10-Phenylundecanoic Acid.—10-Phenylundecanoic acid (50 g., 0.191 mole) was treated with 88.4 g. of dioxane sulfur trioxide reagent (0.25 mole of SO_3). A white waxy sulfonation product was obtained. The S-*p*-chlorobenzylthiuronium salt melted at 152°.

Anal. Calcd. for $C_{33}H_{44}O_5Cl_2N_4S_3$: C, 53.3; H, 5.96. Found: C, 52.96; H, 6.44.

Diphenylacetic Acid.—Treatment of diphenylacetic acid[18] (14.2 g., 0.067 mole) with dioxane sulfur trioxide reagent (8.75 g., 0.11 mole of SO_3) gave no sulfonation product. Unchanged diphenylacetic acid was recovered; weight 10.8 g. (76% recovery).

α-Cyclohexylphenylacetic Acid.—α-Cyclohexylphenylacetonitrile[19] (51.3 g., 0.257 mole) was treated with 250 ml. of concentrated sulfuric acid (sp. gr. 1.84) in 300 ml. of water at reflux temperature for six hours. The solution was cooled and diluted with a liter of water. The organic layer was separated, dried and upon cooling, it solidified; m.p. 145–149°. Recrystallization from petroleum ether gave 29.7 g. of α-cyclohexylphenylacetic acid (53.0%), m.p. 147–149° (lit.[20] m.p. 148–149°).

Dioxane sulfur trioxide (0.2 mole of SO_3) and 29.7 g. (0.136 mole) of α-cyclohexylphenylacetic acid were combined and stirred for the usual time. No heat was evolved, and unreacted α-cyclohexylphenylacetic acid was recovered; 25.3 g. (86%). No sulfonation product was isolated.

α-Phenylbutyric Acid.—α-Phenylbutyric acid (41.2 g., 0.25 mole) was treated with dioxane sulfur trioxide (0.3 mole of SO_3). The sodium salt of the product was isolated; yield 10.1 g. (14.0%).

Anal. Calcd. for $C_{10}H_{10}O_5Na_2$: Na, 15.96. Found: Na, 16.15.

Its S-*p*-chlorobenzylthiuronium derivative had m.p. 155–157°.

---

[18] C. S. Marvel, F. Hager and E. Caudle, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 224.

[19] E. M. Hancock and A. C. Cope, *Org. Syntheses*, **25**, 25 (1945).

[20] H. A. Smith, D. M. Alderman and F. W. Nadig, THIS JOURNAL, **67**, 272 (1945).

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NOTRE DAME]

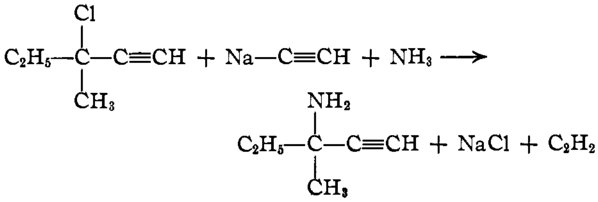
The Preparation of Some Acetylenic Primary Amines[1]

BY G. F. HENNION AND EUGENE G. TEACH[2]

RECEIVED OCTOBER 24, 1952

Secondary and tertiary ethynylcarbinyl chlorides, $R(R')C(Cl)—C\equiv CH$, obtained from the corresponding carbinols, react with sodamide in liquid ammonia to produce primary amines, $R(R')C(NH_2)—C\equiv CH$. Eight compounds of this type were prepared. The method failed (in two cases) where one of the R groups was phenyl, yielding only polymeric material.

Dimethylethynylcarbinyl chloride, $(CH_3)_2C(Cl)—C\equiv CH$, was recently shown[3] to undergo a unique solvolysis in alkaline 80% ethyl alcohol to produce chiefly the corresponding ethyl ether. The reaction was found to obey second order kinetics and it was proposed that the dipolar ion $(CH_3)_2\overset{\oplus}{C}—C\equiv\overset{\ominus}{C}$ is an intermediate. One of the consequences of the suggested mechanism is that reaction with bases in other suitable media should likewise produce the solvolytic products. An especially good test of this idea is found in the reaction of dimethylethynylcarbinyl chloride with sodamide in liquid ammonia: according to our mechanism the amine should be produced, as indeed it is. The ordinary course of sodamide–ammonia reactions on aliphatic halides produces unsaturated hydrocarbons by HX elimination.[4] We have found that many secondary and tertiary ethynylcarbinyl chlorides, $R(R')C(Cl)C\equiv CH$, react atypically to produce primary amines in reasonable yield. This we regard as good evidence for the detailed mechanism proposed previously.[3] These ideas are further supported by the fact that sodium acetylide may be substituted for sodamide in the amine synthesis, showing that the reaction is not a simple nucleophilic displacement. When methylethylethynylcarbinyl chloride was added to sodium acetylide in liquid ammonia, evolution of acetylene occurred and the amine was produced in 52% yield.



