pH 7 and 13 (unstable), 252, 267, 317; $\bar{\nu}$ 3490, 3380, 3313, 3140 (NH), 2990–2700 (CH), 1648 (NH_2), 1592, 1577, 1520, 1497 (ring stretching), 750, 683 cm^{-1} (monosubstituted phenyl); pmr (4% DMSO-d_6 w/v), 1.53 (2-H), 3.15 (phenyl), ~3.33 (NH_2), ~4.15 (NH_2), 4.10 (8-H), 5.35 (CH_2), 6.92 (CH_3), (ethanol, 6.58 (CH_2), 8.93 (CH_3)).

Anal. Calcd for $C_{15}H_{16}N_6 \cdot {}^1/_3C_2H_6O$: C, 63.63; H, 6.14; N, 28.43. Found: C, 63.59; H, 6.20; N, 28.51.

Ethyl 8-Amino-2-[(N-methylanilino)methyl]pyrido[2,3-*b*]pyrazine-6-carbamate (**16**).—A suspension of crude **12** (1.45 g, 3.60 mmoles) in ethanol (70 ml) was stirred with Raney nickel (3.0 g weighed wet with ethanol) in the presence of hydrogen at room temperature and atmospheric pressure for 16 hr. The resulting solution was filtered under N_2, and evaporated to dryness under reduced pressure. The residue was redried *in vacuo* over P_2O_5 to give **ethyl 8-amino-3,4-dihydro-2-[(N-methylanilino)-methyl]pyrido[2,3-*b*]pyrazine-6-carbamate** (**15**): mp *ca.* 115° with softening from 107° (Mel-Temp); λ_{max} in mμ ($\epsilon \times 10^{-3}$), pH 1, 232 (24.2), 265 (sh) (9.81), 317 (10.1), pH 7, 225 (32.5), 245 (sh) (24.8), 331 (8.13), pH 13, 245 (sh) (24.5), 332 (8.21); $\bar{\nu}$ 3500–3100 (NH), 2970, 2920, 2848 (CH), 1730 (C=O), 1615 (NH_2), 1595, 1535, 1500 (ring stretching), 1200 (C–O–C), 742, 685 cm^{-1} (monosubstituted phenyl).

Anal. Calcd for $C_{18}H_{22}N_6O_2 \cdot {}^1/_4C_2H_6O$: C, 60.72; H, 6.47; N, 22.97. Found: C, 60.68; H, 6.64; N, 22.95.

A stirred solution of the above-described solid (**15**) in acetone (70 ml) was treated dropwise with a 0.27% solution of potassium permanganate in acetone until the color of permanganate persisted (about 150 ml was required). The solution was filtered to remove manganese dioxide and evaporated to dryness *in vacuo*. The residue was crystallized from ethanol (100 ml) to give yellow platelets of **16** which were collected by filtration, washed with cold ethanol, and dried at 135° *in vacuo* over P_2O_5 to yield 950 mg (75%): mp >350° (darkens from 280°); λ_{max} in mμ ($\epsilon \times 10^{-3}$), pH 1, 225 (19.1), 258 (7.32), 327 (11.0), pH 7, 220 (18.7), 265 (18.0), 333 (6.87), pH 13, 228 (13.6), 266 (16.4), 336 (6.25); $\bar{\nu}$ 3445, 3315, 3235, 3190 (NH), 3092, 3052, 2981, 2970, 2920 (CH), 1696 (C=O), 1623 (NH_2), 1588, 1570, 1546, 1533, 1504 (ring stretching), 1230 (C–O–C), 737, 685 cm^{-1} (monosubstituted phenyl).

Anal. Calcd for $C_{18}H_{20}N_6O_2$: C, 61.35; H, 5.72; N, 23.85. Found: C, 61.08; H, 5.64; N, 24.19.

6,8-Diamino-2-[(N-methylanilino)methyl]pyrido[2,3-*b*]pyrazine (**17**).—A solution of **16** (200 mg, 0.475 mmole) and KOH (670 mg, 12.0 mmoles) in ethanol (10 ml) was refluxed under N_2 for 7 hr. The reaction mixture was diluted with water (4 ml), cooled to 0°, and acidified with 6 *N* HCl to pH 3. This mixture was warmed and the resulting solution was filtered and carefully adjusted to pH 8 with 50% aqueous sodium hydroxide. After cooling the mixture in an ice bath, the yellow precipitate of **17** was collected by filtration under N_2, washed with cold water (2 ml), and dried *in vacuo* over P_2O_5 to yield 110 mg (73%) mp *ca.* 153–157°. Elemental analysis indicated that this product was a partial hydrochloride, partial hydrate. A portion of the product (100 mg) was purified by trituration with water (2 ml) containing 1 *N* NaOH (0.32 ml). The resulting solid was collected by filtration, washed with water, and dried at 65° *in vacuo* over P_2O_5 to yield 81.0 mg: mp *ca.* 79–86° (Mel-Temp); λ_{max} in mμ ($\epsilon \times 10^{-3}$), pH 1, 225 (39.5), 245 (sh) (8.94), 339 (15.9), pH 7, 221 (35.8), 249 (20.1), 343 (12.3), pH 13, 261 (23.6), 355 (10.7); $\bar{\nu}$ 3600–2400 (NH, OH, CH), 1620 (NH_2), 1595, 1530, 1503 (ring stretching), 747, 688 cm^{-1} (monosubstituted phenyl); pmr (5% DMSO-d_6 w/v), τ 1.50 (3-H), 3.12 (phenyl), 3.60 (NH_2), 3.92 (7-H), 5.26 (CH_2), 6.85 (CH_3).

Anal. Calcd for $C_{15}H_{16}N_6$: C, 64.27; H, 5.75; N, 29.98. Found: C, 64.02; H, 5.98; N, 29.98.

Registry No.—Folic acid, 59-30-3; **2**, 15223-95-7; **3**, 15223-96-8; **4**, 15223-97-9; **6**, 15223-98-0; **9**, 15223-99-1; **12**, 15275-66-8; **13**, 15224-00-7; **14**, 15224-01-8; **15**, 15224-02-9; **16**, 15224-03-0; **17**, 15224-04-1.

Acknowledgment.—The authors are indebted to Mr. W. E. Fitzgibbon and the Organic Preparations Section of Southern Research Institute for the large-scale synthesis of intermediates and to Dr. W. J. Barrett and the members of the Analytical and Physical Chemistry Division of Sothern Research Institute for the spectral and micro-analytical determinations. Some of the analyses reported were performed by the Galbraith Microanalytical Laboratories, Knoxville, Tenn.

