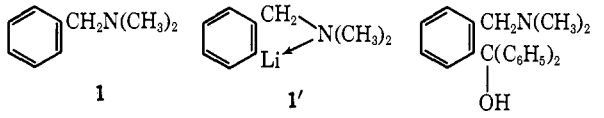
Lithiations of α- and β-Dimethylaminomethylnaphthalenes with *n*-Butyllithium and Condensations with Benzophenone. Some Related Results[1]

Robert L. Gay and Charles R. Hauser

Contribution from the Department of Chemistry, Duke University, Durham, North Carolina 27706. *Received November 18, 1966*

Abstract: α-Dimethylaminomethylnaphthalene was lithiated with *n*-butyllithium in ether–hexane to form a mixture of the 8- and 2-lithioamines in which the former predominated in a ratio of about 91:9; this was shown by treatment of the mixture with benzophenone and nmr analysis of the resulting carbinolamines. The 8 derivative was isolated in 58% yield, suggesting a useful new route for the synthesis of *peri* compounds. β-Dimethylaminomethylnaphthalene was treated similarly to produce a mixture of the 3- and 1-lithioamines in a ratio of about 55:45; after treatment with benzophenone, the 2,3-disubstituted naphthalene compound was isolated in 25% yield. These lithioamine ratios were found not to change significantly over a wide range of lithiation times. Independent syntheses of three of the four carbinolamines indicated above were carried out and some further reactions of these compounds were effected.

Recently,[2] benzyldimethylamine (**1**) was lithiated with *n*-butyllithium in ether–hexane to form *o*-lithioamine **1′**, which was condensed with benzophenone to give carbinolamine **2**. This product was converted to several derivatives.



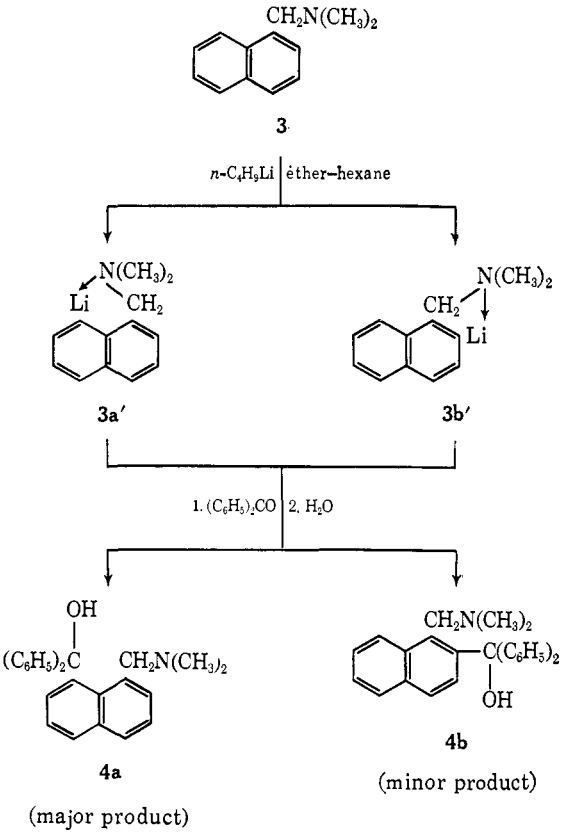
1 **1′** **2**

In the present investigation, a similar study was made of α- and β-dimethylaminomethylnaphthalenes which promised to be of special interest because of the possibility of lithiation at two nonequivalent positions in each case.

Results with α-Dimethylaminomethylnaphthalene (3). This amine might conceivably undergo lithiation at either the 8 position to form lithioamine **3a′** or the 2 position to form lithioamine **3b′**; condensations of **3a′** and **3b′** with benzophenone would afford carbinolamines **4a** and **b**, respectively (Scheme I).

This lithiation–condensation reaction was found to afford largely carbinolamine **4a**, which was readily isolated in 58% yield. The crude reaction product, obtained in about 79% yield, was shown by thin layer chromatography (tlc) to consist not only of **4a** but also of another component, presumably the isomeric carbinolamine **4b**; evidence for **4b** as the minor product is presented below. Actually, predominant *ortho* lithiation of **3** leading to **4b** had been expected, since such *ortho* lithiation of amine **1** occurs exclusively.[2,3] The

Scheme I



product isolated was shown to be carbinolamine **4a** or **b** by analysis and by infrared and nmr spectra (see Tables I and II). Its structure was established as **4a** by independent synthesis from anhydride **5** through the known bromo acid **6** (Scheme II).

Bromo acid **6** agreed with its previously reported description.[4] The structures of the intermediate bromo

(1) Supported by the Petroleum Research Fund administered by the American Chemical Society and by the Army Research Office (Durham).

(2) F. N. Jones, R. L. Vaulx, and C. R. Hauser, *J. Org. Chem.*, 28, 3461 (1963).

(3) For further demonstration of the strong tendency of the lithium atom to occupy an *ortho* positiion in lithioamine **1′** see W. H. Puterbaugh and C. R. Hauser, *J. Am. Chem. Soc.*, 85, 2467 (1963).

(4) H. G. Rule, W. Purcell, and R. R. H. Brown, *J. Chem. Soc.*, 170 (1934).

