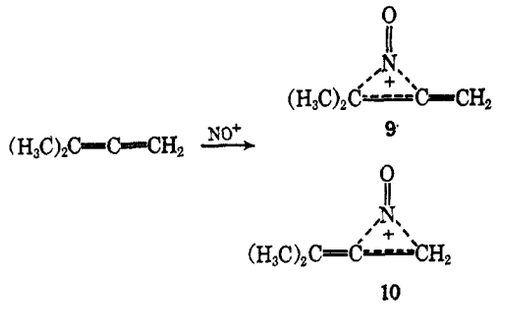
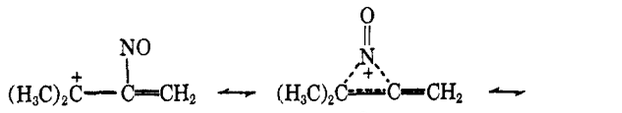


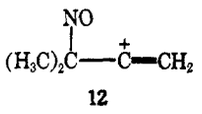
9

10

be explained by considering cation **9** to be a resonance hybrid with canonical structures **11** and **12** as major contributors. The ability of the alkyl groups to stabilize adjacent positive charge by hyperconjugation would make structure **11** of greater importance to the



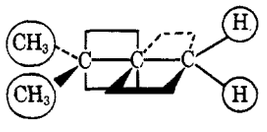
11 9



12

hybrid. Attack of Cl^- would then be directed toward the more electron-deficient tertiary carbon forming 2-nitroso-3-chloro-3-methylbutene (**1**).

Addition to the internal double bond may also be explained on a stereochemical basis. The methyl groups of 3-methylbutadiene-1,2 are in closer proximity to the terminal π orbital than to the internal π



orbital. To form the primary carbonium ion **6** or the cyclic nitrosonium ion **10**, NO^+ must approach in the plane of the terminal π orbital. The methyl groups lie in this plane and pose severe steric restrictions to approach of NO^+ in this manner. Less severe restrictions are imposed by the protons for approach of NO^+ in the plane of the internal π orbital leading to formation of cations **5**, **7**, or **9**. Arguments stated previously can be invoked to explain exclusive formation of the tertiary halide.

Experimental Section

To a 50-ml round-bottom flask fitted with a Dry Ice condenser was added 2.31 g (0.034 mol) of 3-methylbutadiene-1,2, 15 ml of ether, and 2 drops of water. The flask was cooled to 0° and 2.2 g (0.034 mol) of gaseous nitrosyl chloride passed through the reaction solution causing a green color to develop. When the allene was nearly gone as shown by glpc, the mixture was dried over anhydrous $MgSO_4$ and solvent removed at reduced pressure. The resulting yellow-green oil was transferred to a sublimation apparatus and the blue monomer sublimed at 2 μ pressure onto a cold finger containing liquid nitrogen. It was found necessary to store the monomer at −196° prior to characterization to prevent polymerization. Nuclear magnetic resonance spectrometry of the yellow-green oil indicated that 95% of the oil was 2-nitroso-3-chloro-3-methylbutene. Attempts to identify other products were unsuccessful.

Registry No.—**1**, 16162-33-7; nitrosyl chloride, 2696-92-6; 3-methylbutadiene-1,2, 598-25-4.

Acknowledgment.—The authors gratefully acknowledge financial support from the Atmospheric Science Research Center of the State University of New York and from the United States Army Research Office, Durham, N. C.

The Nucleophilic Displacement of One Dianion by Another

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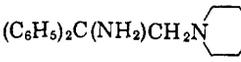
Although it has been known since 1911[1] that benzophenone forms a disodio adduct that can be alkylated, the synthetic utility of this reagent only recently has become the subject of a number of systematic investigations.[2] To add to this number, we have now found that disodiobenzophenone and its analogs can be aminomethylated in fair to excellent yields by sodium aminomethanesulfonates (**1**).

$$R_2NH + HOCH_2SO_3Na \longrightarrow R_2NCH_2SO_3Na$$
$$\mathbf{3} \qquad\qquad \mathbf{1}$$

$$Ar_2CO + 2Na \xrightarrow{DME} [Ar_2\bar{C}-\bar{O}]\,2Na^+ \xrightarrow[2.\ H_2O]{1.\ \mathbf{1}} Ar_2C(OH)CH_2NR_2$$
$$\mathbf{2}$$

The solid sulfonate salt **1** is added to a solution of the disodio derivative prepared in 1,2-dimethoxyethane (DME) and stirred at room temperature for 16–19 hr before work-up. Results of a number of such reactions listed in Table I serve to indicate the scope of the reaction. Those amino alcohols derived from the tricyclic diaryl ketones are not readily accessible by other known methods.[3,4]

Extension of this scheme to diphenylketimine gave a low yield (19%) of the triamine **4** in the one reaction tried. Similar reductive alkylations of N-arylimines[5] and oximes[6] with alkylhalides have been reported.