Azetidines. II.[1] The Synthesis and Stevens Rearrangement of 2-Phenyl-1,1,3,3-tetramethylazetidinium Iodide[2,3]

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Received July 11, 1967

The title compound (**2**) was synthesized by two routes. 1-Chloro-2,2-dimethyl-3-dimethylamino-1-phenylpropane (**5**), prepared from 2,2-dimethyl-3-dimethylaminopropanol (**3**) *via* 2,2-dimethyl-3-dimethylamino-1-phenyl-1-propanol (**4**), gave **2** when treated with sodium iodide. Methyl-3-bromo-2,2-dimethyl-3-phenylpropylammonium bromide (**8**) was obtained from the benzamide (**9**) of 2,2-dimethyl-3-methylaminopropanal (**6**) *via* 2,2-dimethyl-3-(N-methylbenzamido)-1-phenyl-1-propanol (**10**) and 2,2-dimethyl-3-methylamino-1-phenyl-1-propanol (**7**). Treatment of **8** with aqueous hydroxide gave fragmentation products plus 2-phenyl-1,3,3-trimethylazetidine (**1**), which reacted with methyl iodide to form **2**. Reaction of **2** with phenyllithium gave 1-dimethylamino-2,2-dimethyl-3,3-diphenylpropane (**11**), 2-phenyl-1,2,3,3-tetramethylazetidine (**12**), plus small amounts of **1** and two compounds tentatively identified as rearrangement products. Reaction of **2** with potassium amide in liquid ammonia gave 2,2-dimethyl-3-dimethylaminopropiophenone (**15**), 4,4-dimethyl-3-dimethylamino-5-phenyl-2-isoxazoline (**16**), and small amounts of rearrangement products.

Relatively few azetidines or azetidinium salts have been prepared by direct ring closure,[4-6] probably because of the occurrence of competing reactions which can preclude formation of the four-membered ring. One of these, which has been called "fragmentation" and has been studied extensively by Grob and coworkers,[7] was observed in the preparation of **1** and in the thermal decomposition of **2**.

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[1] Part I: A. G. Anderson, Jr., and M. T. Wills, *J. Org. Chem.*, **32**, 3241 (1967).

[2] From the Ph.D. Thesis of M. T. Wills, University of Washington, Seattle, Wash.

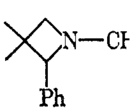
[3] Supported in part by State of Washington Initiative 171 Funds for Research in Biology and Medicine.

[4] For a recent review, see J. A. Moore, "The Chemistry of Heterocyclic Compounds," Vol. 10, part II, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, Chapter VII.

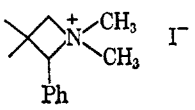
[5] The method of Wadsworth, *J. Org. Chem.*, **32**, 1184 (1967), appeared after the present work was completed.

[6] V. R. Gaertner, *Tetrahedron Letters*, 4691 (1966); V. R. Gaertner, *ibid.*, 343 (1967); N. H. Cromwell and E. Doomes, *ibid.*, 4037 (1966); J. L. Imbach, E. Doomes, R. P. Rebman, and N. H. Cromwell, *J. Org. Chem.*, **32**, 78 (1967).

[7] C. A. Grob and P. W. Schiess, *Angew. Chem.*, **79**, 1 (1967); C. A. Grob, "Kekule Symposium on Theoretical Chemistry," Butterworth and Co. Ltd., London, 1959, pp 114–127.

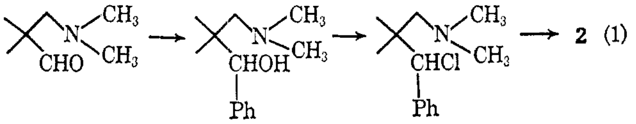


1



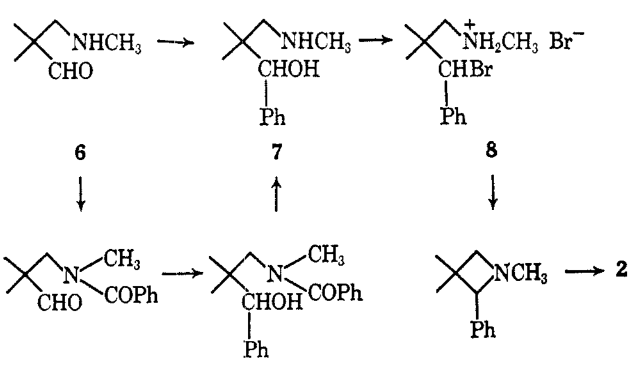
2

One route to **2** consisted of the addition of phenylmagnesium bromide to 2,2-dimethyl-3-dimethylaminopropanal (**3**) to give 2,2-dimethyl-3-dimethylamino-1-phenyl-1-propanol (**4**), conversion of **4** with thionyl chloride into 1-chloro-2,2-dimethyl-3-dimethylamino-1-phenylpropane (**5**), and ring closure of **5** with sodium iodide in acetone. This sequence (eq 1) was satisfactory except for the cyclization which gave at best 11% of **2** along with considerable tarry material.



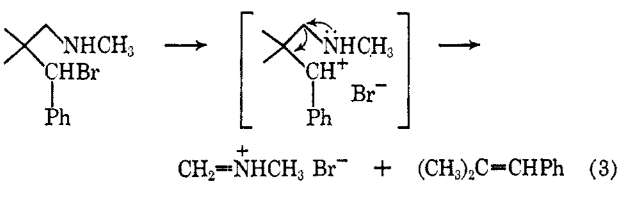
3 4 5 (1)

In the second route (eq 2) direct conversion of 2,2-dimethyl-3-methylaminopropanal (**6**) (which tended to dimerize spontaneously with the loss of water to form 2,4,4,6,8,8-hexamethyl-9-oxa-2,6-diazabicyclo-[3.3.1]nonane[8]) into **7** was found to give low (4%) yields despite the use of a molar excess of the Grignard reagent and carefully purified amino aldehyde. This difficulty was partially overcome (31% over-all yield) by carrying out the Grignard reaction on the more stable benzamide derivative **9**, with subsequent hydrolysis of the product **10** to **7**. Treatment of **7** with hydrobromic acid gave **8** (68%) and reaction of the latter with sodium hydroxide afforded **1** (65%) plus 26–30% (relative to yields of **1**) of the fragmentation products of **8**, methylamine, and 1,1-dimethyl-2-phenylethene. The side reaction can be pictured as a two-step carbonium ion fragmentation[7] (eq 3). The cyclization of 2,2-dimethyl-3-methylamino-1-phenyl-1-sulfatopropane (formed from the reaction of **7** with chlorosulfonic acid) also gave approximately the same relative amounts of **1** and fragmentation products.