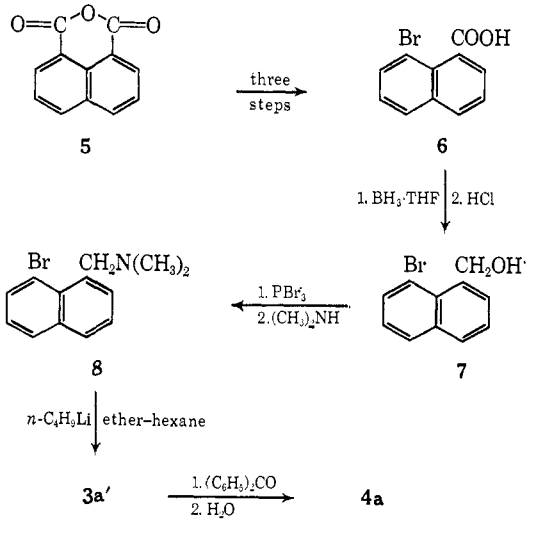
Table I. Infrared Data

Compd	Functional Group	Functional group absorptions, Peak, cm^{-1}	Aromatic absorptions, cm^{-1} [a]
3	$CH_2N(CH_3)_2$	840[b]	765[c] 790[d]
4a	$CH_2N(CH_3)_2$	852[b]	776, 703[f]
	OH (tertiary)	3425 (1171, 1379)[e]	763[d]
7	OH (primary)	3401 (1058, 1304)[e]	759[d]
8	$CH_2N(CH_3)_2$	847[b]	765[d]
11	C-O-C (cyclic)	1078, 1062[g]	779, 699[f] 768[d]
16	$CH_2N(CH_3)_2$	839[b]	775[c] 791[d]
17a	$CH_2N(CH_3)_2$	833[b]	759, 702[f]
	OH (tertiary)	3436 (1175, 1346)[e]	750[c] 894[h]
17b	$CH_2N(CH_3)_2$	841[b]	775, 702[f]
	OH (tertiary)	3413 (1167,1368)[e]	760[c] 812[i]
20	C=O (amide)	1633[i]	744[c] 888[h]
21	$CH_2N(CH_3)_2$	837[b]	743[c] 881[h]
24	$CH_2N(CH_3)_2$	847[b]	754[c] 812[i]
25	$CH_2N(CH_3)_2$	845[b]	754, 701[f]
	OH (tertiary)	3436 (1167, 1359)[e]	776[c] 901[h]
28	C-O-C (cyclic)	1032, 1025[g]	759, 697[f] 748[c] 810[i]

[a] See L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, pp 75–79. [b] See W. Q. Beard, Jr., and C. R. Hauser, *J. Org. Chem.*, **25**, 334 (1960). [c] Four adjacent aromatic hydrogens. [d] Three adjacent aromatic hydrogens. [e] See footnote *a*, p 96. [f] Five adjacent aromatic hydrogens. [g] See footnote *a*, p 119. [h] One aromatic hydrogen. [i] Two adjacent aromatic hydrogens. [j] See footnote *a*, p 205.

alcohol **7** and bromo amine **8** were supported by analysis and absorption spectra (see Tables I and II). The over-all yield of carbinolamine **4a** from anhydride **5** was 23%, which is considerably lower than that (58%) obtained from amine **3** (see Scheme I).

Scheme II



Although carbinolamine **4b** was not isolated from the product mixture obtained according to Scheme I, it was indicated to be present in relatively small amount by comparison of the nmr spectrum of this mixture

Table II. Nmr Data

Compd[a]	Type of hydrogen	Peak character	Peak center or over-all range, ppm[b]	No. of hydrogens[c]
3	Methyl	Singlet	2.13	5.9(6)
	Methylene	Singlet	3.63	2.0(2)
	Aromatic	Multiplet	7.10–8.30	7.2(7)
4a	Methyl	Singlet	1.95	5.9(6)
	Methylene	Singlet	3.24	2.0(2)
	Aromatic	Multiplet	6.90–7.99	16.8(17)[d]
4a + 4b (mixt)[e]	Methyl	Two singlets	1.95 2.17	5.46(6) 0.52(6)
	Methylene	Two singlets	3.25 3.66	1.75(2) 0.17(2)
	Aromatic	Multiplet	6.96–8.00	16.7(17)[d]
7	Hydroxyl	Singlet	3.05	1.1(1)
	Methylene	Singlet	5.38	1.9(2)
	Aromatic	Multiplet	6.90–7.92	5.9(6)
8	Methyl	Singlet	2.12	6.0(6)
	Methylene	Singlet	4.16	2.0(2)
	Aromatic	Multiplet	6.76–7.90	6.0(6)
11	Methylene	Singlet	4.88	2.0(2)
	Aromatic	Multiplet	6.70–7.85	16.3(16)
16	Methyl	Singlet	1.84	5.9(6)
	Methylene	Singlet	3.14	2.0(2)
	Aromatic	Multiplet	7.00–7.77	6.9(7)
17a	Methyl	Singlet	2.07	5.8(6)
	Methylene	Singlet	3.04	2.1(2)
	Aromatic	Multiplet	6.92–7.75	17.4(17)[d]
17b	Methyl	Singlet	2.06	6.1(6)
	Methylene	Singlet	3.60	1.9(2)
	Aromatic	Multiplet	6.58–7.79	17.5(17)[d]
17a + 17b (mixt)[f]	Methyl	Singlet	2.07	6.1(6)
	Methylene	Two singlets	3.06 3.63	1.12(2) 0.85(2)
	Aromatic	Multiplet	6.67–7.86	17.0(17)[d]
20	Methyl	Two singlets	2.83 3.16	2.9(3) 3.1(3)
	Aromatic	Multiplet	7.26–8.24	6.1(6)
21[g]	Methyl	Singlet	2.16	5.9(6)
	Methylene	Singlet	3.49	2.0(2)
	Aromatic	Multiplet	6.97–7.94	6.1(6)
24	Methyl	Singlet	1.79	6.0(6)
	Methylene	Singlet	3.27	2.0(2)
	Aromatic	Multiplet	6.65–8.16	6.0(6)
25	N-Methyl	Singlet	2.06	5.7(6)
	C-Methyl	Singlet	2.18	3.0(3)
	Hydroxyl	Singlet	3.14	1.0(1)
	Methylene	Singlet	3.67	1.9(2)
	Aromatic	Multiplet	6.93–8.20	15.6(15)
28	Methylene	Singlet	5.22	2.9(2)
	Aromatic	Multiplet	7.00–8.00	16.3(16)

[a] The solvent used was deuteriochloroform unless otherwise stated. [b] Downfield from tetramethylsilane (TMS) = 0 (internal standard). [c] Obtained by integration of peak areas; usually the reported value is the average of three integrations. The value in parentheses is the theoretical number of hydrogens, based on the proposed structure. [d] See ref 5. [e] Data for a 1-hr lithiation of amine **3**; see Table III, entry two, for calculations based on this data. [f] Data for a 24-hr lithiation of amine **16**; see Table IV, entry three, for calculations based on this data. [g] Run as a neat liquid.

with that of authentic carbinolamine **4a** (see Table II). Thus, the methylene and N-methyl peaks observed in the spectrum of **4a** were found also in that of the mixture. In addition, the latter spectrum showed two similar, but much smaller, peaks that may be ascribed to the same groups in **4b** (see Table II). In support of these conclusions, the areas (by integration) of the methyl and methylene peaks assigned to **4b** afforded a ratio of 3.1:1 (theoretical ratio, 3:1). Also, the total values of the integrations for each type of hydrogen in

the spectrum of the mixture afforded a ratio of 6:1.9:16.7 for methyl:methylene:aromatic[5] hydrogens (theoretical ratio, 6:2:17).

