Registry No.—**1**, 577-61-7; **2**, 16156-17-5; **3**, 657-70-5; **4a**, 16156-19-7; **4b**, 16156-20-0; **5**, 655-67-4; **6a**, 16156-22-2; **6b**, 720-49-0; **6c**, 16156-24-4; **6e**, 16156-25-5; **6f**, 16156-26-6; **8a**, 98-10-2; **8b**, 70-55-3; **8c**, 88-19-7; **8d**, 1869-24-5; **8e**, 672-58-2; **8f**, 830-43-3; **9**, 724-94-7; **10**, 3144-09-0; 2,3-dihydro-3-methyl-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine 1,1 dioxide, 16156-28-8.

Alkylation of Alkylidenebisdimethylamines

CHARLES F. HOBBS AND H. WEINGARTEN

Central Research Department, Monsanto Company, Saint Louis, Missouri 63166

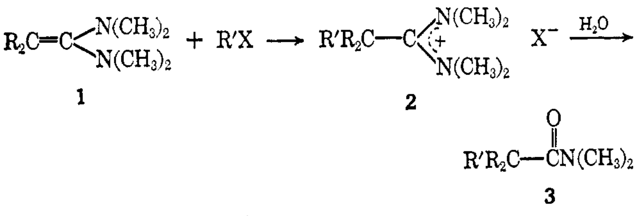
Received January 23, 1968

Alkylation of alkylidenebisdialkylamines (enediamines) with alkyl halides gave both C and N alkylation. Carbon alkylation afforded the amidinium salts, **2**, which were readily hydrolyzed to the amides, **3**. This carbon–carbon bond-forming reaction thus provides a convenient new route to substituted amides. The initial products of N alkylation are unstable and react with the starting enediamine, in the case of 2-methylpropenylidenebisdimethylamine, to yield condensation product, **6**, and an N,N-dimethylalkylamine. Elimination of hydrogen halide from butyl halides by the strongly basic enediamines also was observed.

Alkylation of enamines has become an important synthetic tool for the preparation of substituted ketones and aldehydes.[1,2] Analogously, the alkylation of alkylidenebisdialkylamines (enediamines), which have recently become conveniently accessible,[3] offers a new route to carboxylic acids and amides. Although the alkylation of enediamines with methyl and ethyl iodides has been observed previously,[4] the scope of this reaction and its utility for organic synthesis have not been elaborated.

Results

Alkylation of vinylidenebisdimethylamine (**1a**) and 2-methylpropenylidenebisdimethylamine (**1b**) with methyl iodide, benzyl bromide or chloride, and allyl bromide in acetonitrile solution gave the amidinium salts **2c–h** in good yield. The salts were characterized by elemental analysis and nmr spectroscopy and in the case of **2c** and **2e** by comparison with authentic samples prepared by independent syntheses. The reaction of vinylidenebisdimethylamine with butyl bromide and of 2-methylpropenylidenebisdimethylamine with butyl bromide and iodide, as well as benzyl chloride, afforded mixtures of salts from which the amidinium salts could not be isolated.