4

$HOCH_2OSO_2Na$

5

(1) W. Schlenk and T. Weikel, *Ber.*, **44**, 1182 (1911); C. B. Wooster [*J. Amer. Chem. Soc.*, **50**, 1388 (1928)] also showed that disodiobenzophenone could be alkylated with ethyl bromide.

(2) (a) P. J. Hamrick, Jr., and C. R. Hauser, *ibid.*, **81**, 493 (1959); (b) D. V. Ioffe, *Zh. Obshch. Khim.*, **34**, 3900 (1964); *ibid.*, **35**, 1851 (1965); D. V. Ioffe and I. N. Somin, *ibid.*, **34**, 703 (1964); B. Z. Askinazi and D. V. Ioffe, *Zh. Org. Khim.*, **3**, 367 (1967); D. V. Ioffe, *ibid.*, **3**, 535 (1967); (c) M. Miocque and C. Fauran, *Compt. Rend.*, **259** 408 (1964); J. A. Gautier, M. Miocque, C. Fauran, and M. D. d'Engenières, *Bull. Soc. Chim. Fr.*, 3162 (1965); (d) S. Selman and J. F. Eastham, *J. Org. Chem.*, **30**, 3804 (1965); (e) E. L. Anderson and J. E. Casey, Jr., *ibid.*, **30**, 3959 (1965).

(3) A. Schönberg, E. Singer, and W. Knöfel [*Chem. Ber.*, **99**, 3813 (1966)] have reported the preparation of 9-acyloxy-9-aminomethylfluorenes by treating 9-diazofluorene with diaminomethanes in the presence of carboxylic acid anhydrides.

(4) (a) H. E. Zaugg, R. J. Michaels, H. J. Glenn, L. R. Swett, M. Freifelder, G. R. Stone, and A. W. Weston, *J. Amer. Chem. Soc.*, **80**, 2763 (1958); (b) H. E. Zaugg and R. J. Michaels, *ibid.*, **80**, 2770 (1958).

(5) (a) W. Schlenk and E. Bergmann, *Ann. Chem.*, **463**, 281 (1928); (b) B. M. Mikhailov and K. Kurdiumova, *Zh. Obshch. Khim.*, **25**, 1687 (1955), (c) J. G. Smith and C. D. Veach, *Can. J. Chem.*, **44**, 2245 (1966).

(6) J. A. Gautier, M. Miocque, C. Fauran, and A. Y. Cloarec, *Compt. Rend.*, **263**, 1164 (1966).

