixture of 99.0 g (1.35 mol) of *n*-butylamine and 156.0 g (about 36%) aqueous diacetonamine was added dropwise. By adjustment of the addition rate, the pot temperature was maintained at 20–35 °C. As the reaction progressed the reaction mixture became thicker. The addition took about 20 min. The reaction mixture was allowed to stand over the weekend at room temperature.

The resulting light gray slurry was stirred, heated to 90 °C, cooled, and filtered. The filtrate was treated with about 15 g of sodium hydroxide pellets to form two layers. The top layer was removed. The aqueous layer was extracted twice with 100 mL of ether, and the combined ether extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated. The combined organic material was distilled to give 76.9 g (91.1% based on diacetonamine) of **2a**: bp 74–78 °C (0.93 kPa); IR (neat) 3350 (w), 3290 (m), 2940 (s), 1570 (m), 1460 (s), 1370 (s), 1190 (s), 860 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.2–3.0 (m, 3 H), 1.54 (br s, 3 H), 1.25–1.60 (m, 6 H), 1.12 (s, 6 H), 0.7–1.10 (m, 6 H).

Anal. Calcd for $C_{10}H_{24}N_2$: C, 69.70; H, 14.04; N, 16.26. Found: C, 68.16; H, 13.80; N, 15.81.

***N*,*N*′-Bis(3-amino-1,3-dimethylbutyl)-1,6-hexanediamine (4c).** Following the general procedure 157.0 g (3.73 mol) of 27.3% aqueous diacetonamine and 302.3 g (1.82 mol) of 70% aqueous 1,6-hexanediamine were reacted in the presence of 3.5 g of mercuric chloride, 300 mL of water, and 105 g of 20-mesh aluminum. After the mixture reacted overnight, the reaction product was worked up as usual. The combined organic layer was distilled through a 10-cm, vacuum-jacketed column packed with protruded stainless-steel packing material. The desired product boils at 144–145 °C (0.020 kPa). A total 348.0 g (52.4% yield) of **4c** was collected: IR (neat) 3355 (w), 3290 (m), 2975 (s), 1470 (m), 1370 (s), 1190 (s), 870 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20–3.15 (m, 6 H), 1.55 (s, 6 H), 1.25–1.50 (m, 12 H), 1.15 (s, 12 H).

Anal. Calcd for $C_{18}H_{42}H_4$: C, 68.73; H, 13.46; N, 17.81. Found: C, 68.26; H, 13.41; N, 17.41.

General Procedure for the Preparation of Hexahydro-2*H*-1,4-diazepin-2-ones 3a–d and 5a–g. For a 0.1-mol-scale reaction in the preparation of **3** derivatives, 0.12 mol of a 1,3-diamine, 0.1 mol of acetone, 0.3 g of benzyltriethylammonium chloride (BTEAC), and 40 mL of chloroform are placed in a 250-mL, three-necked flask. To the above cooled (about 0 °C) mixture is added dropwise 20 g of 50% aqueous sodium hydroxide solution while the reaction temperature is maintained at 0–17 °C. After the completion of the addition of the sodium hydroxide solution, the reaction temperature is allowed to come to ambient temperature and the mixture allowed to react overnight. Enough water is added to the white slurry to result in the formation of two layers. The aqueous layer is extracted twice with 70 mL of methylene chloride. The organic layers are combined, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a crude product. A simple wash with hexane usually gives a snow-white product.

Representative examples are shown below. Spectral data and elemental analyses for other hexahydro-2*H*-1,4-diazepin-2-ones listed in Tables II and III are given in the supplementary material.

1-Dodecylhexahydro-3,3,5,5,7-pentamethyl-2*H*-1,4-diazepin-2-one (3b). Method A. In a 500-mL, three-necked flask were placed 113.8 g (0.4 mol) of *N*^{2}-dodecyl-4-methyl-2,4-pentanediamine (**2b**), 25.5 g (0.3 mol) of acetone cyanohydrin, 100 mL of chloroform, and 1.5 g of benzyltriethylammonium chloride. The above mixture was stirred while it was cooled to −2 °C. About 55 mL of 50% aqueous sodium hydroxide solution was added dropwise to the stirred mixture. The addition took 2.2 h, during which time the pot temperature was maintained between −2 and +2 °C. The reaction was stirred 2 days at 12–27 °C. After the usual workup, 33.7 g (31.9%) of the desired product was collected by fractional distillation: bp 180–185 °C (0.047 kPa); IR (neat) 3340 (m), 2965 (s), 2930 (s), 2860 (s), 1625 (s), 1468 (m), 1410 (s), 1360 (m), 1300 (m), 1260 (m), 1212 (m), 1160 (m), 1130 (m), 1090 (w), 1030 (w), 760 (w), 725 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.95–4.66 (m, 2 H), 3.08–3.60 (m, 4 H), 0.90, 1.13, 1.26, 0.8–2.0 (3 s, m, 38 H).