6 7 8

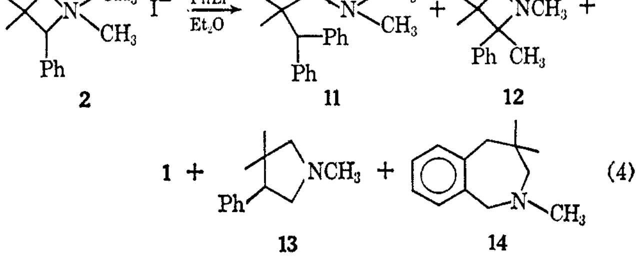
9 10 1 (2)



$$CH_2{=}\overset{+}{N}HCH_3\ Br^- + (CH_3)_2C{=}CHPh \quad (3)$$

The azetidinium salt (**2**), obtained in 80% yield from **1**, decomposed at its melting point and a fragmentation product, 1,1-dimethyl-2-phenylethene, was identified. This behavior provides a possible explanation for the low yield obtained in the direct formation of **2** from **5**.

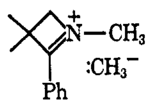
The reaction of **2** with a 1–3 molar excess of phenyllithium in ether (eq 4) was carried out at 10 and at 27°. The major product in both cases was **11**, corresponding to nucleophilic attack at position 2 with ring opening. The analogous product which would have been formed *via* the scission of the other carbon–nitrogen ring bond was not detected, but a small amount of **1**, which presumably arose from nucleophilic attack at one of the N-methyl groups, was found. Other products were the Stevens rearrangement compound (**12**) and two other substances, found in small quantities, which were tentatively identified as rearrangement products **13** and **14**.

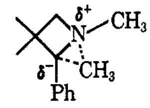


2 11 12

13 14 (4)

The formation of **12** is analogous to the rearrangement of benzyltrimethylammonium bromide to give 1-phenylethyldimethylamine,[9] and is of interest with respect to the ion-pair and concerted mechanisms which have been proposed[10] for the Stevens rearrangement.[11] The first would require a methyl carbanion as the negative species, and the second would involve a transition state having, apparently, appreciable strain energy.





An alternative possibility is the formation of a carbene intermediate and subsequent reaction of this by intramolecular insertion into a nitrogen–carbon bond to form the rearrangement product **12**. Reaction of the carbene with phenyllithium would provide an additional pathway to **11** (Scheme I). Support for the hypothesis of carbene formation is found in the chemistry of nitrogen ylides,[12] including the decomposition to carbenes of the conjugate bases of tetramethylammonium bromide,[13–16] *n*-butoxymethyltrimethylammonium bro-

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[8] C. Mannich and H. Wieder, *Ber.*, **65**, 385 (1932).

[9] Other examples of selective nucleophilic attack at the benzylic carbon of insoluble quaternary salts have been reported: G. Wittig, R. Mangold, and G. Felletschin, *Ann.*, **560**, 116 (1948).

[10] For a review and leading references, see (a) H. E. Zimmerman, "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp 372–382; (b) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 223–229.

[11] T. S. Stevens, E. M. Creighton, A. B. Gordon, and M. MacNicol, *J. Chem. Soc.*, 3193 (1928); T. S. Stevens, *ibid.*, 2107 (1930).

[12] A. W. Johnson, "Ylid Chemistry," Academic Press Inc., New York, N. Y., 1966, pp 251–283.

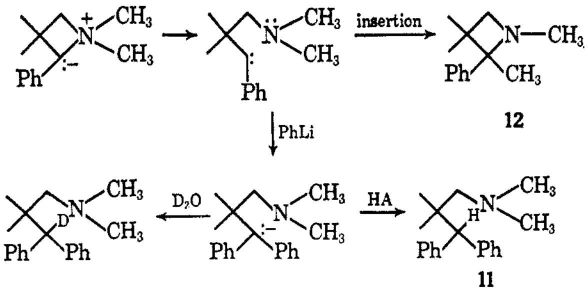
[13] G. Wittig and R. Polster, *Ann.*, **599**, 1 (1956).

[14] V. Franzen and G. Wittig, *Angew. Chem.*, **72**, 417 (1960).

[15] G. Wittig and D. Kraus, *Ann.*, **679**, 34 (1964).

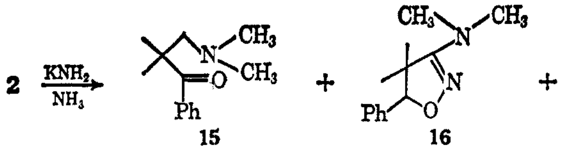
[16] F. Weygand, H. Daniel, and A. Schroll, *Ber.*, **97**, 1217 (1964).

SCHEME I



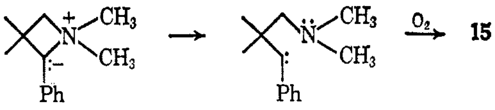
mide,[15] phenoxymethyltrimethylammonium bromide,[15] and fluoryl-9-trimethylammonium bromide.[17–19] There does not appear to be a definitive example of a carbene insertion into a carbon–nitrogen bond; however Franzen and Kuntze[20] found a product which could have resulted from this process in the reaction of benzyldimethylamine with externally generated carbethoxycarbene, but the formation of an ylide and rearrangement of this by another route was not excluded. Experimental evidence for the carbene pathway in the present case was obtained by quenching the reaction mixture with deuterium oxide. If the reaction proceeded as proposed, the anion formed from reaction of the carbene with phenyllithium would react with the deuterium oxide to give **11** containing a deuterium on the carbon bearing the phenyl groups. The nmr spectrum of the product showed 80% incorporation of deuterium at this position. Alternatively, the anion intermediate could have arisen *via* nucleophilic attack by phenide ion at position 2 of the quaternary salt with ring opening (which is less attractive since this involves displacement at a phenyl substituted neopentyl carbon) and subsequent proton abstraction. This possibility was tested by treating a sample of **11** with excess phenyllithium for 5 hr and then quenching with deuterium oxide. The nmr spectrum of the product indicated 85% retention of the pertinent hydrogen. Thus this alternative process cannot be the major one involved. Attempts to trap the sterically hindered carbene by the addition of cyclohexene or tetramethylethene were not definitive.

The reaction of **2** with potassium amide in liquid ammonia (eq 5) produced only 14% of rearrangement products (**12**, **13**, and **14** formed in a ratio of 1:2:4). The two major products were 2,2-dimethyl-3-dimethylaminopropiophenone (**15**, 16%) and 4,4-dimethyl-3-dimethylamino-5-phenyl-2-isoxazoline (**16**, 45%). The identity of **15** was determined by an independent synthesis involving the oxidation of 2,2-dimethyl-3-dimethylaminopropanal (**3**) with silver oxide and then reaction of the acid product with phenyllithium. The structural assignment for **16** was based on its spectral characteristics.