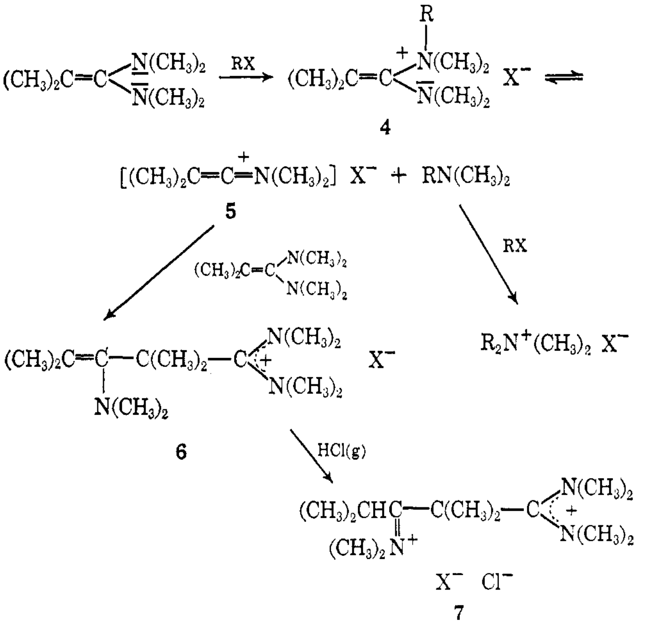


a, $R = H$
b, $R = CH_3$
c, $R = H; R' = CH_3$
d, $R = R' = CH_3$
e, $R = H; R' = C_6H_5CH_2$
f, $R = CH_3; R' = C_6H_5CH_2$
g, $R = H; R' = CH_2{=}CHCH_2$
h, $R = CH_3; R' = CH_2{=}CHCH_2$
i, $R = H; R' = n\text{-}C_4H_9$
j, $R = CH_3; R' = n\text{-}C_4H_9$

The amidinium salts, or the crude salt mixtures in those cases where no amidinium salt could be isolated, were hydrolyzed with dilute sodium hydroxide to afford moderate to good yields of the N,N-dimethylamides, **3e–j**. The yields of amides, shown in Table I, were calculated on the basis of the starting alkylidenebisdimethylamine and therefore represent over-all yields.

The reaction of benzyl chloride with 2-methylpropenylidenebisdimethylamine also afforded 6% of N,N-dimethylbenzylamine in addition to the expected amide (**3f**). Examination by nmr spectroscopy of the aqueous solution remaining after extraction of the amide indicated considerable quantities of ammonium or amidinium salts. These were precipitated as the fluorophosphates and fractionally crystallized to obtain 18% of dibenzyldimethylammonium fluorophosphate and 13% of the condensation product **6**, X = PF_6 (Scheme I). Compound **6** was characterized by elemental analysis and nmr spectroscopy and by conversion with dry hydrogen chloride to a second salt whose nmr spectrum was consistent with structure **7**. Compound **6** in the form of its iodide also was isolated

SCHEME I



---

[1] J. Szmuszkovicz, *Advan. Org. Chem.*, 25, 58, **4** (1963).

[2] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

[3] H. Weingarten and W. A. White, *J. Org. Chem.*, **31**, 2874 (1966); *J. Amer. Chem. Soc.*, **88**, 850 (1966).

[4] D. H. Clemens, A. J. Bell, and J. L. O'Brien, *J. Org. Chem.*, **29**, 2932 (1964).

Table I

Substituted Amides from Alkylation of Alkylidenebisdimethylamines

Reactants	Products	Yield,[a] %
Vinylidenebisdimethylamine		
Benzyl chloride	N,N-Dimethylhydrocinnamamide	48
Allyl bromide	N,N-Dimethyl-4-pentenamide	43
Butyl bromide	N,N-Dimethylhexanamide	33
2-Methylpropenylidenebisdimethylamine		
Benzyl bromide	N,N,2,2-Tetramethylhydrocinnamamide	42
Benzyl chloride	N,N,2,2-Tetramethylhydrocinnamamide	34
Allyl bromide	N,N,2,2-Tetramethyl-4-pentenamide	51
Butyl iodide	N,N,2,2-Tetramethylhexanamide	18
Butyl bromide	N,N,2,2-Tetramethylhexanamide	>1

[a] Over-all yield based on starting reactants.

in 5.4% yield from the reaction of butyl iodide with 2-methylpropenylidenebisdimethylamine.

The reaction of butyl bromide with 2-methylpropenylidenebisdimethylamine gave 69% of the amidinium salt (**2**, R = CH_3; R′ = H; X = Br) corresponding to abstraction of hydrogen bromide by the enediamine. This salt, as the iodide, also was detected by nmr spectroscopy in the product mixture from the reaction of butyl iodide with **1b**, and the analogous salt (**2**, R = R′ = H; X = Br) was detected in the reaction of butyl bromide with **1a**.

Discussion

The results of this study show that the alkylation of enediamines is a convenient new route to substituted amides. Of the amides prepared, those containing a quaternary carbon atom, **3f**, **h**, **i**, are new compounds. The yields obtained here (Table I) for the alkylation of enediamines are comparable with those reported for the alkylation of enamines of aldehydes[5,6] and cyclic ketones.[2] The data in Table I show that higher yields of alkylation product are obtained with the less-hindered enediamines and the more reactive alkyl halides. The effect of halide reactivity parallels that observed for enamine alkylations.[5–7]

Elimination of hydrogen halide was a major side-reaction in the case of the butyl halides and was the only reaction observed with 2-bromopropane. This was not entirely unexpected, since the enediamines are powerful bases, comparable to the amidines,[8] protonation giving an amidinium salt in which the positive charge can be delocalized over both nitrogen atoms and the central carbon.