TABLE I

AMINO ALCOHOLS 2 FROM DISODIODIARYLKETONES AND SODIUM AMINOMETHANESULFONATES 1

Amino alcohol 2 from	Registry no.	Yield, %	Mp or bp (mm), °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
Benzophenone and										
Diethylamine	5554-72-3	53	135 (0.5)	$C_{18}H_{23}NO$	80.24	8.61	5.20	80.18	8.33	5.03
Hydrochloride	16298-94-5		174–175	$C_{18}H_{24}ClNO$	70.70	7.91	4.58	70.90	8.11	4.55
Pyrrolidine	6071-96-1	62	163 (0.8)	$C_{18}H_{21}NO$	80.86	7.92	5.24	80.92	7.77	5.31
Hydrochloride	6071-97-2		204–205	$C_{18}H_{22}ClNO$	71.16	7.30	4.61	71.29	7.15	4.79
Piperidine (hydrochloride)	5345-03-9	43	231–232	$C_{19}H_{24}ClNO$	71.78	7.61	4.41	71.71	7.56	4.47
1-Methylpiperazine		91	81–83[a]							
4-Methylbenzophenone and										
1-Methylpiperazine (dihydrochloride)		47	226–227[b]							
Fluoren-9-one and										
Dimethylamine	16298-98-9	26	82–83	$C_{16}H_{17}NO$	80.30	7.16	5.85	80.58	6.96	5.81
Pyrrolidine	16298-99-0	45	115–116	$C_{18}H_{19}NO$	81.49	7.22	5.28	81.60	7.08	5.16
O-Acetate'	16299-00-6	66	88–89	$C_{20}H_{21}NO_2$	78.14	6.89	4.56	78.41	7.19	4.53
1-Methylpiperazine	16299-01-7	40	175–176	$C_{19}H_{22}N_2O$	77.51	7.53	9.52	77.64	7.55	9.49
Dimaleate	16299-02-8	82	161–162	$C_{27}H_{30}N_2O_9$	61.59	5.74	5.32	61.51	5.86	5.60
5H-Dibenzo[*a*,*d*]cyclohepten-5-one and										
1-Methylpiperazine	16299-03-9	4	124–125	$C_{21}H_{24}N_2O$	78.72	7.55	8.75	78.42	7.98	8.94
10,11-Dihydro-5H-dibenzo[*a*,*d*]cyclo-hepten-5-one and 1-Methylpiperazine	16299-04-0	51	131–132	$C_{21}H_{26}N_2O$	78.23	8.13	8.69	78.23	8.18	8.78
Xanthene-9-one and										
Dimethylamine	16299-05-1	51	105–106	$C_{16}H_{17}NO_2$	75.27	6.68	5.48	75.33	6.58	5.55
Pyrrolidine	16299-06-2	45	115–116	$C_{18}H_{19}NO_2$	76.85	6.81	4.98	76.95	6.94	5.12
1-Methylpiperazine	16299-07-3	55	169–170	$C_{19}H_{22}N_2O_2$	73.51	7.14	9.03	73.51	7.15	9.16
Monomaleate	16299-08-4		128–129	$C_{23}H_{26}N_2O_6$	64.75	6.14	6.57	65.00	6.21	6.59
1-Methylhexahydro-1,4-diazepine	16299-09-5	10	164–166	$C_{20}H_{24}N_2O_2$	74.05	7.46	8.64	74.34	7.45	8.50
Thioxanthene-9-one and										
Pyrrolidine	16299-10-8	60	90–91	$C_{18}H_{19}NOS$	72.69	6.44	4.71	72.81	6.51	4.72
1-Methylpiperazine	16299-11-9	84	111–112	$C_{19}H_{22}N_2OS$	69.89	6.74	8.58	69.64	6.77	8.48
1-Methylhexahydro-1,4-diazepine	16299-12-0	34	132–133	$C_{20}H_{24}N_2OS$	70.54	7.11	8.23	70.69	7.37	8.08
10-Methyl-9-acridanone and										
1-Methylpiperazine	16299-13-1	11	165–166	$C_{20}H_{25}N_3O$	74.28	7.99	12.99	74.35	7.58	12.91

[a] Zaugg, *et al.*,[4a] report mp 83–84°. [b] Zaugg, *et al.*,[4a] report mp 232–233°. [c] From the amino alcohol with acetyl chloride in triethylamine.

Because it has been proved[7] that alkali "formaldehyde bisulfites" are hydroxymethane sulfonates (*i.e.*, **3**) and not the isomeric sulfites (*i.e.*, **5**), it is generally believed[8] that their amine derivatives (*i.e.*, **1**) also have the analogous structure. This means that in the displacement of the sulfite dianion from **1**, a carbon–sulfur bond is broken. That such displacement in an aprotic environment requires a rather high order of nucleophilic reactivity in a reaction partner is suggested by the observations that the monosodium adduct of benzophenone (the ketyl radical anion)[9] and the mono anion derived from benzyl cyanide are both inert to sulfonates of type **1**.

Attempts to extend the reaction to higher homologs of **1** were unsuccessful.[10] A homogeneous product could not be obtained from 1-methylpiperazine and "acetone sodium bisulfite"; and the product from "acetaldehyde sodium bisulfite" could not be obtained in anhydrous form. Using excess disodiobenzophenone to compensate for this hydration led to a mixture apparently (nmr) containing the expected product. However, purification attempts were not successful.

There are other aminomethyl compounds known[11] with leaving groups seemingly more displaceable than the sulfite dianion. Three of these were treated with disodiobenzophenone, with negative results. The butoxy group in 1-*n*-butoxymethyl-4-methylpiperazine was not displaced to give detectable amounts of the amino alcohol **2**. This was a surprising result in view of its ready replaceability by Grignard reagents.[12] Neither did the aminomethyl dithiocarbamate, $R_2NCH_2SC(=S)NR_2$ (R_2N = piperidino),[13] lead to any isolable amino alcohol **2**. In this case, displacement of the dithiocarbamate anion also (as in **1**) would involve carbon–sulfur bond cleavage. Finally, attempts to replace the cyano groups in α-(N-methylpiperazino)-propionitrile and α-(N-methylpiperazino)isobutyronitrile using both disodio- and dilithiobenzophenone failed.[10,14]

Experimental Section

All melting and boiling points are uncorrected. The nmr and infrared spectra of all reported products were consistent with their assigned structures.