12 + 13 + 14 (5)

The finding of oxygenated compounds as the major products was quite unexpected even though no precautions were taken to prevent the ingress of air into the reaction vessel. It is planned to examine this reaction more closely, and at this time we can only propose the reaction of oxygen with an intermediate phenyl carbene as a plausible possibility for the incorporation of the oxygen.[21]



Experimental Section[22]

2,2-Dimethyl-3-dimethylamino-1-phenyl-1-propanol (4).—To the Grignard reagent prepared from 6 g (0.25 g-atom) of magnesium and 25 ml (0.25 mole) of bromobenzene in 100 ml of dry ether was added a solution of 32.3 g (0.25 mole) of 2,2-dimethyl-3-dimethylaminopropanal (**3**), bp 49–53° (20 mm), n^{25}_{D} 1.4230 (lit.[23] bp 39–43° (10 mm)), prepared as described by Wenner,[23] in 50 ml of dry ether over a period of 1.5 hr. The mixture was refluxed for 1 hr and was then poured with stirring into 100 g of ice and 150 ml of 10% sulfuric acid. The separated aqueous phase was basified with excess 50% sodium hydroxide and the organic layer which formed was extracted into ether. Removal of the solvent from the dried (sodium sulfate) solution and distillation of the residue *in vacuo* gave 32.6 g (63%) of **4** as a colorless oil, bp 107–112° (0.6 mm) (lit.[24] bp 115° (0.4 mm)). The infrared spectrum was recorded.

1-Chloro-2,2-dimethyl-3-dimethylamino-1-phenylpropane (5).—To a stirred solution of 15.5 g (75 mmoles) of **4** in 25 ml of chloroform at 0° (ice bath) was added, dropwise, a solution of 18 g (150 mmoles) of thionyl chloride in 75 ml of chloroform over a period of 30 min. The bath was then removed and the stirring was continued for 1 hr. The solvent was removed under reduced pressure, the residual oil was treated with 50 ml of ethanol, and the extract was evaporated to dryness. Repetition of this process two more times afforded a colorless solid cake which was dissolved in 35 ml of absolute ethanol. Dilution of the solution with 200 ml of ether caused slow crystallization to occur and gave 16.7 g (90%) of the hydrochloride salt of **5** as short, colorless needles, mp 174–176°.

Anal. Calcd for $C_{13}H_{21}NCl_2$: C, 59.54; H, 8.07; N, 5.34. Found: C, 59.32; H, 8.05; N, 5.41.

The salt (16.7 g, 64 mmoles), was treated with an excess of 50% sodium hydroxide solution and the organic layer which formed was extracted into ether. The ethereal solution was washed with water and then with saturated sodium chloride solution. Evaporation of the solvent from the dried (sodium sulfate) solution and distillation of the residual oil under reduced pressure gave 11.4 g (79%) of **5** as a colorless oil: bp 110–113° (2.2 mm); n^{25}_{D} 1.5188. The infrared spectrum was recorded.

2-Phenyl-1,1,3,3-tetramethylazetidinium Iodide (2). A. By Ring Closure.—To a solution of 10.4 g (46 mmoles) of distilled **5** in 80 ml of dry acetone was added 6.5 g (43 mmoles) of oven-dried (100°) sodium iodide. The resulting homogeneous solution was stirred at room temperature for 5 days during which time sodium chloride separated and the solution became yellow. The mixture was filtered and the solvent was evaporated from the filtrate under reduced pressure. The oily residue was dissolved

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[17] C. K. Ingold and J. A. Jessop, *J. Chem. Soc.*, 2357 (1929).

[18] V. Franzen, *Ber.*, **93**, 557 (1960).

[19] G. Wittig and H. Laib, *Ann.*, **580**, 57 (1953).

[20] V. Franzen and H. Kuntze, *ibid.*, **627**, 15 (1959).

[21] Diphenylcarbene has been reported to react with oxygen to form benzophenone: W. Kirmse, L. Horner, and H. Hoffman, *ibid.*, **614**, 19 (1958); P. D. Bartlett and T. G. Traylor, *J. Am. Chem. Soc.*, **84**, 3408 (1962).

[22] Boiling points and melting points are uncorrected. The latter were taken on a Thomas–Hoover capillary melting point apparatus. Infrared spectra were obtained with a Perkin-Elmer Model 21 recording spectrophotometer. Ultraviolet spectra were recorded with a Cary Model 14 recording spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian Associates Model A-60 analytical nmr spectrometer and, unless otherwise noted, with carbon tetrachloride as the solvent. Values are reported in parts per million (δ) relative to tetramethylsilane as the internal standard. Elemental analyses were performed by Dr. A. Bernhardt, Max-Planck Institut, Mülheim (Ruhr), Germany.

[23] W. Wenner, U. S. Patent 2,477,842 (Aug 2, 1949); *Chem. Abstr.*, **43**, P9080*h* (1949).

[24] J. Matti and E. Barman, *Bull. Soc. Chim. France*, **5**, 1742 (1935).

in a miniuum amount of 2-butanone and just enough ether was added to the yellow solution to precipitate the amine salt. Two repetitions of this dissolution and precipitation gave 1.5 g (11%) of **2** as colorless crystals, mp 122° dec, which were identical (nmr and infrared spectra, mixture melting point) with the product from B.

B. By Alkylation.—To a solution of 2.2 g (12.6 mmoles) of 2-phenyl-1,3,3-trimethylazetidine (**1**) in 15 ml of freshly distilled acetonitrile was added 2.1 g (14.8 mmoles) of methyl iodide. The mixture was stirred overnight and the solvent was then evaporated under reduced pressure. The pale yellow oil which remained solidified to a hard mass on standing. This solid was pulverized and washed with ether to afford 3.2 g (80%) of **2** as a colorless powder, mp 119–121° dec. Recrystallization from the minimum of absolute ethanol gave colorless cubes, mp 122° dec. The nmr spectrum of a trifluoroacetic acid solution showed singlets at 1.60, 1.79, 3.08, 3.42, and 5.60, doublets centered at 4.22 (J = 11 cps) and 4.49 (J = 11 cps), and a multiplet centered at 7.65 ppm with relative areas of 3, 3, 3, 3, 1, 1, 1, and 5, respectively. The infrared spectrum was recorded.

Anal. Calcd for $C_{13}H_{20}NI$: C, 49.22; H, 6.36; N, 4.42. Found: C, 49.12; H, 6.21; N, 4.58.