The relative amounts of isomeric carbinolamines **4a** and **b** in the mixture obtained according to Scheme I were estimated from the ratio of the integration values of their respective methyl (or methylene) peaks. Table III contains ratios of **4a** and **b** obtained in this manner from a series of experiments in which amine **3** was lithiated for various lengths of time followed by standardized periods for condensation with benzophenone and hydrolysis. These values show that the lithiation of amine **3** at the 8 position was favored over lithiation at the 2 position by about 91:9. The slight but steady increase in the amount of **4a** relative to lengths of reaction time may or may not be of significance. If a conversion of intermediate lithioamine **3b′** to lithioamine **3a′** occurs, it must do so very slowly, since the range of lithiation times employed was wide.

Table III. Reaction of Amine **3** According to Scheme I for Different Lithiation Times, Product Mixture Proportions by Nmr[a]

Reaction time	Total yield **4a** + **4b**, %	Ratio[b] **4a**:**4b**	% **4a**[c]	% **4b**[d]
5 min	27.7[e]	9.8	90.7	9.3
1 hr[f]	66.4	10.4	91.2	8.8
24 hr[g]	79.4	11.3	91.8	8.2
48 hr	52.7[h]	11.5	92.0	8.0

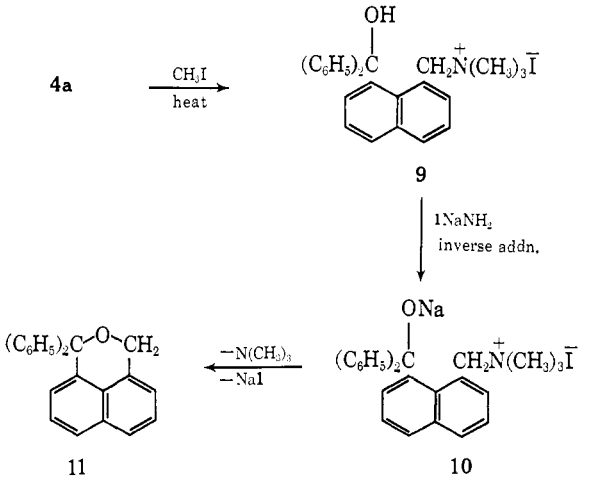
[a] In all cases, three integrations were recorded and their average value was used for further calculations. [b] This ratio was obtained by dividing the average integration value for the methylene peak at 3.25 ppm by the average value for the methylene peak at 3.66 ppm. [c] This percentage was obtained by dividing the average integration value for the methylene peak at 3.25 ppm by the sum of the average values for both methylene peaks, and multiplying the resulting number by 100. [d] This percentage was obtained by subtracting the percentage obtained in *c* from 100. [e] In this experiment 53.8% of starting amine **3** was recovered by distillation. [f] See Table II, entry three, for additional data on this mixture. [g] In a similar experiment in which the *n*-butyllithium used was prepared in ether [see H. Gilman, J. Beel, C. Brannen, M. Bullock, G. Dunn, and L. Miller, *J. Am. Chem. Soc.*, **71**, 1499 (1949)], the total yield (**4a** + **4b**) was 85%, the ratio (**4a**:**4b**) was 9.5, and the percentage of **4a** was 90.3. [h] In this experiment 30.2% of starting amine **3** was recovered by distillation.

Further evidence that lithiation of amine **3** involved mainly the 8-hydrogen (*peri* hydrogen) was obtained by treatment of a lithiation mixture of **3a′** and **3b′** (after 24 hr) with deuterium oxide. The nmr spectrum of the resulting deuterated amine showed that the 8-hydrogen, which appears downfield from the rest of the aromatic hydrogens because of deshielding,[6] had been substituted by deuterium to the extent of 79%.

The highly preferential lithiation at the 8 position of amine **3** furnishes a new route to the synthesis of *peri* compounds, as illustrated by the condensation of the resulting lithioamine **3a′** with benzophenone to form carbinolamine **4a**. Presumably intermediate **3a′** could be condensed with other electrophilic compounds to form the corresponding *peri* products.

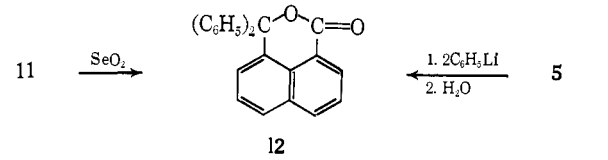
Moreover, such *peri* compounds may be converted to other 1,8 derivatives. For example, carbinolamine **4a** was converted to its methiodide **9**, which was cyclized by means of sodium amide to cyclic ether **11** in 89% yield (Scheme III).

Scheme III



The structure of **11** was supported by analysis and by infrared and nmr spectra (see Tables I and II). Also **11** was converted to lactone **12**, which was independently synthesized from anhydride **5** by a known method[7] (Scheme IV).

Scheme IV



Although the selenium dioxide oxidation of ether **11** afforded lactone **12** in only 11% yield, no other product was isolated; probably the yield of **12** from **11** could be improved. Attempts to reduce lactone **12** back to ether **11** with lithium aluminum hydride in ethyl ether were unsuccessful; instead of **11**, an acetal was obtained on recrystallization from ethanol. A similar observation has previously been reported.[8]

Interestingly, the preferential lithiation at the 8 position of α-dimethylaminomethylnaphthalene **3** is to be contrasted with the previously observed[9,10] preferential lithiation at the 2 position of α-methoxynaphthalene **13**.[11] Thus, lithiation of **13**, followed by carbonation, has afforded much more of acid **14** than acid **15**; the ratio of **14** to **15** was 83:17 with commercial *n*-butyllithium in hexane but 65:35 with the reagent prepared in ether.[9a] Incidentally, we observed no appreciable

(5) It is assumed that the peak for the hydroxyl hydrogen, which could be found nowhere else in the spectra of either the pure carbinolamines or their mixtures, is hidden within the aromatic multiplet; when deuteriochloroform solutions of these compounds were treated with deuterium oxide prior to analysis, the area of the aromatic portion of their spectra was reduced.

(6) For a discussion (and other examples) of such deshielding of the *peri* hydrogen of other 1-substituted naphthalenes see G. O. Dudek, *Spectrochim. Acta*, **19**, 697 (1963). We are indebted to Dr. P. W. Jeffs for help in the interpretation of our nmr data.

(7) G. Wittig, M. Leo, and W. Wiemer, *Ber.*, **64**, 2410 (1931).

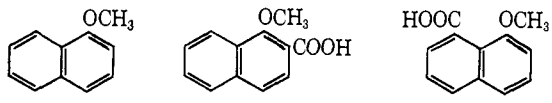
(8) R. L. Letsinger and P. T. Lansbury, *J. Am. Chem. Soc.*, **81**, 939 (1959).