A second side reaction observed was alkylation on nitrogen. This was demonstrated in the reaction of benzyl chloride and 2-methylpropenylidenebisdimethylamine by the isolation of N,N-dimethylbenzylamine, the dibenzyldimethylammonium salt, and condensation product **6**. Minor amounts of these products also were detected by nmr spectroscopy in the product mixture from the reaction of benzyl bromide with this enediamine. Isolation of compound **6** from the reaction of butyl iodide with **1b** indicated that N-alkylation had taken place in this case as well. No direct evidence was found for N-alkylation in the vinylidenebisdimethylamine alkylations. However, nmr spectroscopy revealed residual ammonium or amidinium species in the hydrolysate from the crude butyl bromide adduct, indicating that N-alkylation probably had occurred. Certainly some N-alkylation is to be expected with the unsubstituted enediamine since self-condensation is the major reaction observed in the alkylation of enamines from unhindered aldehydes.[5,9]

The formation of the condensation product **6** and the other products of N-alkylation can be rationalized in terms of the processes outlined in Scheme I. Nucleophilic attack by nitrogen affords the initial ammonium salt **4**, which can eliminate 1 mol of trialkylamine to give the ketenimmonium salt **5**. Attack by a second mole of enediamine on **5** affords **6**. The trialkylamine can attack a second mole of alkyl halide to afford the dialkyldimethylammonium salt. An alternate view is that enediamine attacks **4** displacing trialkylamine and giving **6** directly. In view of the steric requirements which would be involved in such a displacement, however, the alternative process appears more attractive.

The failure of compound **6** to undergo hydrolysis under the same conditions as the amidinium salts, **2**, can be explained on the basis of steric hindrance[10] to hydrolysis. Hydrolysis can be effected under forcing conditions, *i.e.*, 30 hr in refluxing 2 *N* sodium hydroxide, but a complex mixture of products was obtained from which no single product could be isolated.

Experimental Section

Melting points are corrected; boiling points are uncorrected. Nmr data are reported in τ units using tetramethylsilane as internal standard. Molecular weights were determined by mass spectroscopy. All manipulations, reactions, and distillations, except those dealing with the amides, were carried out in a dry nitrogen atmosphere.

Materials.—Vinylidenebisdimethylamine, propenylidenebisdimethylamine, and 2-methylpropenylidenebisdimethylamine were prepared as described previously.[3] Allyl bromide, benzyl chloride and bromide, butyl bromide and iodide, and acetone were dried over magnesium sulfate and distilled before use. Acetonitrile (Matheson Coleman and Bell Spectroquality) was used as received.

N,N,N′,N′-Tetramethyl-3-phenylpropionamidinium hexafluorophosphate.—A solution of 5.28 g (0.30 mol) of N,N-dimethylhydrocinnamamide[11] (bp 111–112° (0.6 mm), $n^{25}{}_{D}$ 1.5300), 3.06 g (0.15 mol) of tetrakis(dimethylamino)titanium,[12] and 10 ml of dry ether was heated to reflux for 2 hr. The reaction mixture was filtered and the filtrate distilled to obtain 2.0 g (33%)

---

(5) G. Opitz and H. Mildenberger, *Ann.*, **649**, 26 (1961).

(6) G. Opitz, H. Hellmann, H. Mildenberger, and H. Suhr, *ibid.*, **649**, 36 (1961).

(7) G. Opitz, H. Mildenberger, and H. Suhr, *ibid.*, **649**, 47 (1961).

(8) P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. 1, W. A. Benjamin, Inc., New York, N. Y., 1965, p 178.

(9) E. Elkik, *Bull. Soc. Chim. Fr.*, 972 (1960).

(10) M. S. Newman in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 227.

(11) H. J. Taverne, *Rec. Trav. Chim. Pays Bas*, **16**, 31 (1897).