$$C_2H_5—\overset{Cl}{\underset{CH_3}{C}}—C\equiv CH + Na—C\equiv CH + NH_3 \longrightarrow C_2H_5—\overset{NH_2}{\underset{CH_3}{C}}—C\equiv CH + NaCl + C_2H_2$$

The acetylenic amine synthesis involves three steps: reaction of a carbonyl compound (aldehyde or ketone) with sodium acetylide, conversion of the carbinol so obtained to the chloride by treatment with hydrochloric acid or thionyl chloride, and ammonolysis with sodamide in liquid ammonia. These steps were applied successfully to *n*-butyraldehyde, *n*-heptaldehyde, acetone, methyl ethyl ketone, diethyl ketone, methyl *n*-propyl ketone, methyl *n*-amyl ketone and cyclohexanone. Benzaldehyde and propiophenone failed in the last step; the acetylenic chlorides derived from these compounds gave only tar by reaction with sodamide in liquid ammonia.

The acetylenic amines manifest the usual acetylenic properties and undergo the ordinary primary amine reactions. Each compound gave a copious curdy precipitate with ammoniacal silver nitrate solution, confirming the presence of the $—C\equiv CH$ group. They formed crystalline hydrochlorides and sulfates in the usual way and reacted with acetic anhydride, benzoyl chloride, benzenesulfonyl chloride, potassium cyanate, etc., in typical fashion. Every derivative responded to the silver nitrate test showing that the ethynyl radical does not interfere in the reactions of the amino group.

The amines are described in Table I and some assorted derivatives in Table II. Further work is in progress.

---

[1] Paper LVIII on substituted acetylenes; previous paper, *J. Org. Chem.*, **16**, 1289 (1951).

[2] Eli Lilly Company Fellow, 1951–1953.

[3] G. F. Hennion and D. E. Maloney, THIS JOURNAL, **73**, 4735 (1951).

[4] F. W. Bergstrom and W. C. Fernelius, *Chem. Revs.*, **12**, 92 (1933); **20**, 433 (1937).

TABLE I

ACETYLENIC PRIMARY AMINES, R(R′)C(NH_2)—C≡CH

Compd.	R	R′	B.p., °C.	Press., mm.	$n^{25}D$	d^{25}	Yield,[a] %
I[b]	CH_3	CH_3	79–80	Atm.	1.4183	0.790	41
II	C_2H_5	CH_3	55–56	120	1.4302	.804	57
III	C_2H_5	C_2H_5	73–74	100	1.4392	.824	60
IV	n-C_3H_7	H	70–71	100	1.4378	.815	68
V	n-C_3H_7	CH_3	69–70	100	1.4346	.811	49
VI	n-C_5H_{11}	CH_3	76–77	25	1.4391	.811	70
VII[c]	n-C_6H_{13}	H	74	10	1.4452	.821	76
VIII[d]	$-CH_2-(CH_2)_3-CH_2-$		65–66	20	1.4796	.913	72

[a] Yield of once distilled product based on chloride taken. [b] M.p. 18°. [c] M.p. 10°. [d] Compound VIII is 1-amino-1-ethynylcyclohexane.

TABLE II

ANALYTICAL DATA, DERIVATIVES OF ACETYLENIC PRIMARY AMINES

Compd.	Derivative	Formula	M.p., °C. (uncor.)	Nitrogen, % Calcd.	Nitrogen, % Obsd.
I	Sulfate	$2C_5H_9N \cdot H_2SO_4$	.....	10.57	10.29
I	Benzoyl	$C_{12}H_{13}NO$	152–153	7.48	7.35
II	Acetyl	$C_8H_{13}NO$	62–64	10.06	9.99
II	Benzoyl	$C_{13}H_{15}NO$	106–107	6.96	6.70
III	Acetyl	$C_9H_{15}NO$	55–56	9.14	9.01
III	Benzoyl	$C_{14}H_{17}NO$	64–66	6.51	6.23
IV	Sulfate	$2C_6H_{11}N \cdot H_2SO_4$	.....	9.57	9.47
IV	Benzoyl	$C_{13}H_{15}NO$	70–71	6.96	6.79
V	Benzoyl	$C_{14}H_{17}NO$	116–117	6.51	6.11
VI	Benzoyl	$C_{16}H_{21}NO$	80–81	5.76	5.34
VII	Benzoyl	$C_{16}H_{21}NO$	55–56	5.76	5.84
VIII	Acetyl	$C_{10}H_{15}NO$	150–152	8.48	8.58
VIII	Benzoyl	$C_{15}H_{17}NO$	131–132	6.16	6.07
VIII	Urea	$C_9H_{14}N_2O$	134–135	16.86	16.82

Experimental

Acetylenic Carbinols.—All of the starting materials were prepared in the usual way by reaction of the aldehyde or ketone with sodium acetylide in liquid ammonia. An excellent review of the literature is available.[5]