(9) (a) B. M. Graybill and D. A. Shirley, *J. Org. Chem.*, **31**, 1221 (1966); (b) S. V. Sunthankar and H. Gilman, *ibid.*, **16**, 8 (1951).

(10) R. A. Barnes and L. J. Nehmsmann [*ibid.*, 27, 1939 (1962)] proposed that, initially, 8-lithio-1-methoxynaphthalene was formed predominantly, followed by isomerization to 2-lithio-1-methoxynaphthalene; later work[9a] presented evidence that such a change is negligible.

(11) The reason for this difference and the mechanism of the lithiation of these compounds are under investigation.

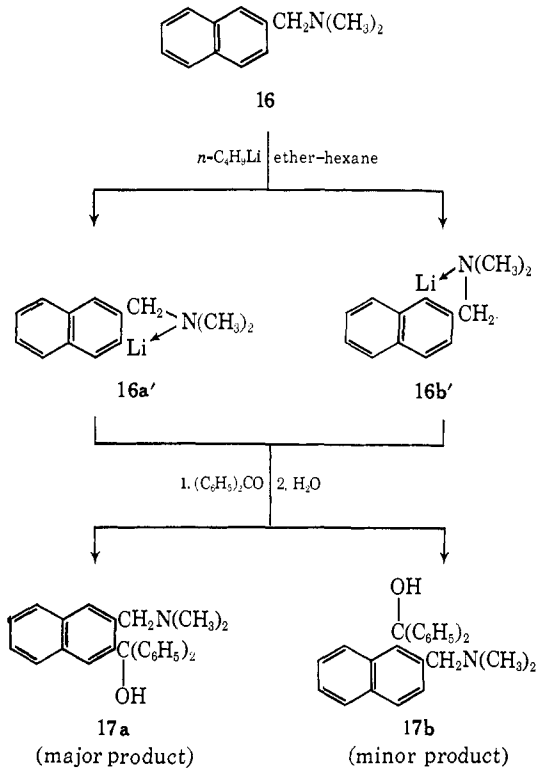
difference in lithiations of amine **3** under these two conditions (see Table III, footnote *g*).



13 14 15

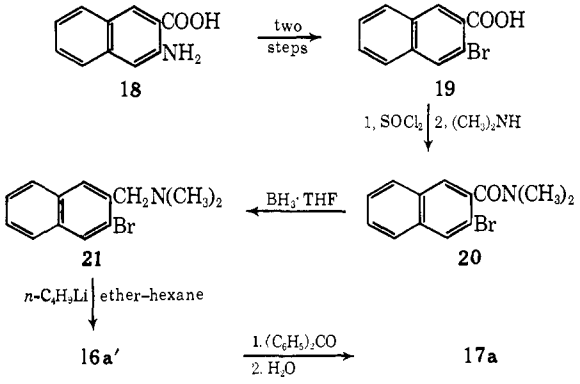
Results with β-Dimethylaminomethylnaphthalene (16). This amine might undergo lithiation at either the 3 position to form lithioamine **16a′** or the 1 position to form lithioamine **16b′**; condensations of **16a′** and **16b′** with benzophenone would afford carbinolamines **17a** and **b**, respectively (Scheme V).

Scheme V



Actually, the crude condensation product, obtained in 79% yield, was shown by tlc to consist of two components, one of which was isolated in 25% yield by fractional crystallization. That the compound thus isolated was **17a** was supported by analysis and by infrared and nmr spectra (see Tables I and II); its structure was confirmed by independent synthesis from amino acid **18** through the known bromo acid **19** (Scheme VI).

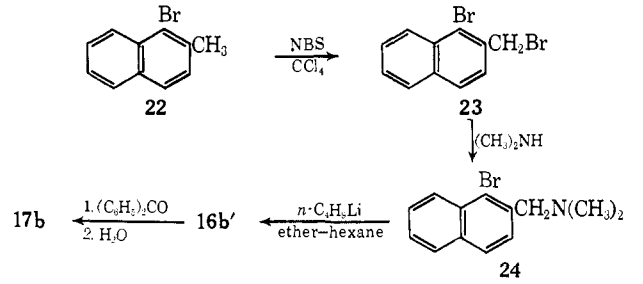
Scheme VI



Bromo acid **19** agreed with its previously reported description.[12] The structures of intermediate bromo amide **20** and bromo amine **21** were supported by analysis and absorption spectra (see Tables I and II). The over-all yield of carbinolamine **17a** from amino acid **18** was 20%, which is lower than that (25%) obtained by the much easier method shown in Scheme V.

Although carbinolamine **17b** was not isolated from the reaction mixture obtained according to Scheme V, it was shown to be present by comparison of the nmr spectrum of this mixture with those of independently synthesized samples of **17a** (Scheme VI) and **17b**; the latter was prepared from **22** through the known dibromide **23** (Scheme VII). Clearly the peaks exhibited by **17a** and **17b** accounted fully for those shown by the mixture (see Table II).

Scheme VII



Dibromide **23** agreed with its previously reported description.[13] The structure of bromo amine **24** was supported by analysis and by infrared and nmr spectra (see Tables I and II). The over-all yield of carbinolamine **17b** from bromide **22** was 46%.

The relative amounts of isomeric carbinolamines **17a** and **17b** in the mixture obtained according to Scheme V were estimated from the ratio of the integration values for their respective methylene peaks. Table IV contains ratios of **17a** and **b** obtained in this manner for a series of experiments in which amine **16** was lithiated for various lengths of time followed by standardized periods for

Table IV. Reaction of Amine **16** According to Scheme V for Different Lithiation Times, Product Mixture Proportions by Nmr[a]

Reaction time	Total yield **17a** + **17b**, %	Ratio[b] **17a**:**17b**	% **17a**[c]	% **17b**[d]
5 min	7.4[e]	1.11	52.7	47.3
1 hr	53.8[f]	1.27	55.8	44.2
24 hr[g]	78.3	1.32	56.8	43.2
48 hr	79.4	1.37	57.8	42.2

[a] In all cases, three integrations were recorded and their average value was used for further calculations. [b] This ratio was obtained by dividing the average integration value for the methylene peak at 3.06 ppm by the average value for the methylene peak at 3.63 ppm. [c] This percentage was obtained by dividing the average integration value for the methylene peak at 3.06 ppm by the sum of the average values for both methylene peaks, and multiplying the resulting number by 100. [d] This percentage was obtained by subtracting the percentage obtained in *c* from 100. [e] In this experiment 78.8% of the starting amine **16** was recovered by distillation. [f] In this experiment 21% of the starting amine **16** was recovered by distillation. [g] See Table II, entry ten, for additional data on this mixture.

