BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3606—3608 (1969)

N-Alkylation of Primary and Secondary Amines by Alkyl Halides and Lithium Naphthalene

Kyoichi SUGA, Shoji WATANABE, Tsutomu FUJITA and Tsu Pai PAN

Department of Applied Chemistry, Faculty of Engineering, Chiba University, Yayoi-cho, Chiba

(Received June 10, 1969)

Alkylation of trivalent nitrogen can be effected in a variety of ways, such as the action of alcohol on ammonia or an amine for the preparation of the lower amines, and for higher amines by the action of an alkyl halide on ammonia in the liquid phase. Certain organoalkali compounds are used under various conditions. Lithium dialkylamides can be made from dialkylamine and phenyllithium. Lithium diethylamide reacts with phenyl halide in ether to form diethylaniline.[1] This paper deals with a new convenient procedure for the alkylation of various higher amines.[2]

Recently, the authors have reported that lithium naphthalene in tetrahydrofuran solution is an excellent agent for the ethynylation of α,β-unsaturated ketones,[3] and for the oligomerization of various dienes.[4,5] To a solution of lithium naphthalene in tetrahydrofuran, dibenzylamine (I) was added. *n*-Butyl bromide was added to this solution and the mixture was allowed to react in the usual way to give dibenzylbutylamine (II) in good yeild. Identity was confirmed by elementary analyses, titration and spectral data. From the combination of other various amines and alkyl halides, high conversion into the corresponding alkylamines was achieved by this method. Typical results are presented in Table 1. When authentic samples were available, identity was also confirmed by com parison of the infrared absorption spectra and the retension time of gas chromatography with those of authentic samples. The effect of reaction variables on the alkylation of dibenzylamine has been examined, and typical results are presented in Table 2. Alkylation products are obtained in higher yields with organic bromides than with organic chlorides. Both metallic sodium and potassium gave lower yields of *N*-alkylated products than in the case where lithium was used. Other products were obtained. The results indicate that lithium naphthalene can be applicable for selective *N*-alkylation of various higher primary and secondary amines.

Experimental

Materials. Commercial tetrahydrofuran was purified by drying with metallic sodium and distilling over metallic sodium under nitrogen. Naphthalene was recrystallized from benzene. All amines, organic halides and other compounds were distilled before use. All the experiments were carried out in a dry apparatus under purified nitrogen.

Alkylation of Amines. *Dibenzylbutylamine.* To a mixture of 0.05 mol (6.5 g) of naphthalene and 100 m*l* of tetrahydrofuran, 0.1 mol (0.7 g) of metallic lithium cuttings was added, and the mixture was agitated at room temperature in an atmsphere of dry nitrogen.[3,4] After 1 hr, 0.1 mol (19.7 g) of dibenzylamine was added slowly. The reaction mixture was stirred for an additional 2 hr 0.1 mol (13.7 g) of *n*-butyl bromide was gradually added, and the mixture was stirred for an additional 1 hr at room temperature. The reaction mixture was decomposed with methanol, the insoluble matter was dissolved in water, and the organic material was transferred into isopropyl ether. The isopropyl ether extracts were washed with water, dried over anhydrous sodium sulfate, and distilled to give the following fractions: (a) bp 74—80°C/4 Torr, yield 6.7 g; (b) bp 121—158°C/4 Torr, yield 7.0 g; and (c) bp 158—160°C/4 Torr, yield 15 g. Gas-liquid chromatography of fraction (a) with a column (2 m) of Reoplex 400 on Celite 545 at a temperature of 140°C with Helium as a carrier gas (40 m*l*/min) showed two peaks: peak No. 1 (1, 4-dihydronaphthalene), retention time 23 min, peak area ratio 50%; and peak No. 2 (naphthalene), retention time 35 min, peak area ratio 50%. Quantitative data were obtained by comparison of peak areas to those of internal standard of known concentration. Fraction (b) was dibenzylamine. Fraction (c) was redistilled to give pure dibenzylbutylamine, bp 159—160°C/4 Torr, n_D^{20} 1.5681, infrared (IR); 2960, 1600, 1460, 1120, 740 and 695 cm^{-1}; nuclear magnetic resonance (NMR) (δ, ppm): 0.8 ($\text{C}\underline{\text{H}}_3$-, 3H), 1.5 ($\text{-C}\underline{\text{H}}_2\text{-C}\underline{\text{H}}_2\text{-}$, 4H), 2.4 ($\text{-C}\underline{\text{H}}_2\text{-}\underset{\text{CH}_2\text{ph}}{\text{N}}\text{-C}\underline{\text{H}}_2\text{-ph}$, 2H), 3.5 ($\text{ph-C}\underline{\text{H}}_2\text{-N-C}\underline{\text{H}}_2\text{-ph}$, 4H), 7.3 (aromatic protons, 10H), molecular weight from titrimetric procedure 240 (Calcd for $C_{18}H_{23}N$: 253).