Anal. Calcd for $C_{22}H_{44}N_2O$: C, 74.94; H, 12.58; N, 7.94. Found: C, 74.74; H, 12.30;, N, 8.16.

Method B. In a 500-mL, three-necked flask were placed 93.9 g (0.33 mol) of *N*^{2}-dodecyl-4-methyl-2,4-pentanediamine (**2b**), 17.4 g (0.3 mol) of acetone, 1.0 g of benzyltriethylammonium chloride, and 120 mL of chloroform. To the above stirred mixture was added dropwise 60 g of 50% aqueous sodium hydroxide solution while the pot temperature was kept below 17 °C. The reaction was allowed to react overnight at room temperature. After the usual workup, 77.4 g (66.5%) of the desired product (**3b**) was isolated.

Separation of Diastereoisomers of 5a. Sixteen grams of the product containing two isomers was suspended in 170 mL of heptane and 25 mL of acetone and heated with stirring. The slurry was filtered while it was hot. The hot heptane–acetone insoluble solid weighed 7.5 g after being dried and had a melting point of 205–209 °C. The filtrate was cooled in a refrigerator overnight to form a white solid. It was filtered, dried, and weighed to isolate 7.9 g of a low-melting isomer which melts at 148–151 °C.

Spectral data for the high-melting isomer: IR (KBr pellet) 3350 (s), 2980 (s), 1617 (s), 1470 (s), 1460 (s), 1410 (s), 1380 (m), 1362 (s), 1310 (m), 1285 (m), 1270 (m), 1220 (s), 1170 (m), 1150 (s), 1100 (m), 1030 (m), 865 (w), 750 (m), 635 (m), 540 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.00–4.60 (m, 2 H), 3.40 (s, 4 H), 1.15, 1.45, 1.35–2.20 (2 s, m, 36 H); ^{13}C NMR ($CDCl_3$) δ 176.58, 78.46, 77.03, 75.60, 58.99, 51.52, 50.38, 47.55 (NCH_2), 42.06, 34.68, 33.02, 29.67, 18.46.

Spectral data for the low-melting isomer: IR (KBr pellet) 3370 (s), 2980 (s), 2920 (s), 1595 (s), 1470 (m), 1450 (s), 1420 (s), 1400 (s), 1380 (s), 1370 (s), 1365 (s), 1350 (s), 1345 (s), 1330 (m), 1310 (m), 1290 (m), 1270 (s), 1233 (s), 1210 (s), 1165 (s), 1140 (m), 1105 (m), 1080 (m), 1035 (m), 757 (m), 650 (m), 540 (m) cm^{-1}; ^1H NMR

($CDCl_3$) δ 4.00–4.60 (m, 2 H), 3.47 (s, 4 H), 1.12, 1.13, 1.33, 1.35, 1.30–2.20 (4 s, m, 36 H); ^{13}C NMR ($CDCl_3$) δ 176.71, 78.43, 77.03, 75.60, 59.35, 51.78, 50.67, 48.46 (NCH_2), 42.06, 34.94, 33.28, 30.03, 18.82.

Anal. Calcd for $C_{22}H_{42}N_4O_2$: C, 66.96; H, 10.73; N, 14.20. Found: C, 67.19; H, 10.54; N, 14.40 (for the isomer with higher melting point). Found: C, 66.67; H, 10.47; N, 14.13 (for the isomer with lower melting point).