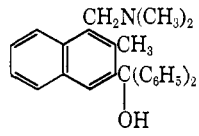
(12) J. Kenner, W. H. Ritchie, and R. L. Wain, *J. Chem. Soc.*, 1528 (1937).

(13) J. B. Shoesmith and H. Rubli, *ibid.*, 3102 (1927).

condensation with benzophenone and hydrolysis. These values show that the lithiation of amine **16** at the 3 position was favored over lithiation at the 1 position by about 55:45. The slight but steady increase in the amount of **17a** relative to lengths of reaction time may or may not be of significance.

The preferential lithiation of amine **16** at the 3 position furnishes an easy route to the synthesis of certain 2,3-substituted naphthalene compounds, as illustrated by the condensation of lithioamine **16a'** with benzophenone to form **17a**. Presumably intermediate **16a'** could be condensed with other electrophilic compounds to afford other 2,3-substituted naphthalenes.

Moreover, such 2,3-substituted naphthalenes may be converted to other 2,3 derivatives. Thus, carbinolamine **17a** was converted to its methiodide which was rearranged by means of excess potassium amide to tertiary amine **25** in 70% yield.[14] The structure of **25** was supported by analysis and by infrared and nmr spectra (see Tables I and II). Also, **17a** was treated with hydrobromic acid to form apparently quaternary salt **26** in 95% yield.



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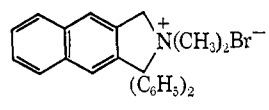

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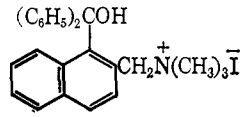
In connection with this work, carbinolamine **17b** (see Scheme VII) was converted to its methiodide **27**, which was thermally cyclized to naphthofuran **28** by a method previously developed in this laboratory.[15] The structure of cyclic ether **28** was supported by analysis and by infrared and nmr spectra (see Tables I and II).



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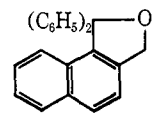

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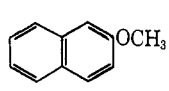
The preferential lithiation at the 3 position of amine **16** is comparable to that at the 3 position of β-methoxynaphthalene **29** observed previously.[9b] The latter reaction was evidenced by carbonation to form methoxy acid **30** in 50% yield; none of the isomeric acid **31** was reported.[9b]



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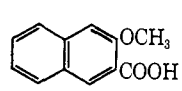

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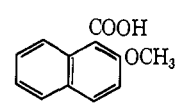

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We have observed that lithiation of methoxy compound **29** with *n*-butyllithium in ether–hexane appears to produce a mixture of lithio intermediates, since treatment with benzophenone afforded two products (by tlc).

(14) For previous work on the *ortho*-substitution rearrangement of similar quarternized carbinolamines see R. L. Vaulx, G. C. Jones, and C. R. Hauser, *J. Org. Chem.*, **27**, 4385 (1962).

(15) R. L. Vaulx, F. N. Jones, and C. R. Hauser, *ibid.*, **29**, 505 (1964).

Experimental Section

Melting points, taken on a Thomas-Hoover capillary melting point apparatus, are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 137 Infracord. Solids were prepared as potassium bromide pellets and liquids were run neat between sodium chloride plates. Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer using deuteriochloroform solutions and tetramethylsilane as an internal standard. These spectra were integrated three times and the average value used to calculate the relative number of hydrogens associated with each peak. Thin layer chromatographic (tlc) analyses were performed on microscope slides covered with a thin layer of Silica Gel G (Merck). Chloroform solutions of the material to be tested were spotted onto the plates, which were eluted with benzene and subsequently developed by standing in a jar containing crushed iodine crystals. Elemental analyses were performed by Paul Demoen, Janssen Pharmaceutical Research Laboratories, Beerse, Belgium.

α-Dimethylaminomethylnaphthalene (3). A solution of 500 g (2.83 moles) of 1-chloromethylnaphthalene and 550 g (12.2 moles) of anhydrous dimethylamine in 4 l. of absolute ethanol was stirred magnetically in a tightly stoppered flask at room temperature for 1 week. The solvent was removed, and the residue was stirred with excess 6 *M* sodium hydroxide and ether. The layers were separated. The alkaline aqueous layer was extracted with ether and the ethereal extracts were combined with the original ether layer. This ether solution was extracted with 3 *M* hydrochloric acid, and the acidic extracts were then made strongly alkaline. The resulting mixture was shaken with ether, and the layers were separated. The ether layer was dried over anhydrous magnesium sulfate, and the solvent was removed. The residual oil was distilled to give 475 g (91%) of α-dimethylaminomethylnaphthalene (**3**), bp 98–103° (0.5 mm) [lit.[16] bp 148–152° (16 mm)]. The picrate, after several recrystallizations from 95% ethanol, melted at 144–146° (lit.[16] mp 145°).

Lithiation of Amine 3 and Condensation with Benzophenone. In Table III are summarized the total yields and the estimated ratios of carbinolamines **4a** and **b** obtained after various lithiation times. A typical experiment is described below.

To a stirred solution of 4.63 g (0.025 mole) of α-dimethylaminomethylnaphthalene (**3**) in 200 ml of dry ether was added 17.7 ml (0.0275 mole) of 1.55 *M* *n*-butyllithium in hexane[17] to form lithioamines **3a'** and **3b'** (see Scheme I). The mixture was stirred magnetically in a tightly stoppered flask for 24 hr. The resulting dark red solution was added cautiously to a solution of benzophenone in 50–75 ml of dry ether, which had been brought to reflux on a steam bath. The resulting blue solution was refluxed on the steam bath for about 5 min, the volume being reduced to about 100 ml. The flask was then tightly stoppered and the solution was stirred magnetically for 12 hr to produce a precipitate. The reaction mixture was hydrolyzed with 100 ml of water, stirred for 12 hr, and filtered. The solid was washed with water and a little cold ether and dried to give 6.58 g of a mixture of carbinolamines **4a** and **b**, mp 190–197°. The layers of the filtrate were separated. The ethereal layer was combined with three ethereal extracts of the aqueous layer. This ether solution was extracted three times with 1*M* hydrochloric acid, and the combined acidic extracts were made strongly alkaline with 6 *M* sodium hydroxide. The resulting mixture was extracted three times with ether and the combined ethereal extract was dried over anhydrous magnesium sulfate. The solvent was removed and the residue was recrystallized from hexane to give 0.72 g of a mixture of carbinolamines **4a** and **b**, mp 150–190°; total yield, 7.30 g (79.4%).