Found: C, 85.24; H, 9.22; N, 5.43%. Calcd for $C_{18}H_{23}N$: C, 85.23; H, 9.15; N, 5.53%.

---

[1] C. H. Horning and F. W. Bergstrom, *J. Am. Chem. Soc.*, **67**, 2110 (1945).

[2] K. Suga, S. Watanabe, T. P. Pan and T. Fujita, *Chem. & Ind.*, **1969**, 78.

[3] K. Suga, S. Watanabe and T. Suzuki, *Can. J. Chem.*, **46**, 3041 (1968).

[4] K. Suga, S. Watanabe, H. Kikuchi and T. Watanabe, *ibid.*, **46**, 2619 (1968).

[5] K. Suga and S. Watanabe, This Bulletin, **40**, 1257 (1967).

[6] H. Pleininger, *Chem. Ber.*, **87**, 127 (1954).

TABLE 1. ALKYLATION OF VARIOUS PRIMARY AND SECONDARY AMINES BY ALKYL HALIDES AND LITHIUM NAPHTHALENE

Amine	Halide	Product*	Yield %	Bp (°C/Torr)	n_D^{20}	Infrared (cm^{-1})
Laurylamine	Butyl bromide	Butyllaurylamine	40	167—170/4	1.4489	3320, 2925, 1470, 1380, 1130, 720
Oleilamine	Butyl bromide	Butyloleilamine	40	225—230/4	1.5021	3340, 2925, 1480, 750
Benzylamine	Butyl bromide	Benzylbutylamine	55	133—135/2	1.5048	3320, 2960, 1460
Aniline	Methyl bromide	*N*-Methylaniline	50	78—79/10	1.6032	
Aniline	Ethyl bromide	*N*-Ethylaniline	70	80—84/10	1.5559	
Aniline	Butyl bromide	*N*-Butylaniline	74	120—122/10	1.5349	3360, 2960, 1500, 1320, 2925, 1470,
Aniline	Cyclohexyl bromide	*N*-Cyclohexylaniline	70	133—135/4	1.5620	1600, 745, 690
Dibenzylamine	Butyl bromide	Dibenzylbutylamine	60	159—160/4	1.5681	2960, 1460, 1600, 1120, 740, 695
Cyclohexylamine	Butyl bromide	Butylcyclohexylamine	55	78—84/12	1.4499	3340, 2960, 1460, 1370, 1130
Di-*n*-butylamine	Butyl bromide	Tri-*n*-butylamine	32	120—126/70	1.4583	2950, 1470, 1380
Dicyclohexylamine	Butyl bromide	Butyldicyclohexylamine	30	130—135/3	1.4860	2960, 1460
Pyrrolidine	Butyl bromide	*N*-Butylpyrrolidine	35	79—81/53	1.5288	2960, 2925, 1470, 1460
Diphenylamine	Butyl bromide	Butyldiphenylamine	30	122—125/2	1.5681	2960, 1600, 1500, 1370, 2925, 745, 690
N-Methylaniline	Methyl bromide	*N,N*-Dimethylaniline	60	71—73/10	1.5586	
Indole**	Butyl bromide	*N*-Butylindole	25	130—134/2	1.5695	2960, 2925, 1460, 1320, 760, 735, 710
		3-Butylindole	3	130—134/2		3400, 2960, 1460, 2925, 1350, 830, 730

* Elementary nitrogen analyses and neutral equivalent of these amines agreed with the calculated data.