(12) D. C. Bradley and T. M. Thomas, *J. Chem. Soc.*, 3857 (1960).

of 3-phenylpropenylidenebisdimethylamine: bp 83–87° (0.55 mm); nmr spectrum (in CCl_4), (s) 2.83, (m) ∼8.50, (s) 7.32, (s) 7.57 (5:3:6:6).

A benzene solution of 3-phenylpropenylidenebisdimethylamine was treated with dry hydrogen chloride and the resulting N,N,N′,N′-tetramethyl-3-phenylpropionamidinium chloride was collected by filtration. Addition of sodium hexafluorophosphate solution to an aqueous solution of the amidinium chloride afforded the corresponding hexafluorophosphate, mp 146–147.5° (acetone–ethyl acetate).

Alkylation of Vinylidenebisdimethylamine. With Methyl Iodide—To a solution of 4.56 g (0.040 mol) of vinylidenebisdimethylamine in 20 ml of dry acetonitrile was added 6.24 g (0.044 mol) of methyl iodide with cooling. After standing overnight, the acetonitrile was evaporated under vacuum and the solid recrystallized from dry acetone to afford 9.11 g (84%) of N,N,N′,N′-tetramethylpropionamidinium iodide (**2c**): mp 225–229°; nmr spectrum (in methylene chloride), (s) 6.67, (q) 7.13, $J = 7.5$ Hz, (t) 8.74, $J = 7.5$ Hz (12:2:3).

Anal. Calcd for $C_7H_{17}IN_2$: C, 32.81; H, 6.68; I, 49.51; N, 10.94. Found: C, 32.73; H, 6.80; I, 49.65; N, 10.83.

An authentic sample of the amidinium salt, mp 232–233°, prepared by addition of dry hydrogen iodide to propenylidenebisdimethylamine, had identical nmr and infrared spectra; mmp 230–231.5°.

With Benzyl Chloride.—A mixture of 6.4 g (0.05 mol) of benzyl chloride, 5.7 g (0.05 mol) of vinylidenebisdimethylamine, and 20 ml of acetonitrile was heated to reflux for 80 hr. The acetonitrile was evaporated under vacuum to give a viscous orange residue which was taken up in dry acetone and recrystallized to yield 10.6 g (86%) of N,N,N′,N′-tetramethyl-3-phenylpropionamidinium chloride (**2e**): mp 105–107°; nmr spectrum (methylene chloride), (s) 2.69, (s) 6.78, (m) 6.91 (5:12:4). Because of the extreme hygroscopicity of the salt, a satisfactory analysis could not be obtained. Addition of sodium hexafluorophosphate to an aqueous solution of the chloride salt afforded the hexafluorophosphate, recrystallized from acetone: mp 146–146.5°; mmp with authentic sample, 146.5–147.5°.

Anal. Calcd for $C_{13}H_{21}F_6N_2P$: C, 44.57; H, 6.04; N, 8.00. Found: C, 44.63; H, 6.08; N, 7.79.

N,N,N′,N′-Tetramethyl-3-phenylpropionamidinium chloride (8.0 g, 0.033 mol) was dissolved in 20 ml of 2 *N* sodium hydroxide and allowed to stand overnight. Extraction of the aqueous solution with ether, followed by distillation, afforded 3.3 g (56%) of N,N-dimethylhydrocinnamamide (**3e**): bp 102° (0.35 mm); n^{25}_{D} 1.5303. The nmr spectrum (in CCl_4) was identical with that of an authentic sample[11] with peaks at (s) 2.85, (s) 7.21, (m) 7.32 (5:6:4).

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90; mol wt, 177. Found: C, 74.42; H, 8.64; N, 7.88; mol wt, 177.

With Allyl Bromide.—A solution of 3.6 g (0.03 mol) of allyl bromide, 3.4 g (0.03 mol) of vinylidenebisdimethylamine, and 10 ml of acetonitrile was heated to reflux for 24 hr. The acetonitrile was removed under vacuum and the resulting solid recrystallized from acetone to yield 5.45 g (77%) of N,N,N′,N′-tetramethyl-4-pentenamidinium bromide (**2g**): mp 153–154.5°; nmr spectrum (in $CDCl_3$), (m) ∼4.25, (m) 4.83, (s) 6.62 (m) ∼6.95, (t) 7.51 (1:2:12:2:2).