This product mixture was crushed and mixed well in a mortar. A sample was dissolved in deuteriochloroform for nmr analysis. The data for a similar case are listed in Table II, entry three, and the calculations based on these data are listed in Table III, entry two.

From a similar reaction (larger scale), in which the lithiation time was 48 hr, 13.55 g (73.7%) of a mixture of **4a** and **b** was obtained. One recrystallization from acetonitrile afforded 10.72 g (58.3%) of pure 1-dimethylaminomethyl-8-diphenylhydroxymethylnaphthalene (**4a**), mp 198–201°, and 200–201° after further recrystallization from this solvent.

Anal. Calcd for $C_{26}H_{25}NO$: C, 85.00; H, 6.85; N, 3.82. Found: C, 85.32; H, 6.69; N, 4.05.

(16) J. V. Braun and K. Moldaehke, *Ber.*, **56B**, 2169 (1923).

(17) Used as obtained from Foote Mineral Co., New Johnsonville, Tenn.

Independent Synthesis of Carbinolamine 4a. 1,8-Naphthalic anhydride (**5**) was converted in 55% yield to 8-bromo-1-naphthoic (**6**), mp 177–179° (lit.[4] mp 177–178°), as described previously.[4]

A solution of 25.15 g (0.10 mole) of bromo acid **6** in 60 ml of dry diglyme[18] was added slowly to a stirred suspension of 3.5 g (0.093 mole) of sodium borohydride in 40 ml of dry diglyme[18] under a positive nitrogen pressure, followed by a solution of 24.5 g (0.12 mole) of freshly distilled boron trifluoride etherate in 25 ml of dry diglyme,[18] essentially as described previously for a similar reduction.[19] After stirring for 8 hr, the thick white suspension was poured onto ice (1500 ml) and 3 *M* hydrochloric acid (100 ml). After the ice had melted, the cold suspension was filtered, and the solid obtained was treated with sodium bicarbonate solution to remove 2.18 g (3.7%) of bromo acid **6**, mp 176–178.5°. The bicarbonate-insoluble material was boiled with 100 ml of hexane, and the mixture was filtered; this treatment was repeated several times, and the combined filtrates were concentrated to afford 16.0 g (67%) of 8-bromo-1-naphthylmethanol (**7**), mp 86–88°, and 87–88.5° after several more recrystallizations from hexane.

Anal. Calcd for $C_{11}H_9BrO$: C, 55.72; H, 3.82; Br, 33.71. Found: C, 55.78; H, 3.79; Br, 33.92.

The phenylurethan, recrystallized from benzene, melted at 140–141°.

Anal. Calcd for $C_{18}H_{14}BrNO_2$: N, 3.93; Br, 22.43. Found: N, 4.04; Br, 22.32.

To a solution of 14.5 g (0.06 mole) of bromocarbinol **7** in 500 ml of dry ether at −80° was added 10.8 g (0.04 mole) of phosphorus tribromide; the mixture was stirred at room temperature for 7 hr. Work-up afforded the crude dibromide (white solid), which was dissolved in 700 ml of absolute ethanol and treated with 25 ml of anhydrous dimethylamine. After stirring in a tightly stoppered flask for 24 hr, the mixture was processed as described above for the preparation of **3**. Distillation of a portion of the yellow oil obtained seemed to cause decomposition, so the remaining portion was chromatographed on alumina, eluting with dry ether. The colorless oil obtained by this process was magnetically stirred *in vacuo* (1 mm) for 30 min to afford 12.23 g (75%) of 8-bromo-1-dimethylaminomethylnaphthalene (**8**). This colorless oil was used for spectral samples and for the further reactions described below. The picrate of **8**, recrystallized three times for 95% ethanol, melted at 187–188°.

Anal. Calcd for $C_{19}H_{17}BrN_4O_7$: C, 46.27; H, 3.47; N, 11.36; Br, 16.21. Found: C, 46.22; H, 3.60; N, 11.66; Br, 16.48.

A stirred solution of 4.5 g (0.017 mole) of bromo amine **8** in 100 of dry ether was treated with 16.5 ml (0.026 mole) of 1.55 *M n*-butyllithium in hexane.[17] The clear orange-red solution was stirred for 60 min in a stoppered flask and then poured cautiously into a refluxing solution of 4.97 g (0.027 mole) of benzophenone in 100 ml of dry ether. After refluxing for 1 min, the flask was stoppered, and the solution was stirred for 6 hr. The resulting suspension was hydrolyzed with 100 ml of water and processed as described above for the lithiation of amine **3** to give 4.76 g (76.3%) of carbinolamine **4a**, mp 198–200°, undepressed on admixture with a sample of **4a** prepared from **3**. The infrared spectra of the two samples of **4a** were identical.

Preparation of Methiodide 9. A solution of 9.19 g (0.025 mole) of carbinolamine **4a** in 25 ml of methyl iodide was refluxed for 3 hr. Evaporation of the excess methyl iodide afforded 12.56 g (98.4%) of 1-(8-diphenylhydroxymethyl)naphthylmethyltrimethylammonium iodide (**9**), mp 213.5–215°, and 212–213° after precipitation from an acetonitrile solution with ether.

Anal. Calcd for $C_{27}H_{28}INO$: C, 63.65; H, 5.54; N, 2.75. Found: C, 63.34; H, 5.50; N, 2.80.

Cyclization of Methiodide 9 to Ether 11. To a stirred suspension of 26 g (0.051 mole) of methiodide **9** in 600 ml of commercial anhydrous liquid ammonia was added, during 5 min, a solution of 0.054 mole of sodium amide in 150 ml of liquid ammonia.[20] After 1 hr, the ammonia was replaced with 500 ml of dry ether (steam bath), and the resulting suspension was shaken with 150 ml of water. Filtration afforded 8.35 g of 1,1-diphenyl-3*H*-naphtho[1,8-*cd*]pyran (**11**), mp 158–160°. The ether layer of the filtrate was separated and washed with dilute hydrochloric acid, followed by dilute sodium hydroxide. After drying over anhydrous magnesium sulfate, the solvent was removed to afford 6.40 g more of **11**, mp 158–160°; total yield 14.74 g (89%). Several recrystallizations from ethanol failed to raise the melting point.

Anal. Calcd for $C_{24}H_{18}O$: C, 89.41; H, 5.63. Found: C, 89.12; H, 5.76.