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Registry No. 1, 625-04-7; **2a**, 75812-95-2; **2b**, 75812-96-3; **2c**, 75812-97-4; **3a**, 71620-95-6; **3b**, 75812-98-5; **3c**, 75812-99-6; **3c'**, 75813-00-2; **3d**, 75813-01-3; **4a**, 75813-02-4; **4b**, 75813-03-5; **4c**, 75813-04-6; **4d**, 75813-05-7; **4e**, 75813-06-8; **4f**, 75813-07-9; **5a** (isomer 1), 75813-08-0; **5a** (isomer 2), 75813-09-1; **5b**, 75813-10-4; **5c** (isomer 1), 75813-11-5; **5c** (isomer 2), 75813-12-6; **5d**, 75813-13-7; **5e**, 75813-14-8; **5f**, 75813-15-9; **5g**, 75813-16-0; mesityl oxide, 141-79-7; *n*-butylamine, 109-73-9; 1,6-hexanediamine, 124-09-4; acetone, 67-64-1; acetone cyanohydrin, 75-86-5; *n*-dodecylamine, 124-22-1; ethanolamine, 141-43-5; ethylenediamine, 107-15-3; 1,3-diaminopropane, 109-76-2; 3,3'-diamino-*N*-methyldipropylamine, 105-83-9; *p*-xylene-α,α'-diamine, 539-48-0; *m*-xylene-α,α'-diamine, 1477-55-0; cyclohexanone, 108-94-1.

Supplementary Material Available: Elemental analyses and IR and ^1H NMR spectral data of compounds **2b,c**, **3a,c,d**, **4a,b,d–f**, and **5a–g** (8 pages). Ordering information is given on any current masthead page.

Schiff Bases as External and Internal Electrophiles in Reactions of Functionalized Organolithium Reagents. A New Route to Isoindoline Derivatives and 1,2,3,4-Tetrahydroisoquinolines[1]

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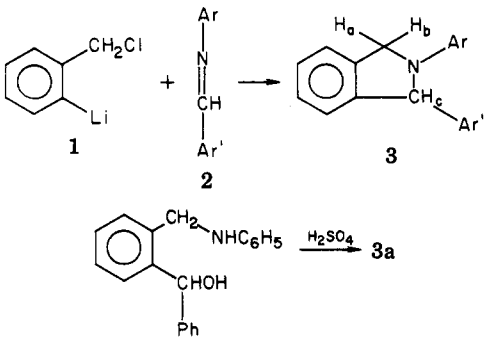
Reaction of Schiff bases with certain functionalized organolithium reagents is useful in the synthesis of 1,2-diarylisoindolines and 2,3-diarylphthalimidines. Schiff bases derived from 2-(2-bromophenyl)ethylamines on halogen–metal exchange with butyllithium undergo a Parham-type cyclization to yield 1-aryl-1,2,3,4-tetrahydroisoquinolines.

Parham et al.[2] discovered that at low temperatures certain aryl halides bearing electrophilic groups can be induced to undergo halogen–metal exchange selectively with butyllithium, affording synthetically useful functionalized organolithium reagents. When the organolithium reagents thus generated have the proper electrophilic group in the ortho position, cyclization reactions are possible. If the geometry of these functionalized organolithium reagents is correct, *direct* cyclization may occur through attack of the anionic center on the electrophilic substituent of the molecule.[3] The majority of the cyclizations studied have been *indirect* and involve the preliminary reaction of the anionic center with an added electrophile, followed by cyclization of the newly created anion.

Recently[2,4] it was shown that 3,4-dihydroisoquinolines could be prepared by the indirect method, through the addition of suitable nitriles to *o*-(2-bromoethyl)phenyllithium. One purpose of the present work was to investigate the possibility of forming dihydroisoindole derivatives by the indirect method using Schiff bases as the added electrophile.

The use of Schiff bases as electrophiles seemed promising since it is known[5] that in the presence of organolithium reagents N-substituted imines without hydrogens α to the imine carbon undergo simple addition at the imine double bond. When benzalaniline (**2a**) was added at −100 °C to the organolithium reagent (**1**) derived from *o*-bromobenzyl chloride and the mixture was allowed to warm to room temperature, 1,2-diphenylisoindoline (**3a**) was formed (Scheme I). The only known 1,2-diarylisoindoline was prepared earlier in this laboratory by Ludt and Hauser[6] through the acid-catalyzed cyclization of *o*-[(phenylamino)methyl]benzhydrol (**4**). Samples prepared

Scheme I[a]



[a] a, Ar = Ar' = Ph; b, Ar = 4-BrC_6H_4, Ar' = Ph; c, Ar = 2-Br-4-MeC_6H_3, Ar' = Ph; d, Ar = Ph, Ar' = 3,4-$(OCH_3)_2C_6H_3$.

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