Sodium 1-Methyl-4-piperazinomethanesulfonate (1, R_2N = 4-Methylpiperazino).—To a stirred solution of 80.5 g (0.6 mol) of sodium hydroxymethane sulfonate (sodium formaldehyde bi-

(7) W. M. Lauer and C. M. Langkammerer, *J. Amer. Chem. Soc.*, **57**, 2360 (1935).

(8) H. Hellman and G. Opitz, "Aminoalkylierung," Verlag Chemie, G.m.b.H., Weinheim, Germany, 1960, p 227.

(9) Compare G. O. Schenck and G. Matthias, *Tetrahedron Lett.*, 699 (1967).

(10) We are indebted to Miss N. Buczynski for these experiments.

(11) Reference 8, pp 223–245.

(12) G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **123**, 532 (1923).

(13) R. A. Donia, J. A. Shotton, L. O. Bentz, and G. E. P. Smith, Jr., *J. Org. Chem.*, **14**, 952 (1949).

(14) Compare H. R. Henze, G. L. Sutherland, and G. B. Roberts, *J. Amer. Chem. Soc.*, **79**, 6230 (1957); C. Fabre and Z. Welvart, *Tetrahedron Lett.*, 3801 (1967).

sulfite) in 50 ml of water, 65 g (0.65 mol) of 1-methylpiperazine was added over a period of 15 min. By cooling in an ice bath the temperature was not allowed to exceed 50°. After stirring at room temperature for 1 hr, the solution was poured into 500 ml of acetone. After cooling in ice, the precipitated product was collected at the filter and dried at 100° under reduced pressure (50 mm) for 48 hr. The product (105 g, 81% yield) was sufficiently pure for use in the next step. It could be recrystallized from dimethylformamide, mp 188–190° dec, but the best obtainable samples still were not quite analytically pure.

Anal. Calcd for $C_6H_{13}N_2NaO_3S$: C, 33.33; H, 6.06; N, 12.96. Found: C, 32.72; H, 6.24; N, 13.14.

In a similar manner were prepared the corresponding sodium salts derived from dimethylamine (61% yield, mp 197–200° dec), diethylamine[15] (67% yield), pyrrolidine (84% yield, mp >325°), piperidine (91% yield, mp >325°), and 1-methylhexahydro-1,4-diazepine (N-methylhomopiperazine) (71% yield, mp >325°). In D_2O, the NCH_2S peak in the A-60 nmr spectra of all these sodium salts fell within the range of 225–235 cps relative to TPS (sodium 3-trimethylsilyl-1-propanesulfonate).

1-(2′,2′-Diphenyl-2′-hydroxyethyl)-4-methylpiperazine (2, Ar = Phenyl, R_2N = 4-Methylpiperazino).—To a stirred suspension of sodium sand (3.5 g, 0.15 mol) in 50 ml of freshly distilled (from lithium aluminum hydride) 1,2-dimethoxyethane (DME) was added dropwise under an atmosphere of nitrogen, a solution of 9.1 g (0.05 mol) of benzophenone in 50 ml of DME. The temperature rose to 45° (no external cooling) and the color of the mixture went from blue to deep purple. After stirring for 1.5 hr at room temperature, the mixture was cooled to −50° by an acetone–CO_2 bath and 13.0 g (0.06 mol) of solid sodium 1-methyl-4-piperiazinomethanesulfonate was added in one portion. The cooling bath was removed and the mixture was stirred under nitrogen at room temperature for 19 hr. To the deeply colored mixture, still under nitrogen, was added dropwise with stirring 50 ml of water. (The first few drops decolorized the mixture.) The decomposed reaction mixture was then extracted with ether and dried over anhydrous magnesium sulfate. Filtration and removal of the ether by distillation gave 13.5 g (91%) of product that required only washing with pentane to give the pure amino carbinol, mp 81–83°, identical with an authentic[4a] sample. The dihydrochloride, mp 226–227°, also was identical with known material.[4]

Other compounds prepared by this method are listed in Table I. In several cases crystalline bases were not obtainable. Using ethereal or alcoholic solutions of appropriate acids they were converted into their corresponding crystallizable salts. In other cases distillation of the liquid bases followed by crystallization of the solidified distillates was required to effect purification. In some cases aqueous acid extraction of the original organic layer followed by reprecipitation of the base with excess aqueous alkali was necessary to separate the water-insoluble base from neutral and water-soluble by-products. The foregoing procedure probably does not represent optimum conditions for the preparation of all of the other compounds listed.