Oxidation of cyclic ether **11** was effected by heating a 1.0-g (0.0031 mole) sample with 0.5 g (0.0045 mole) of selenium dioxide at 180° for 30 min, then at 150–160° for 2.5 hr (Woods metal bath). After cooling the solid was crushed under dry ether, and the mixture was filtered. The ethereal filtrate was washed with water and dried over anhydrous magnesium sulfate. The solvent was removed to afford 0.30 g of a solid, mp 170–190°. Two recrystallizations from absolute ethanol gave 0.11 g (11%) of 1,1-diphenyl-3-oxonaphtho[1,8-*cd*]pyran (**12**), mp 200–202.5°. Two more recrystallizations raised the melting point to 203–205° (lit.[7] mp 203–205°), undepressed on admixture with authentic lactone **12** (mp 204–205.5°) prepared from anhydride **5** and phenyllithium.[7] The infrared spectra of the two samples of **12** were identical.

Attempted reduction of lactone **12** (prepared from **5** by Wittig's method)[7] with lithium aluminum hydride in dry ether employing a Soxhlet extracter[21] afforded, after treatment with absolute ethanol, apparently 1,1-diphenyl-3-ethoxynaphtho[1,8-*cd*]pyran, mp 196–198°, and 198.5–201° after several more recrystallizations from absolute ethanol (lit.[8] mp 197.5–198.5°). The yield was 76%.

β-Dimethylaminomethylnaphthalene (16). 2-Chloromethylnaphthalene, bp 102–108° (0.8 mm) [lit.[22] bp 125–132° (2 mm)], was prepared in 64% yield from 2-naphthoic acid as described previously.[22]

A solution of 32.6 g (0.185 mole) of this chloride and 100 ml (1.51 moles) of anhydrous dimethylamine in 300 ml of absolute ethanol was allowed to stand in a tightly stoppered flask in an ice–salt bath (dewar) for several days. The reaction mixture was then processed as described above for the preparation of amine **3** to give 23.1 g (67.4%) of β-dimethylaminomethylnaphthalene (**16**), bp 89–91° (0.45 mm) [lit.[16] bp 130–132° (14 mm)]. The picrate of **16**, recrystallized from 95% ethanol, melted at 151–152° (lit.[16] mp 152°).

Lithiation of Amine 16 and Condensation with Benzophenone. In Table IV are summarized the total yields and the estimated ratios of carbinolamines **17a** and **17b** obtained after various lithiation times. A typical expriment is described below.

To a stirred solution of 4.63 g (0.025 mole) of β-dimethylaminomethylnaphthalene (**16**) in 200 ml of dry ether was added 17.7 ml (0.0275 mole) of 1.55 *M n*-butyllithium in hexane[17] to form lithioamines **16a′** and **16b′** (Scheme V). The mixture was stirred magnetically in a tightly stoppered flask to produce a dark red suspension containing an orange precipitate. This suspension was added to benzophenone and processed as described above for the lithiation of amine **3** to give 7.19 g (78.3%) of a mixture of **17a** and **b**, mp 142–178°. A sample was prepared for nmr analysis as there described; the resulting data for this experiment are listed in Table II, entry three, while calculations based on these data may be found in Table IV, entry three.

From a similar reaction (larger scale), in which the lithiation time was 45 hr, 19.04 g (76.4%) of a mixture of **17a** and **b** was obtained. This product was refluxed with 500 ml of acetonitrile; after filtering, the solution was allowed to stand undisturbed overnight. The precipitated crystals were filtered and the process was repeated. Filtration afforded 6.3 g (25.3%) of pure 2-dimethylaminomethyl-3-diphenylhydroxymethylnaphthalene (**17a**), mp 194–197°. The analytical sample of **17a**, isolated similarly, but recrystallized twice from acetonitrile and once each from ligroin and hexane, melted at 193–194.5°.

Anal. Calcd for $C_{26}H_{25}NO$: C, 85.00; H, 6.85; N, 3.82. Found: C, 84.87; H, 6.96; N, 3.72.

Independent Synthesis of Carbinolamine 17a. Amino acid[23] **18** was converted in 65% yield to 3-bromo-2-naphthoic acid (**19**), mp 216–218.5° (lit.[12] mp 219–220°), as described previously.[12]

A solution of 15.86 g (0.063 mole) of bromo acid **19** and 50 ml of thionyl chloride in 50 ml of dry benzene was refluxed for 30 min. After removing the excess thionyl chloride and benzene, the residue was cooled and dissolved in 100 ml of methylene chloride. This solution was added to a cold suspension of 50 ml of dimethylamine and 250 ml of 1 *M* sodium hydroxide. After stirring for 3 hr, the

(18) Freshly distilled from lithium aluminum hydride.

(19) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **82**, 686 (1960).

(20) See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 122 (1954).

(21) See R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, **69**, 1198 (1947).

(22) C. R. Hauser, D. N. van Eenam, and P. L. Bayless, *J. Org. Chem.*, **23**, 354 (1958).

(23) The preparation of amino acid **18** by Dr. D. L. Heywood and C. E. Moyer, Jr., of Union Carbide Corp., Olefins Division, South Charleston, W. Va., is gratefully acknowledged.

mixture was heated until the temperature of the escaping vapors reached 80°, then cooled and extracted with ether. The ethereal extract was washed with dilute acid and alkali and dried. The solvent was removed to give a red liquid, which solidified *in vacuo*. This residue was boiled with 1 l. of water and the mixture filtered; the filtrate was cooled to deposit N,N-dimethyl-3-bromo-2-naphthamide (**20**). This treatment was repeated several times with the filtered material to give a total of 12.0 g (68.2%) of **20**, mp 112–115°, and 114–115° after another recrystallization from boiling water.

Anal. Calcd for $C_{13}H_{12}BrNO$: C, 56.21; H, 4.35; N, 5.03. Found: C, 55.94; H, 4.34; N, 5.10.

A solution of 6.2 g (0.022 mole) of bromo amide **20** in 50 ml of dry[18] tetrahydrofuran (THF) was reduced with 66 ml (0.066 mole) of a 1 *M* solution of diborane in THF[24] essentially as described previously for similar amides.[25] After stirring for 1 hr at room temperature and for another hour at reflux, the reaction mixture was cooled and hydrolyzed, first with water dropwise (caution, foaming) and then with 50 ml of 6 *M* hydrochloric acid. The solvents were distilled until the temperature of the vapor reached 90°, and the residual mixture was cooled and extracted with ether. The solvent was removed from the dried ethereal solution and the residual oil was distilled to afford 3.69 g (63%) of 3-bromo-2-dimethylaminomethylnaphthalene (**21**), bp 82–83° (0.03 mm).

Anal. Calcd for $C_{13}H_{14}BrN$: C, 59.10; H, 5.36; N, 5.32. Found: C, 58.88; H, 5.41; N, 5.21.