Thermal Decomposition of 2.—A sample of **2** (*ca.* 1 g) in a small distilling flask was heated (oil bath) slowly to 200° over a 30-min period. The pressure was then reduced to 20 mm and the colorless oil which distilled was collected. This material was identified as 1,1-dimethyl-2-phenylethene by its refractive index, $n^{25}D$ 1.5371 (lit.[25] 1.5367), and by comparison (nmr spectrum and gas chromatography retention time) with a sample obtained from a different source (see below). The brown solid residue in the flask, presumed to be N,N-dimethylmethyleniminium iodide, decomposed on standing in air.

2,2-Dimethyl-3-(N-methylbenzamido)propanal (9).—To a well-stirred suspension of 150 g (1.3 moles) of crude (bp 50–70° at 15 mm) 2,2-dimethyl-3-methylaminopropanal (**6**), prepared as described in the literature,[7] in 700 ml of 8% sodium hydroxide cooled in an ice bath was added 160 ml (1.39 moles) of benzoyl chloride over a period of 1 hr. Ether (750 ml) was then added and, after 2 hr of continued stirring, the ethereal layer was separated and washed with three 150-ml portions of dilute hydrochloric acid and then with 150 ml of water. Removal of the solvent from the dried (sodium sulfate) solution left an oily solid which was dissolved in the minimum amount of ether. The solution was cooled in a Dry Ice–acetone bath and the white powder, mp 58–64°, which separated was collected by filtration. Recrystallization from ether gave 153 g (53%) of **9** as colorless plates, mp 68–70° (lit.[7] mp 69°).

2,2-Dimethyl-3-(N-methylbenzamido)-1-phenyl-1-propanol (10).—A solution of the Grignard reagent prepared from 25 g (1.0 g-atom) of magnesium turnings and 157 g (1.0 mole) of bromobenzene in 400 ml of ether was added, dropwise, to 132 g (0.68 mole) of **9** in 300 ml of ether at a rate (*ca.* 1.5 hr) to maintain gentle reflux. An oily layer formed at the bottom of the flask. The mixture was refluxed for 1 hr and then was poured into a mixture of 700 g of ice and 300 ml of concentrated hydrochloric acid. The ether layer was separated and washed with water and saturated sodium chloride solution. Evaporation of the solvent followed by recrystallization from fresh ether gave 138 g (67%) of **10** as colorless needles, mp 116–117°. The infrared spectrum (carbon tetrachloride) showed absorption at 3.0 (OH stretching) and 6.15 μ (C=O stretching).

Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.79; N, 4.71. Found: C, 77.05; H, 7.86; N, 4.94.

2,2-Dimethyl-3-methylamino-1-phenyl-1-propanol (7). A. From 10.—To a solution of 132 g (0.44 mole) of **10** in 800 ml of ethanol was added 200 g of solid potassium hydroxide and 400 ml of water. The mixture was then refluxed for 3 hr. More water (400 ml) was added and all of the ethanol was removed by distillation. The aqueous solution was extracted with four 500-ml portions of ether and the organic solution was in turn extracted with three 300-ml portions of 5% hydrochloric acid. The acidic extract was washed with ether twice and was then basified with sodium hydroxide. The organic layer which separated was taken up in ether and this solution was washed with saturated sodium chloride solution and then dried over sodium sulfate. Evaporation of the ether left 92.5 g of an oil which solidified on standing. Recrystallization from petroleum ether (20–40°) gave 75 g (88%) of **7** as colorless cubes, mp 51–53°.

The infrared spectrum (carbon tetrachloride) showed absorption at 3.15 μ (OH stretching). The nmr spectrum was in agreement with the assigned structure.

Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.50; H, 9.90; N, 7.31.

A hydrobromide derivative was formed by the addition of dry hydrogen bromide to an ether solution of **7**. After one recrystallization from ethanol the melting point was 108–110°.

B. From 6.—A solution of 81 g (0.71 mole) of freshly distilled **6**[7] was added dropwise over a period of 2 hr to the Grignard reagent prepared from 36.5 g (1.5 g-atoms) of magnesium and 236 g (1.5 moles) of bromobenzene in 600 ml of dry ether. The mixture was refluxed for 4.5 hr and was then poured into a mixture of ice and 300 ml of concentrated hydrochloric acid. The aqueous layer was separated, neutralized to pH 8 with sodium hydroxide solution, and extracted with two portions (200 ml and 100 ml) of ether. Evaporation of the solvent from the dried (sodium sulfate) ethereal solution and distillation of the residual oil *in vacuo* gave 42 g of crude product, bp 98–132° (0.6 mm). Dissolution in petroleum ether (20–40°) and refrigeration for 4 days gave 5.6 g (4.1%) of colorless crystals, mp 51–53°, identical (mixture melting point, infrared spectrum) with the product obtained from A.

Methyl-3-bromo-2,2-dimethyl-3-phenylpropylammonium Bromide (8).—A solution of 25 g (0.13 mole) of **7** in 85 ml of concentrated hydrobromic acid was heated on a steam bath and the water and hydrobromic acid were removed slowly under reduced pressure (20 mm). A fresh portion of 50 ml of concentrated hydrobromic acid was added to the oily residue and the distillation was repeated. Recrystallization of the solid residue twice from absolute ethanol gave 30 g (68%) of **8** as small, colorless needles, mp 208–210° dec.

Anal. Calcd for $C_{12}H_{19}Br_2N$: C, 42.75; H, 5.68; Br, 47.41. Found: C, 42.72; H, 5.72; Br, 47.67.

2-Phenyl-1,3,3-trimethylazetidine (1). A.—To a suspension of 15 g (44 mmoles) of **8** in 250 ml of water was added 50 ml of 50% sodium hydroxide and the mixture was refluxed for 4 hr. After cooling, the separated organic layer was dissolved in 100 ml of ether and the ethereal solution was extracted with 100 ml of 5% sulfuric acid. The acidic aqueous solution was washed with three 50-ml portions of ether and then basified with 100 ml of 50% sodium hydroxide. The organic layer which formed was taken up in 100 ml of ether. Evaporation of the solvent from the dried (sodium sulfate) solution and distillation of the residue under reduced pressure gave 5.2 g (65%) of **1** as a colorless oil: bp 85–89° (9 mm); $n^{25}D$ 1.5016. The nmr spectrum showed singlets at 0.80, 1.16, 2.28, and 3.57, doublets centered at 2.58 (J = 6 cps) and 3.12 (J = 6 cps), and a multiplet centered at 7.20 ppm with relative areas of 3, 3, 3, 1, 1, 1, and 5, respectively. The infrared spectrum was recorded.

Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.16; H, 9.79; N, 7.93.

B. The bromide salt **8** was treated with base as described in A and this basic solution was then steam distilled. Analysis of the oil thus obtained by vapor phase chromatography on a cyanosilicone (XF-1150) column (see below) showed that it was a mixture of *ca.* 70% of **1** and *ca.* 30% of 1,1-dimethyl-2-phenylethene. An ethanol solution of the latter showed λ_{max} 244 mμ (log ϵ 4.09) (lit.[25] λ_{max} 244 mμ (log ϵ 4.16) in methanol). The nmr spectrum exhibited a doublet centered at 1.90 (J = 1.3 cps), a doublet centered at 1.96 (J = 1.3 cps), a multiplet centered at 6.56, and a broad singlet at 7.50 ppm with area ratios of 3, 3, 1, and 5, respectively.

In one run, after the addition of the base to the suspension of **8** in water, the mixture was warmed gently and the gaseous product which was evolved was passed through an ethereal solution of picric acid. The methylammonium picrate which formed was washed several times with ether and then dried, mp 206–208° (lit.[26] mp 207°).

Reaction of 2-Phenyl-1,1,3,3-tetramethylazetidinium Iodide (2) with Phenyllithium. A.—To a suspension of 3.0 g (9.5 mmoles) of finely divided **2** in 100 ml of dry ether under an atmosphere of dry nitrogen was added 10 ml (23 mmoles) of phenyllithium as a solution in benzene–ether (75:25 by volume).[27] The

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[25] J. F. Bunnett, G. T. Davis, and H. Tanida, *J. Am. Chem. Soc.*, **84**, 1606 (1962).

[26] C. D. Hodgman, Ed., "Tables for Identification of Organic Compounds," Chemical Rubber Publishing Co., Cleveland, Ohio, 1960.

[27] Foote Mineral Co., Exton, Pa.

mixture was stirred at 10–11° for 12 hr and had become homogeneous after 2 hr. Excess phenyllithium was destroyed with water (0.2 ml). Sulfuric acid (5%) was added and the mixture was then extracted twice with ether. An excess of 50% sodium hydroxide was added to the acidic solution. The organic layer which formed was taken up in ether and dried over sodium sulfate. Careful evaporation of the solvent left 2.08 g of oil. Chromatographic analysis of a sample on an Aerograph Model 600 (Hy-Fi) apparatus using a $^1/_8$ in. × 5 ft column of 20% cyanosilicone (XF-1150) on 60–80 mesh Chromosorb W at 175° showed the presence of five amines. The yields were determined for the two principal products (Table I). (Samples of known composition of high and low boiling products were chromatographed; the relative peak areas obtained were found to agree with the sample composition within 1%.)

TABLE I

DATA ON REACTION OF **2** WITH PHENYLLITHIUM IN ETHER

Product	Yield, g[a] (mole %[b])		Retention time, min[c]	
	10°	27°	150°	175°
1	Present[d]	0.024 (3)	0.8	0.3
12	0.144 (8)	0.176 (2)	1.5	0.7
13	Present[d]	0.040 (5)	2.1	0.8
14	Present[d]	0.016 (2)	3.0	1.1
11	1.366 (54)	0.544 (46)		8.1

[a] Determined from measurement of calibrated vapor phase chromatogram peak areas. [b] Based on total undistilled, acid soluble product. [c] Measured on an Aerograph Model 600 as described in the Experimental Section. [d] Yields estimated to be less than 2%.

Distillation of the oil under reduced pressure gave a total of 1.73 g of distillate as two fractions: (1) 0.33 g, bp 95–105° (10 mm), and (2) 1.4 g, bp 113–116° (0.2 mm). These fractions were chromatographed on a preparative size (0.25 in. × 6 ft) cyanosilicone column at 135 and 195°, respectively. The first material collected had an nmr spectrum and a retention time (0.3 min at 175° on the Aerograph Model 600) identical with those of an authentic sample of **1**. The second material obtained (retention time of 0.7 at 175° on the Aerograph Model 600) was 2-phenyl-1,2,3,3-tetramethylazetidine (**12**), n^{25}D 1.5108. The nmr showed a singlet at 0.78, 1.07, 1.35, and 2.24, doublets at 2.70 ($J = 6$ cps) and 3.01 ($J = 6$ cps), and a multiplet centered at 7.14 ppm with relative areas of 3, 3, 3, 3, 1, 1, and 5, respectively. The infrared spectrum was recorded.

The picrate of **12**, after recrystallization from ethanol, melted at 171–173°.

Anal. Calcd for $C_{19}H_{22}N_4O_7$: 54.54; H, 5.30; N, 13.39. Found: C, 54.78; H, 5.45; N, 13.32.

The third product (retention time 0.8 min at 175° on the Aerograph Model 600) displayed a nmr spectrum having singlets at 0.63, 1.14, 2.30, and 2.90, and a broad peak at 7.09 ppm with relative areas of 3, 3, 3, 2, and 5, respectively. Several peaks of total area corresponding most closely to three protons were present in the region from 2–3.5 ppm. A possible structure for this compound is 3-phenyl-1,4,4-trimethylpyrrolidine (**13**). It was not characterized further.

A fourth substance (retention time 1.1 min at 175° on the Aerograph Model 600) exhibited a nmr spectrum having singlets at 0.80, 2.30, 2.38, 2.58, and 3.43, and a broad peak at 6.86 ppm with relative areas of 6, 3, 2, 2, 2, and 4, respectively. These data fit with the structure 3,4-benzo-1,6,6-trimethyl-1,5,6,7-tetrahydroazepine (**14**).

The last product obtained (retention time 8.1 min on the Aerograph Model 600) showed a nmr spectrum having singlets at 1.0, 2.08, 2.13, and 4.01, and a multiplet centered at 7.2 ppm with relative areas of 6, 2, 6, 1, and 10, respectively. This and the infrared spectrum were consistent with the structure 1-dimethylamino-2,2-dimethyl-3,3-diphenylpropane (**11**).

The picrate of **11**, after recrystallization from ethanol, melted at 154–156°.

Anal. Calcd for $C_{25}H_{29}N_4O_7$: C, 60.35; H, 5.88; N, 11.26. Found: C, 60.57; H, 5.92; N, 11.43.

B.—A suspension of 1.38 g (4.4 mmoles) of finely divided **2** in 100 ml of ether was allowed to react with 7 ml (16 mmoles) of phenyllithium reagent as described in A except that the reaction temperature was 27°. The treatment of the reaction mixture as given in A afforded 0.8 g of oil which when analyzed by chromatography on the Aerograph Model 600 as described in A gave the results shown in Table I. Samples of each product collected were shown (nmr spectra) to correspond with those obtained in A.