From a number of diaryl ketones no pure product could be isolated although spectral evidence indicated the presence of the desired material in the mixture. These ketones were *p*-chlorobenzophenone, anthrone, 2-benzoyl-, 3-benzoyl-, and 4-benzoylpyridine.

1-(2′,2′-Diphenyl-2′-aminoethyl)-4-methylpiperazine (4).—When diphenylketimine was substituted for benzophenone in the foregoing procedure, two fractions, bp 110–120° (0.5 mm) and bp 150–160° (0.1 mm), were obtained. The second fraction solidified and was recrystallized from hexane to give a 19% yield of **4**, mp 90–92°.[16]

Anal. Calcd for $C_{19}H_{25}N_3$: C, 77.25; H, 8.53; N, 14.22. Found: C, 77.15; H, 8.78; N, 14.25.

Registry No.—**1**, R_2N = 4-methylpiperazino, 16298-92-3; **4**, 16299-14-2.

Acknowledgment.—The authors wish to thank Mr. Orville Kolsto for the microanalyses, Mrs. Ruth Stanaszek for the nmr spectrometry, and Mr. W. H. Washburn for the infrared spectroscopy.

(15) E. Knoevenagel and E. Mercklin, *Ber.*, **37**, 4087 (1904).

(16) We are indebted to Dr. M. Winn for carrying out this experiment.

Octaethylporphyrin

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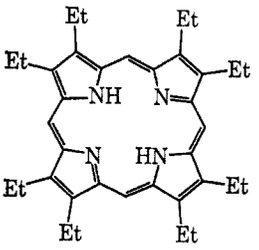
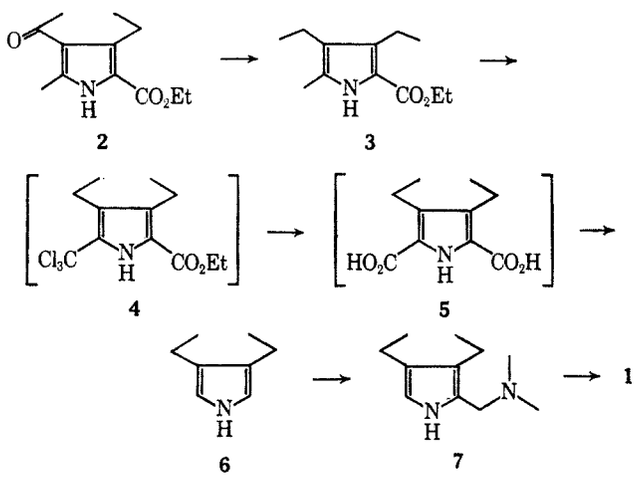
We wish to report a simple procedure for the synthesis of octaethylporphyrin (**1**). The procedure



1

developed is basically an improvement of the synthesis of Eisner, Lichtarowicz, and Linstead.[1] The improvements have eliminated the need for high pressure equipment and chromatography, have resulted in the combination of several steps to minimize purification of intermediates and have raised the yield (40% from ethyl 4-acetyl-3-ethyl-5-methyl-pyrrole-2-carboxylate) of octaethylporphyrin to about three times that originally reported.[1] The synthesis is outlined in Scheme I. The improvements are as follows.

SCHEME I



Conversion of 2 → 3.—Substitution of diborane reduction of **2** for catalytic hydrogenation gave a quantitative yield of **3**. No reduction of the carbethoxy group could be detected.

Conversion of 3 → 4 → 5 → 6 → 7.—Chlorination of **3** and subsequent hydrolysis to first the acid ester (originally isolated and purified by Eisner, *et al.*[1]) and then to diacid **5**, followed by decarboxylation of **5** in boiling quinoline containing barium-promoted copper chromite, was carried out without isolating and purifying intermediates. Entry of **6** into a Mannich reaction afforded a quantitative yield of oily **7**.

(1) U. Eisner, A. Lichtarowicz, and R. P. Linstead, *J. Chem. Soc.*, 733 (1957).