Acetylenic Chlorides.—Dimethyl-, methylethyl-, diethyl- and n-propylethynylcarbinyl chlorides were prepared from the carbinols by methods previously described.[6,7]

Methyl-n-propylethynylcarbinyl chloride, b.p. 69–70° at 100 mm., $n^{25}D$ 1.4350–1.4367, was prepared by reaction of the carbinol with concentrated hydrochloric acid[6] (yield 40%), as was 1-chloro-1-ethynylcyclohexane, b.p. 66° at 20 mm., $n^{25}D$ 1.4770–1.4780, d^{25} 1.008 (yield 21%). Methyl-n-amylethynylcarbinyl chloride was made from the carbinol by saturation with hydrogen chloride gas at room temperature; b.p. 62–65° at 25 mm., $n^{25}D$ 1.4400–1.4410, d^{25} 0.881–0.886 (yield 45%). n-Hexylethynylcarbinyl chloride, b.p. 70° at 10 mm., $n^{25}D$ 1.4470, was prepared by the thionyl chloride method[7] (yield 72%).

Physical constants are given above for the chlorides not previously reported. No attempt was made to obtain them in analytically pure form, although each was tested with ammoniacal silver nitrate solution and observed to give the typical precipitate.

Preparation of Methyl-n-amylethynylcarbinyl Amine (VI).—Ten and one-half grams of sodium (0.45 gram-atom) was converted to the amide[8] in 500 ml. of liquid ammonia contained in a one-liter, three-neck flask provided with a mechanical stirrer. Sixty-seven grams (0.42 mole) of methyl-n-amylethynylcarbinyl chloride diluted with five volumes of anhydrous ether was added dropwise during a period of one hour with continuous stirring. The mixture was stirred for one hour after the addition of chloride was complete. More anhydrous ether (100 ml.) was then added, the stirring discontinued and the mixture was allowed to stand overnight to evaporate most of the ammonia. Chopped ice (250 g.) and ordinary ether were then added. The ether layer was separated and the aqueous layer extracted once with 75 ml. of ether. The combined ethereal extract was washed with a little cold water and dried over anhydrous potassium carbonate. Distillation through a helix-packed column (packed section, 1.4 × 45 cm.) gave 40.8 g. of product (70% yield), b.p. 70–74° at 25 mm., $n^{25}D$ 1.4385–1.4412. The entire product was chilled in an ice-bath and a mixture of 29 ml. of concd. hydrochloric acid and 30 g. of chopped ice was added slowly with stirring. The solution was extracted with two 25-ml. portions of ether (discarded) to remove non-basic impurities. The aqueous solution was then treated with 14 g. of sodium hydroxide in 15 ml. of water to release the amine, recovered by extraction with ether. Distillation yielded 28 g. of pure amine (48% yield), b.p. 76–77° at 25 mm., $n^{25}D$ 1.4391.

The procedure described above was employed in all cases except that some of the products were purified by careful redistillation rather than by ether extraction of aqueous acidic solution. The amount of acetylenic chloride used ranged from 0.2 to 1 mole, with only a slight excess of sodamide. The once distilled products were almost entirely soluble in dilute hydrochloric acid, turbidity or a thin insoluble layer indicating some non-amine impurity, usually estimated at not more than 2–5% of the total product. Purification by way of solution in acid, extraction with ether, etc., as described above, was most effective in producing pure products.

Derivatives.—The acetyl derivatives listed in Table II were prepared by reaction with acetic anhydride, heating for 30 minutes at 70°. The derivatives from II and III were crystallized from Skellysolve F, VIII from aqueous alcohol. Benzoyl derivatives were made by the method of Shriner and Fuson.[9] Sulfates precipitated from 50% sulfuric acid diluted with acetone. 1-Ethynyl-1-ureidocyclohexane was made from 12.3 g. (0.1 mole) of the amine by heating in dilute aqueous hydrochloric acid with 8.9 g. (0.11 mole) of potassium cyanate for 75 minutes. The crystalline product was recovered by cooling with stirring; yield 7.5 g. after recrystallization from aqueous alcohol.

Acknowledgment.—The authors are grateful to the Eli Lilly Company, Indianapolis, Indiana, for the financial support of this work. Special thanks are due Messrs W. J. Schenck, H. L. Hunter, W. L. Brown and G. Maciak of the Lilly Research Laboratories for a large number of microanalyses.

NOTRE DAME, INDIANA

---

(5) A. W. Johnson, "The Chemistry of the Acetylenic Compounds, Vol. I. The Acetylenic Alcohols," Edward Arnold Co., London, 1946.

(6) G. F. Hennion, J. J. Sheehan and D. E. Maloney, THIS JOURNAL, **72**, 3542 (1950).

(7) G. F. Hennion and J. J. Sheehan, *ibid.*, **71**, 1964 (1949).

(8) T. H. Vaughn, R. R. Vogt and J. A. Nieuwland, *ibid.*, **56**, 2120 (1934).

(9) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 177.