The picrate, recrystallized several times from 95% ethanol, melted at 172–173.5°.

Anal. Calcd for $C_{19}H_{17}BrN_4O_7$: N, 11.37. Found: N, 11.71.

A stirred solution of 2.0 g (0.0076 mole) of bromo amine **21** in 100 ml of dry ether was treated with 7.3 ml of *n*-butyllithium in hexane[17] to produce an amber-colored suspension. After stirring magnetically for 75 min, this suspension was added to a refluxing solution of 2.21 g (0.012 mole) of benzophenone in dry ether and processed as described above for the similar reaction of bromo amine **8** to give 2.05 g (73.7%) of carbinolamine **17a**, mp 192–196°, undepressed on admixture with a sample of **17a** prepared as described above. The infrared spectra of the two samples of **17a** were identical.

***ortho*-Substitution Rearrangement of Methiodide of Carbinolamine 17a.** A solution of 7.65 g (0.021 mole) of carbinolamine **17a** in 50 ml of methyl iodide was refluxed for 36 hr. The resulting precipitate was collected to give 8.13 g (77%) of, presumably, 2-(3-diphenylhydroxymethyl)naphthylmethyltrimethylammonium iodide, mp 195–196° (temperature raised from 100°). Evaporation of the filtrate afforded some (20%) of the starting carbinolamine **17a**.

The unrecrystallized methiodide of **17a** (6.0 g, 0.0118 mole) was added to a stirred solution of 0.05 mole of potassium amide in 500 ml of commercial anhydrous liquid ammonia. After 4 hr, the reaction mixture was neutralized with ammonium chloride and processed as described previously[14] for the reaction of the methiodide of the related carbinolamine **2**. There was obtained, on recrystallization of the product from hexane, 3.13 g (70%) of 1-dimethylaminomethyl-2-methyl-3-diphenylhydroxymethylnaphthalene (**25**), mp 126–129°, and 126–128° after several more recrystallizations from this solvent.

Anal. Calcd for $C_{27}H_{27}NO$: C, 85.01; H, 7.13; N, 3.67. Found: C, 85.02; H, 7.05; N, 3.73.

(24) Obtained from Metal Hydrides, Inc., Beverly, Mass.

(25) H. C. Brown and P. Heim, *J. Am. Chem. Soc.*, **86**, 3567 (1964).

Cyclization of Carbinolamine 17a. This compound (0.75 g, 0.002 mole) was refluxed with 25 ml of hydrobromic acid for 6 hr. The resulting solid was collected and washed with small portions of water and dry ether to give 0.81 g (92%) of apparently 2,2-dimethyl-3,3-diphenylbenz[*f*]isoindolinium bromide (**26**), mp 288–290°, and 299–300° after recrystallization from acetonitrile.

Anal. Calcd for $C_{26}H_{24}BrN$: C, 72.60; H, 5.62; N, 3.25. Found: C, 72.64; H, 5.73; N, 3.38.

Independent Synthesis of Carbinolamine 17b. A mixture of 53.4 g (0.242 mole) of 1-bromo-2-methylnaphthalene (**22**) and 49.1 g (0.273 mole) of N-bromosuccinimide (NBS) in 300 ml of dry carbon tetrachloride was stirred and refluxed (no catalyst was used) for 14 hr, essentially as described previously.[13] The product was recrystallized from ligroin to afford 48.80 g (67%) of 1-bromo-2-bromomethylnaphthalene (**23**), mp 105.5–107.5° (lit.[13] mp 107°).

A cold stirred solution of 88 g (0.293 mole) of dibromide **23** in 600 ml of absolute ethanol was treated with 53 g (1.18 moles) of anhydrous dimethylamine. After stirring and heating at 110° in a tightly stoppered flask for 20 hr, the reaction mixture was processed as described above for amine **3** to give 69.7 g (90%) of 1-bromo-2-dimethylaminomethylnaphthalene (**24**), bp 98° (0.14 mm).

Anal. Calcd for $C_{13}H_{14}BrN$: C, 59.10; H, 5.36; N, 5.32. Found: C, 59.29; H, 5.42; N, 5.65.

The picrate, recrystallized from 95% ethanol, melted at 142–143.5°.

Anal. Calcd for $C_{19}H_{17}BrN_4O_7$: C, 46.23; H, 3.47; N, 11.36. Found: C, 45.88; H, 3.57; N, 11.15.

To a stirred solution of 13.31 g (0.05 mole) of bromo amine **24** in 200 ml of dry ether was rapidly added 38 ml (0.059 mole) of 1.55 *M* *n*-butyllithium in hexane.[17] After stirring magnetically in the tightly stoppered flask for 70 min, the solution was added to a refluxing solution of 12.4 g (0.068 mole) of benzophenone in dry ether and processed as described above, for the similar reaction of bromo amine **8**, to give 14.05 g (76.5%) of 1-diphenylhydroxymethyl-2-dimethylaminomethylnaphthalene (**17b**), mp 160–162°. Several more recrystallizations from hexane failed to raise the melting point.

Anal. Calcd for $C_{26}H_{25}NO$: C, 85.00; H, 6.85; N, 3.80. Found: C, 84.94; H, 6.69; N, 3.93.

Thermal Cyclization of Methiodide 27 to Cyclic Ether 28. A solution of 3.67 g (0.01 mole) of carbinolamine **17b** in 25 ml of methyl iodide was refluxed for 7 hr, and the excess methyl iodide was evaporated. The solid residue was dissolved in refluxing acetonitrile and the solution allowed to cool while 500 ml of dry ether was added dropwise. The cold suspension was filtered to afford 4.21 g (82.6%) of 2-(1-diphenylhydroxymethyl)naphthylmethyltrimethylammonium iodide (**27**), mp 204–206°. This melting point was not raised by several more such treatments.

Anal. Calcd for $C_{27}H_{28}INO$: C, 63.65; H, 5.54; N, 2.75. Found: C, 63.36; H, 5.50; N, 3.00.

A 3.69-g (0.0073 mole) sample of methiodide **27** was heated at 210–220° (Woods metal bath) for 15 min under dry nitrogen. After cooling, the solid was processed as described previously[15] for the related cyclization of the methiodide of **2**. Recrystallization of the product afforded 1.87 g (80%) of 1,1-diphenyl-1,3-dihydronaphtho[1,2-*c*]furan (**28**), mp 156–158°, and 157–158.5° after several recrystallizations from hexane.

Anal. Calcd for $C_{24}H_{18}O$: C, 89.41; H, 5.63. Found: C, 89.04; H, 5.63.