** Indole is alkylated with alkyl halides in liquid ammonia or with Grignard reagents to give a mixture of *N*-alkyl- and 3-alkyl-indole.[6] It is interesting that the nitrogen atom of indole can be alkylated selectively by this procedure. NMR of *N*-butylindole: 0.98 ($C\underline{H}_3$-CH_2-, 3H), 1.3—1.7 (-$C\underline{H}_2$-$C\underline{H}_2$- 4H), 4.0 (-$\overset{|}{N}$-$C\underline{H}_2$-, 2H), 6.45 and 6.9 (-$C\underline{H}$=$C\underline{H}$-, 2H), 7.0—7.2 (aromatic protons, 4H). NMR of 3-butylindole: 0.9 ($C\underline{H}_3$-CH_2-, 5H), 1.5 (-$C\underline{H}_2$-, 4H), 2.7 (-$C\underline{H}_2$-$\overset{|}{C}$=, 2H), 6.7 (-$C\underline{H}$=$\overset{|}{C}$-, 1H), 7.5 (-$\overset{|}{N}\underline{H}$, 1H), 7.0 (aromatic protons, 4H).

Table 2. Reaction of dibenzylamine with various halides in the presence of lithium naphthalene

Halides	Product*	Yield (%)	Bp (°C/Torr)	n_{20}^{D}	Infrared (cm^{-1})
Ethyl bromide	Dibenzylethylamine	76	146—150/2	1.5598	2960, 1460, 2930, 1500, 740, 695
n-Propyl bromide	Dibenzyl-*n*-propylamine	48	157—159/2	1.5694	
n-Butyl bromide	Dibenzyl-*n*-butylamine	60	160—166/2	1.5474	
n-Hexyl bromide	Dibenzyl-*n*-hexylamine	90	168—172/2	1.5289	
n-Lauryl bromide	Dibenzyl-*n*-laurylamine	68	220—225/2	1.5203	
Allyl bromide	Allyldibenzylamine	85	150—155/2	1.5621	2950, 990, 910
Benzyl bromide	Tribenzylamine	70	235—245/2	91—92**	2950, 1470, 1600, 740
Bromobenzene	Dibenzylphenylamine	70	180—186/1	1.5741	2950, 1470, 1600, 740
n-Propyl chloride	Dibenzyl-*n*-propylamine	35	157—159/2	1.5694	
n-Hexyl chloride	Dibenzyl-*n*-hexylamine	78	168—172/2	1.5289	
n-Lauryl chloride	Dibenzyl-*n*-laurylamine	62	220—225/2	1.5203	
Allyl chloride	Allyldibenzylamine	67	150—155/2	1.5621	
Methallyl chloride	Dibenzylmethallylamine	36	177—180/2	1.5676	2950, 1470, 990, 910
Benzyl chloride	Tribenzylamine	59	235—245/2	91—92**	
Chlorobenzene	Dibenzylphenylamine	59	180—186/1	1.5740	

* Elementary nitrogen analyses and neutral equivalents of these amines agreed with the calculated data.

** Melting point.

Alkylation of other amines by organic halides and lithium naphthalene was performed and the products were identified in a similar way. Structures were confirmed by elementary nitrogen analyses and titrimetric procedure. Attempted butylation of *N,N*-dimethylaniline by butyl bromide and lithium naphthalene was carried out similarly as mentioned above. A mixture of isomeric butylnapthalenes was obtained, but not a butylated product of *N,N*-dimethylaniline. Alkylation of other tertiary amines by our method was unsuccessful.