Reaction of 2-Phenyl-1,1,3,3-tetramethylazetidinium Iodide (2) with Potassium Amide in Liquid Ammonia.—To a solution of 2 g (38 mmoles) of potassium amide[28] in 100 ml of liquid ammonia was added 2.4 g (7.6 mmoles) of finely divided **2**. Atmospheric moisture was excluded by means of a drying tube containing sodium hydroxide pellets. No provision was made for the exclusion of atmospheric oxygen. A yellow color developed. The mixture was stirred for 10.5 hr at −33° and was then allowed to stand at −80° overnight. Stirring was then continued at −33° for an additional 5.5 hr. Solid ammonium chloride (2.5 g) was added in portions, then 100 ml of ether, and the ammonia was evaporated (water bath). The ethereal solution was separated and set aside. Sulfuric acid (5%, 100 ml) was added to the residual salts and a red-brown (from the presence of iodine) solution containing insoluble black particles formed. After filtration, the solution was extracted several times with ether (until the aqueous layer was colorless) and was then basified with 50% sodium hydroxide solution. This solution was extracted with ether, the extracts were added to the original ether solution, and removal of the solvent from the combined, dried (calcium sulfate) extracts left 1.3 g of yellow oil. Vapor phase chromatographic analysis (as described for the reaction of **2** with phenyllithium) yielded the results given in Table II.

TABLE II

DATA ON REACTION OF **2** WITH POTASSIUM AMIDE IN LIQUID AMMONIA

Product	Yield, mole %[a]	Retention time, min[b]	
		150°	175°
1	3.0	0.8	
12	1.9	1.5	
13	4.2	2.1	
14	7.6	3.0	
15	15.8	7.5	1.7
16	44.8		7.0
Unidentified	4.7		8.3

[a] Determined from measurement of calibrated vapor phase chromatogram peak areas. [b] Measured on an Aerograph Model 600 as described in the Experimental Section.

Fractionation on a preparative size column (as described for the reaction of **2** with butyllithium) at 200° gave a low boiling fraction and a high boiling fraction. Four of the retention times observed (Table II) on analytical chromatography of a sample of the low boiling fraction corresponded exactly to those previously identified with compounds **1**, **12**, **13**, and **14**. A fifth substance (**15**) was also present. Rechromatography of the main portion at 135° on the preparative apparatus permitted the separation of **13**, **14**, and **15**. The identities of **13** and **14** were confirmed by comparison of their nmr spectra with those of authentic samples. An additional chromatographic purification of **15** gave a colorless oil, n^{26}D 1.5149. An ethanol solution showed λ_{max} 240 mμ (log ϵ 3.50) and 273 mμ (log ϵ 2.86). The infrared spectrum showed strong absorption at 5.96 μ. An authentic sample of **15**, prepared from 2,2-dimethyl-3-dimethylaminopropanal (**3**) as described in the literature,[29] showed n^{25}D 1.5115, λ_{max} 239 mμ (log ϵ 3.86) and 273 mμ (log ϵ 2.91). The infrared and nmr spectra of the two samples were essentially identical, but indicated the presence of minor impurities in the product as obtained.

Rechromatography of the higher boiling fraction at 185° gave two products, the second of which was not characterized. The first (**16**), after one further chromatographic purification, had n^{25}D 1.5432 and the nmr spectrum showed singlets at 1.30 (C-

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[28] C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958).

[29] H. R. Snyder and J. H. Brewster, *ibid.*, **71**, 1061 (1949).

methyl), 1.36 (C-methyl), 2.25 (N-methyl), and 4.65 (benzylic hydrogen), and multiplets (phenyl ring) centered at 7.25 and 7.55 ppm with relative areas of 3, 3, 6, 1, 3, and 2, respectively.[30] The nmr spectrum in 75% trifluoroacetic acid possessed singlets at 1.68 (C-methyl), 3.04, and 5.42 ppm with relative areas of 6, 6, and 1, respectively. The infrared spectrum showed no absorption corresponding to N-H or C=O groups. An ethanol solution showed a low intensity band with λ_{max} 255 mμ.

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[30] Separation of the phenyl hydrogen absorption into three- and two-proton multiplets was also observed in the spectrum of 4,4-dimethyl-2-phenyl-1-pyrroline.[1]

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.52; H, 8.31; N, 12.84. Found: C, 71.59; H, 8.31; N, 12.98.

Registry No.—**1**, 15451-12-4; **2**, 15451-13-5; **3**, 15451-14-6; **4**, 15451-15-7; **5**, 15451-16-8; **5** HCl, 15451-17-9; **7**, 15451-18-0; **7** HBr, 15451-19-1; **8**, 15451-20-4; **9**, 15451-21-5; **10**, 15451-22-6; **11**, 15451-23-7; **11** picrate, 15451-24-8; **12**, 15451-25-9; **12** picrate, 15451-26-0; **13**, 15451-27-1; **14**, 15451-28-2; **15**, 15451-29-3; **16**, 15451-30-6; 1,1-dimethyl-2-phenylethene, 768-49-0.

Syntheses of Dicyanoacetylene

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Thermal decomposition of dicyanodiazomethane at 220° gave tetracyanoethylene, cyanogen, and dicyanoacetylene. The two latter products were also formed in the pyrolysis of tetracyanoethylene at 700°. Thermolysis of the easily accessible 4,5-dicyano-1,3-dithiol-2-one (**5**) was found to provide a convenient synthesis of dicyanoacetylene.

Dicyanoacetylene (**1**) was first prepared by Moureu and Bongrand[1] almost 60 years ago by the dehydration of the bisamide of acetylenedicarboxylic acid. While its physical properties have been studied in great detail,[2,3] investigations of its chemical reactions have been hampered by lack of a satisfactory synthesis; despite its unusually high reactivity, only relatively few papers on this subject have appeared so far.[4,5] The original synthesis[1] of dicyanoacetylene proceeds with acceptable yields (30–40%) only on a small scale; attempts to modify it have met with little success.[5e,l] The gas phase pyrolysis of 1,2-dichloro-1,2-dicyanoethylene[6] affords dicyanoacetylene and chlorine in good yields, but the products recombine so rapidly at low temperatures that they must be separated immediately in order to obtain acceptable conversions. The two other reported syntheses of dicyanoacetylene are the retrodiene cleavage of dimethyl 5,6-dicyanooxabicyclo[2.2.1]hepta-2,5-dienedicarboxylate[7] and the reaction of carbon with nitrogen at or above 2500°.[8] We have found that dicyanoacetylene is formed on gas phase pyrolysis of tetracyanoethylene (**2**), 4,5-dicyano-1,3-dithiol-2-one (**5**), and 4,5-dicyano-1,3-dithiol-2-thione (**6**).[9] Pyrolysis of **5** is believed to be the best and most convenient synthetic method for the preparation of dicyanoacetylene presently available.