Anal. Calcd for $C_9C_{19}BrN_2$: C, 45.96; H, 8.14; Br, 33.98; N, 11.91. Found: C, 46.04; H, 8.14; Br, 33.80; N, 11.73.

Hydrolysis of 10.0 g (0.042 mol) of the amidinium bromide with 15 ml of 2 *N* sodium hydroxide afforded, after extraction with ether and distillation, 3.1 g (57%) of N,N-dimethyl-4-pentenamide (**3g**): bp 88° (10 mm); n^{25}_{D} 1.4605 [lit.[13] bp 88–89° (11 mm)]; nmr spectrum (in CCl_4), (m) 4.1, (m) 5.0, (s) 3.02, (s) 2.88, (m) 2.32 (1:2:3:3:4).

Anal. Calcd for $C_7H_{13}NO$: C, 66.11; H, 10.30; N, 11.02; mol wt, 127. Found: C, 65.80; H, 10.27; N, 11.27; mol wt, 127.

With Butyl Bromide.—A mixture of 5.7 g (0.05 mol) of vinylidenebisdimethylamine, 6.9 g (0.05 mol) of *n*-butyl bromide, and 20 ml of acetonitrile was heated to reflux for 3 days, or until the starting materials had disappeared as evidenced by nmr. The acetonitrile was evaporated under vacuum to afford 11.8 g of viscous residue. The viscous residue was treated overnight with 20 ml of 2 *N* sodium hydroxide and the mixture extracted with ether. Distillation afforded 2.4 g (33%) of N,N-dimethylhexanamide (**3i**): bp 50° (0.45 mm); n^{25}_{D} 1.4451 (lit.[14] bp 158° (100 mm); n^{25}_{D} 1.4430); nmr spectrum (in CCl_4), (s) 7.02, (s) 7.14, (m) 7.80, (m) 8.1–9.3 (3:3:2:9).

Anal. Calcd for $C_8H_{17}NO$: C, 67.08; H, 11.97; N, 9.78; mol wt, 143. Found: C, 66.98; H, 12.02; N, 9.80; mol wt, 143.

Vapor phase chromatographic examination of the aqueous sodium hydroxide solution after extraction indicated considerable quantities of N,N-dimethylacetamide along with several unidentified materials. It was estimated from nmr spectra that the aqueous mixture after hydrolysis but before extraction contained N,N-dimethylacetamide and N,N-dimethylhexanamide in the molar ratio of 1:2.

Alkylation of 2-Methylpropenylidenebisdimethylamine. With Methyl Iodide.—Methyl iodide, 15.6 g (0.11 mol), 2-methylpropenylidenebisdimethylamine, 14.2 g (0.10 mol), and 20 ml of dry acetonitrile were maintained at reflux for 24 hr. The mixture was chilled in ice, filtered, and the adduct salt washed with acetone to obtain 17.6 g (62%) of N,N,N′,N′,2,2-hexamethylpropionamidinium iodide (**2d**), sublimes at ∼390°: nmr spectrum (in $CDCl_3$), (s) 6.55, (s) 8.40 (4:3).

Anal. Calcd for $C_9H_{21}IN_2$: C, 38.04; H, 7.45; I, 44.66; N, 9.86. Found: C, 37.83; H, 7.35; I, 44.87; N, 9.78.

With Benzyl Bromide.—A mixture of 7.1 g (0.05 mol) of 2-methylpropenylidenebisdimethylamine, 8.5 g (0.05 mol) of benzyl bromide, and 15 ml of dry acetonitrile was heated to reflux for 40 hr. The acetonitrile was evaporated under vacuum and the crude adduct salt (9.9 g, 63%) was recrystallized from acetone to give N,N,N′,N′,2,2-hexamethylhydrocinnamamidinium bromide (**2f**): mp 181–183°; nmr spectrum (in $CDCl_3$), (m) 2.7, (s) 6.70, (s) 6.88, (s) 8.35 (5:12:2:6).

Anal. Calcd for $C_{15}H_{25}BrN_2$: C, 57.51; H, 8.04; Br, 25.51; N, 8.94. Found: C, 57.24; H, 8.16; Br, 25.72; N, 8.94.

Hydrolysis of 9.5 g (0.033 mol) of the crude adduct salt in 10 ml of 2 *N* sodium hydroxide afforded 4.5 g (66%) of N,N,2,2-tetramethylhydrocinnamamide (**3f**): bp 108–110° (0.55 mm); n^{25}_{D} 1.5257; nmr spectrum (in CCl_4), (s) 2.80, (s) 7.08, (s) 7.11, (s) 8.81 (5:6:2:6).

Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33; N, 6.82; mol wt, 205. Found: C, 75.94; H, 9.47; N, 6.80; mol wt, 205.

With Benzyl Chloride.—The reaction between 11.4 g (0.08 mol) of 2-methylpropenylidenebisdimethylamine and 11.2 g (0.09 mol) of benzyl chloride in 20 ml of acetonitrile required 8 days at reflux to reach completion. Evaporation of the acetonitrile under vacuum yielded a viscous residue which could not be made to crystallize. The viscous product was hydrolyzed in 2 *N* sodium hydroxide and the aqueous solution extracted with ether. Distillation yielded 0.6 g (6%) of N,N-dimethylbenzylamine, bp 30° (0.55 mm), identified by comparison of nmr spectra and vapor phase chromatographic retention times with an authentic sample, and 5.7 g (34%) of N,N,2,2-tetramethylhydrocinnamamide. The aqueous solution remaining from the hydrolysis was treated with sodium hexafluorophosphate to precipitate soluble salts as their hexafluorophosphates. These were collected by filtration and fractionally crystallized from acetone–ethyl acetate to yield two salts, mp 214–218 and 185–186.5° dec. The 214–218° salt, 5.3 g (18% yield based on 2-methylpropenylidenebisdimethylamine), was identified as dibenzyldimethylammonium hexafluorophosphate on the basis of its nmr spectrum and elemental analysis: nmr spectrum (in acetone-d_6), (m) 2.25, (s) 5.10, (s) 6.80 (5:2:3).

Anal. Calcd for $C_{16}H_{20}F_6NP$: C, 51.76; H, 5.43; N, 3.77. Found: C, 51.66; H, 5.48; N, 3.67.

The 185–186.5° salt, 2.0 g (13% based on 2-methylpropenylidenebisdimethylamine), was identified as 3-dimethylamino-N,N,N′,N′,2,2,4-heptamethyl-3-pentenamidinium hexafluorophosphate (**6**, X = PF_6): nmr spectrum (in CD_3CN), (s) 6.78 (s) 7.24, (s) 8.29, (s) 8.44, (s) 8.53 (4:2:1:2:1).

Anal. Calcd for $C_{14}H_{30}F_6N_3P$: C, 43.63; H, 7.85; N, 10.90. Found: C, 43.47; H, 7.80; N, 10.89.

A sample of the 185–186.5° salt, dissolved in chloroform, was treated with dry hydrogen chloride, whereupon crystals formed immediately. The crystals were collected by filtration: nmr spectrum (in CD_3CN), (s) 6.06, (s) 6.43, (s + m) 6.70, (s) 8.07, (d) 8.43, $J = 7.5$ Hz (3:3:13:6:6).

---

(13) H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Ann.*, **641**, 1 (1961).

(14) J. R. Ruhoff and E. E. Reid, *J. Amer. Chem. Soc.*, **59**, 4012 (1937).

With Allyl Bromide.—A solution of 11.4 g (0.08 mol) of 2-methylpropenylidenebisdimethylamine and 10.9 g (0.09 mol) of allyl bromide in 20 ml of dry acetonitrile was heated to reflux for 3 days. The acetonitrile was evaporated under vacuum to yield 20.5 g (92%) of crude adduct. Recrystallization from acetone gave N,N,N′,N′,2,2-hexamethyl-4-pentenamidinium bromide (**2h**): mp 212–213°; nmr spectrum (in $CDCl_3$), (m) ~4.2, (m) 4.7, (s) 6.52, (d) 7.37, J = 7.0 Hz, (s) 8.37 (1:2:12:2:6).

Anal. Calcd for $C_{11}H_{23}BrN_2$: C, 50.19; H, 8.81; Br, 30.26; N, 10.64. Found: C, 50.23; H, 8.94; Br, 30.13; N, 10.47.