Results and Discussion

As part of our investigations of the chemistry of dicyanocarbene,[10] we were interested in the reactions of this species in the absence of added carbene acceptors. To this purpose, solid dicyanodiazomethane (**4**)[11] was pyrolyzed in a stream of helium at 220° [12] in the preheater of a gas chromatograph. The products were separated by gas chromatography and identified by their mass spectra. In addition to nitrogen and tetracyanoethylene (30–40% yield), cyanogen (**3**) and dicyanoacetylene (**1**) were formed in considerable but undeter-

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[1] C. Moureu and J. C. Bongrand, *Bull. Soc. Chim. France*, 846 (1909); *Ann. Chim.* (Paris), [9] **14**, 5 (1920); *Compt. Rend.*, **170**, 1025 (1920).

[2] The following physical data have been published: crystal structure,[3a] heat of combustion and formation,[3b] flame temperatures,[3f] heat of vaporization and vapor pressure,[3c] molecular orbital calculations,[3d] resonance energy,[3e] thermodynamic functions,[3m] ultraviolet spectrum,[3g] infrared spectrum,[3h,n] Raman spectrum,[3h,m] mass spectrum,[3i] molecular refraction,[1,3j] molecular polarizability,[3m] magneto-optical properties,[3k] melting point curves with maleonitrile and fumaronitrile,[3j] lifetime in space,[3o] and toxicity.[3l]

[3] (a) R. B. Hannan and R. L. Collin, *Acta Cryst.*, **6**, 350 (1953); (b) G. T. Armstrong and S. Marantz, *J. Phys. Chem.*, **64**, 1776 (1960); (c) A. J. Saggiomo, *J. Org. Chem.*, **22**, 1171 (1957); (d) J. B. Moffat, *Can. J. Chem.*, **42**, 1323 (1964); (e) M. M. Kreevoy, *J. Am. Chem. Soc.*, **81**, 1608 (1959); (f) A. D. Kirshenbaum and A. V. Grosse, *ibid.*, **78**, 2020 (1956); A. V. Grosse and C. S. Stokes, U. S. Department of Commerce, Office of Technical Services, P. B. Report 171, 460 (1960); *Chem. Abstr.*, **52**, 8696 (1962); (g) F. A. Miller and R. B. Hannan, Jr., *Spectrochim. Acta*, **12**, 321 (1958); (h) F. A. Miller and R. B. Hannan, Jr., *J. Chem. Phys.*, **21**, 110 (1953); F. A. Miller, R. B. Hannan, Jr., and L. R. Cousins, *ibid.*, **23**, 2127 (1955); (i) V. H. Dibeler, R. M. Reese, and J. L. Franklin, *J. Am. Chem. Soc.*, **83**, 1813 (1961); (j) H. Mommaerts, *Bull. Soc. Chim. Belges*, **52**, 79 (1943); (k) A. Turpin and D. Voigt, *Compt. Rend.*, **256**, 1712 (1963); F. Galais and J. F. Labarre, *J. Chim. Phys.*, **61**, 717 (1964); (l) A. Desgret, *Compt. Rend.*, **152**, 1707 (1911); (m) C. Nagarjan, E. R. Lippincott, and J. M. Stutman, *Z. Naturforsch.*, **20a**, 786 (1965); (n) F. A. Miller, D. H. Lemon, and R. E. Witkowski, *Spectrochim. Acta*, **21**, 1709 (1965); (o) A. E. Potter and B. DelDuca, *Icarus*, **3**, 103 (1964).

[4] The following reactions of dicyanoacetylene have been reported: halogenation and hydrohalogenation;[1] addition of alcohols,[1,5a] amines,[1,5a,b] and mercaptans;[3k] reaction with phosphines,[5c] mercuric chloride,[5b] and pentacyanocobaltate ion;[5d] cycloadditions;[5b,e–j,m] and polymerization.[5k,l]

[5] (a) E. Winterfeldt, W. Krohn, and H. Preuss, *Chem. Ber.*, **99**, 2572 (1966); (b) C. D. Weis, *J. Org. Chem.*, **28**, 74 (1963); (c) G. S. Reddy and C. D. Weis, *ibid.*, **28**, 1822 (1963); *cf.*, however, G. Märkl, *Angew. Chem.*, **77**, 1109 (1965); (d) M. E. Kimball, J. P. Martella, and W. C. Kaska, *Inorg. Chem.*, **6**, 414 (1967); (e) A. T. Blomquist and E. C. Winslow, *J. Org. Chem.*, **10**, 149 (1945); (f) R. C. Cookson and J. Dance, *Tetrahedron Letters*, 879 (1962); (g) H. E. Zimmerman and G. L. Grunewald, *J. Am. Chem. Soc.*, **86**, 1434 (1964); (h) P. G. Gassman and K. Mansfield, *Chem. Commun.*, 391 (1965); (i) C. Dufraisse, J. Rigaudy, and M. Ricard, *Tetrahedron Suppl.*, **8**, Part II, 491 (1966); (j) E. Ciganek, *Tetrahedron Letters*, 3321 (1967); (k) M. Beneš, J. Peška, and O. Wichterle, *Chem. Ind.* (London), 562 (1962); *J. Polymer Sci.*, Part C, No. 4, 1377 (1964); (l) N. R. Byrd, NASA Accession No. N64-20601, Report No. NASA-CR-56035; Report 166-F, 1964; *Chem. Abstracts*, **62**, 2831 (1965); (m) C. D. Smith, *J. Am. Chem. Soc.*, **88**, 4273 (1966).

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[8] P. D. Zavitzanos, French Patent 1,460,282 (1966); *Chem. Abstr.*, **67**, 63861 (1967).

[9] The synthesis of dicyanoacetylene from **5** and **6** is subject of a patent: E. Ciganek and J. R. Roland, U. S. Patent 3,322,816 (1967); *Chem. Abstr.*, **67**, 90414 (1967).

[10] E. Ciganek, *J. Am. Chem. Soc.*, **88**, 1979 (1966).

[11] E. Ciganek, *J. Org. Chem.*, **30**, 4198 (1965).

[12] Thermal decomposition of **4** occurs at *ca.* 70°; the higher pyrolysis temperature was used to ensure vaporization of the products.