Treatment of 17.1 g of the crude adduct salt with 20 ml of 2 *N* sodium hydroxide overnight yielded 5.3 g (51% based on 2-methylpropenylidenebisdimethylamine) of N,N,2,2-tetramethyl-4-pentenamide (**3h**): bp 75–80° (4 mm); $n^{25}D$ 1.4641; nmr spectrum (in CCl_4), (m) ~4.2, (m) ~5.0, (s) 6.99, (d) 7.64, J = 7.0 Hz, (s) 8.78 (1:2:6:2:6).

Anal. Calcd for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02; mol wt, 155. Found: C, 69.53; H, 10.96; N, 9.16; mol wt, 155.

With Butyl Iodide.—A mixture of 8.5 g (0.06 mol) of 2-methylpropenylidenebisdimethylamine, 11.1 g (0.06 mol) of butyl iodide, and 20 ml of acetonitrile was heated to reflux for 11 days. The acetonitrile was removed under vacuum to give 15.2 g of yellow semisolid. Recrystallization afforded 0.5 g of crude N,N,-N′,N′,2-pentamethylpropionamidinium iodide, whose nmr spectrum was identical with that of the bromide prepared by addition of dry hydrogen bromide to 2-methylpropenylidenebisdimethylamine. The bulk of the crude product could not be induced to crystallize. The crude product was dissolved in 15 ml of 2 *N* sodium hydroxide and allowed to stand overnight. The mixture was extracted with ether and the extract distilled to obtain 1.8 g (18%) of N,N,2,2-tetramethylhexanamide (**3j**): bp 61–62° (0.7 mm); $n^{25}D$ 1.4512; nmr spectrum (in CCl_4), (s) 7.02, (s) 8.81, (m) 8.70, (m) 9.05 (2:2:2:1).

Anal. Calcd for $C_{10}H_{21}NO$: C, 70.12; H, 12.36; N, 8.18; mol wt, 171. Found: 69.92; H, 12.28; N, 8.18; mol wt, 171.

The aqueous layer remaining after ether extraction was filtered and the crystals so obtained were recrystallized from acetone–tetrahydrofuran to yield 0.6 g (5.4% yield based on 2-methylpropenylidenebisdimethylamine) of material identified as 3-dimethylamino-N,N,N′,N′,2,2,4-heptamethyl-3-pentenamidinium iodide (**6**, X = I): mp 189–191° dec; nmr spectrum (in $CDCl_3$), (s) 6.58, (s) 7.27, (s) 8.30, (s) 8.40, (s) 8.49 (4:2:1:2:1).

Anal. Calcd for $C_{14}H_{30}IN_3$: C, 45.78; H, 8.23; I, 34.55; N, 11.44. Found: C, 45.64; H, 8.27; I, 34.81; N, 11.28.

When butyl bromide was used in place of the iodide, 17 days were required for complete disappearance of the reactants. A total of 15.4 g (69%) of N,N,N′,N′,2-pentamethylpropionamidinium bromide, mp 263° dec, was recovered by crystallization from the reaction mixture. The nmr spectrum was identical with that of an authentic sample of the salt, mp 267° dec, prepared by addition of dry hydrogen bromide to 2-methylpropenylidenebisdimethylamine: mmp 266° dec; nmr spectrum (in CH_2Cl_2), (m) ~6.4, (s) 6.58, (d) 8.53, J = 7.2 Hz (12:6:1).

Anal. Calcd for $C_8H_{19}BrN_2$: C, 43.05; H, 8.58; Br, 35.81; N, 12.55. Found: C, 42.94; H, 8.67; Br, 35.94; N, 12.42.

The remainder of the reaction mixture was hydrolyzed in 2 *N* sodium hydroxide. Extraction with ether, followed by distillation of the extract, afforded less than 1% yield of crude N,N,2,2-tetramethylhexanamide.

Registry No.—N,N,N′,N′-Tetramethyl-3-phenylpropionamidinium hexafluorophosphate, 12260-64-9; 3-phenylpropenylidenebisdimethylamine, 16487-48-2; **2c**, 16487-49-3; **2d**, 16520-61-9; **2e**, 16487-50-6; **2f**, 16487-51-7; **2g**, 16487-52-8; **2h**, 16487-53-9; **3e**, 5830-31-9; **3f**, 16487-55-1; **3g**, 16487-56-2; **3h**, 16487-57-3; **3i**, 5830-30-8; **3j**, 16487-59-5; **6** (X = PF_6), 12260-65-0; **6** (X = I), 16487-60-8; dibenzyldimethylammonium hexafluorophosphate, 12260-70-7; N,N,N′,N′,2-pentamethylpropionamidinium bromide, 16487-61-9.

Acknowledgment.—The authors thank Mrs. Nancy K. Edelmann for nmr analyses and for preparation of intermediates.

Reductive Alkylation of Imines and Esters with Sodium in Ammonia

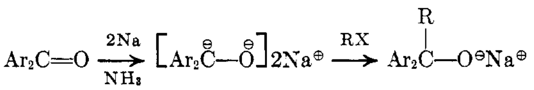
M. WINN, D. A. DUNNIGAN, AND H. E. ZAUGG

Organic Chemistry Department, Research Division, Abbott Laboratories, North Chicago, Illinois

Received December 18, 1967

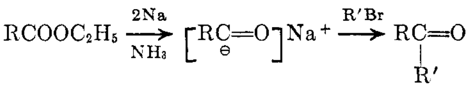
Diphenyl- or pyridylketimines and pyridylaldimines were alkylated at carbon by the addition of sodium metal in liquid ammonia, followed by an organic halide. The same products were obtained by treating the corresponding amine with sodamide in liquid ammonia, followed by the halide. Similar reductive alkylations of methyl isonicotinate with benzyl chlorides gave the corresponding 4-pyridyl ketones.

Numerous reactions in organic synthesis involve the alkylation of carbanions. One route to such intermediates is the addition of electrons from alkali metals to an unsaturated center. The addition of the first electron gives a radical anion, which in the case of most double bonds is so reactive that it dimerizes or reacts with the solvent. In some instances, however, a second electron can be added to give a stable dianion. Schlenk[1] was first to show that a relatively stable dianion can be formed by treating diaryl ketones with sodium in ether and that this dianion can be alkylated with ethyl or methyl iodides. Later workers[2] showed that the dianions, formed from diaryl ketones with sodium in liquid ammonia, alkylated preferentially at carbon with a variety of alkylating agents, but aryl alkyl or dialkyl ketones would not alkylate under these conditions.



$$Ar_2C{=}O \xrightarrow[NH_3]{2Na} \left[Ar_2\overset{\ominus}{C}{-}\overset{\ominus}{O}\right]2Na^{\oplus} \xrightarrow{RX} Ar_2\overset{\overset{\displaystyle R}{|}}{C}{-}O^{\ominus}Na^{\oplus}$$

Kharasch[3] studied the reductive alkylation of esters and obtained 30–35% yields of ketones from the following esters and alkyl halides.



$$RCOOC_2H_5 \xrightarrow[NH_3]{2Na} \left[R\underset{\ominus}{C}{=}O\right]Na^{+} \xrightarrow{R'Br} R\underset{\underset{\displaystyle R'}{|}}{C}{=}O$$

R = C_6H_5, *i*-Pr, *t*-Bu; R′ = *n*-Bu, Et

However, with benzyl chloride and ethyl benzoate, only a 5% yield of ketone was detected.

---

[1] W. Schlenk and T. Weikel, *Chem. Ber.*, **44**, 1182 (1911).

[2] (a) P. J. Hamrick and C. R. Hauser, *J. Amer. Chem. Soc.*, **81**, 493 (1959); (b) D. V. Ioffe, *Zh. Obshch. Khim.*, **34**, 703 (1964); **35**, 1851 (1965); (c) E. L. Anderson and J. E. Casey, Jr., *J. Org. Chem.*, **30**, 3960 (1965); (d) S. Selman and J. Eastham, *ibid.*, **30**, 3804 (1965); (e) J. A. Gautier, M. Miocque, C. Fauran, and M. D. D'Engenieres, *Bull. Soc. Chim. Fr.*, 3762 (1965).

[3] M. S. Kharasch, E. Sternfeld, and F. Mayo, *J. Org. Chem.*, **15**, 362 (1940).