TABLE III

β-DIAZINEPROPIONIC ACIDS, METHYL ESTERS AND AMIDES

R	RCH_2CH_2COOH Yield, %	M. p., °C.	Anal. N, % Calcd.	Found	$RCH_2CH_2COOCH_3$ M. p., °C.	Anal. N, % Calcd.	Found	$RCH_2CH_2CONH_2$ M. p., °C.	Anal. N, % Calcd.	Found
2-Quinoxaline	92[a]	115–115.5	13.86	13.95	39–40[d]	12.96	13.14	152–152.5[f]	20.88	20.95
2-Pyrazine	79[b]	91.5–92	18.42	18.71	Liquid			125–126[g]	[h]	
3-Pyridazine	93[b]	168–170 dec.	[c]		42.5–43[e]	16.86	16.76	141–142[g]	27.80	27.50
2-Pyrimidine	84[b]	179–180	18.42	18.60	Liquid			135–136[g]	27.80	27.88
4-Pyrimidine	75[b]	198–199	18.42	18.46	Liquid			117–118[g]	27.80	27.77

[a] Empirical formula, $C_{11}H_{10}N_2O_2$. [b] Empirical formula, $C_7H_8N_2O_2$. [c] Calcd.: C, 55.26; H, 5.30. Found: C, 54.90; H, 5.45. [d] Empirical formula, $C_{12}H_{12}N_2O_2$. [e] Empirical formula, $C_8H_{10}N_2O_2$. [f] Empirical formula, $C_{11}H_{11}N_3O_2$. [g] Empirical formula, $C_7H_9N_3O_2$. [h] Calcd.: C, 55.62; H, 6.01. Found: C, 55.90; H, 6.19.

mole) had been absorbed. Ninety grams of ice was added to the resulting solution followed by 11.8 g. (0.078 mole) of β-(2-pyridazine)-propionamide (Table III). The mixture was stirred until all of the solid had dissolved, and then it was allowed to stand at room temperature for one hour after which it was heated on the steam-bath for one hour. The cooled solution was extracted with three 150-ml. portions of isoamyl alcohol. This extract was washed with a little water after which it in turn was extracted with three 100-ml. portions of 2 *N* hydrochloric acid. Evaporation of the hydrochloric acid solution in vacuum left a sirup which soon crystallized. The product was triturated with hot absolute ethanol, in which it was sparingly soluble, and air dried.

The β-aminoethylquinoxaline, pyrazine and pyrimidines were best extracted from the hypochlorite–reaction mixture with ethyl acetate instead of isoamyl alcohol. The ethyl acetate solutions were dried with magnesium sulfate, and the amine hydrochlorides were precipitated with dry hydrogen chloride. The products were purified by solution in hot methanol, decolorization with carbon and precipitation with dry ether. They were obtained as white crystalline solids; readily soluble in water or warm methanol, insoluble in non-polar solvents.

Acknowledgment.—The authors are grateful to W. L. Brown, H. L. Hunter and W. J. Schenck for the microanalyses reported here.

Summary

The syntheses of 2-β-aminoethylquinoxaline, 2-β-aminoethylpyrazine, 3-β-aminoethylpyridazine, 2-β-aminethylpyrimidine and 4-β-aminoethylpyrimidine are described.

INDIANAPOLIS, INDIANA RECEIVED JANUARY 25, 1950

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

The Reaction of Dimethylethynylcarbinol with Hydrochloric Acid[1]

BY G. F. HENNION, J. J. SHEEHAN AND D. E. MALONEY

Discussion

It is not surprising that treatment of dimethylethynylcarbinol (I) with hydrochloric acid produces a variety of products. There is, however, a good deal of uncertainty about the nature of these materials as well as the yields and properties of those which are isolable. Furthermore, no attempt has been made previously to ascertain the mechanisms by which the various products are formed. Hurd and McPhee[2,3] observed that 2-chloro-3-methyl-1,3-butadiene (II) was in their product and claimed the amount to be "far in excess of 36%" on the basis of ozonolysis (36% yield of formaldehyde) and 42% yield of a maleic anhydride adduct reported to melt at 124–126°. Carothers and Coffman[4] first prepared II and presented an adequate description and proof of structure, both confirmed in the present study. The Hurd–McPhee product admittedly differed from that of Carothers and Coffman and no definite explanation could be offered.

There are two plausible mechanisms for the formation of II from I: (a) that the carbinol dehydrates *in situ* to form isopropenylacetylene (III) which then adds hydrogen chloride across the triple bond; (b) that the reaction initially produces the tertiary chloride (IV), then adding hydrogen chloride to form an unstable dichloride, $(CH_3)_2C(Cl)—C(Cl)=CH_2$, which loses the tertiary chlorine as hydrogen chloride. The addition of hydrogen chloride to III is known to yield II (Carothers–Coffman synthesis[4]) and the reaction is catalyzed by cuprous and ammonium chlorides.

The behavior of the carbinol (I) with hydrochloric acid *in the presence of cuprous and ammonium chlorides* has been studied by Favorskii and Favorskaya.[5] These investigators did not report II among the products which were said to be dimethylethynylcarbinyl chloride (IV), 1-chloro-3-methyl-1,2-butadiene (V), 1-chloro-3-methyl-1,3-butadiene (VI) and a dichloride, $C_6H_8Cl_2$, of unknown structure.

Since we have been engaged for some time in a

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[1] Paper LIV on substituted acetylenes; previous paper, THIS JOURNAL, **71**, 2813 (1949).

[2] Hurd, U. S. Patent 2,274,611 (Feb. 24, 1942).

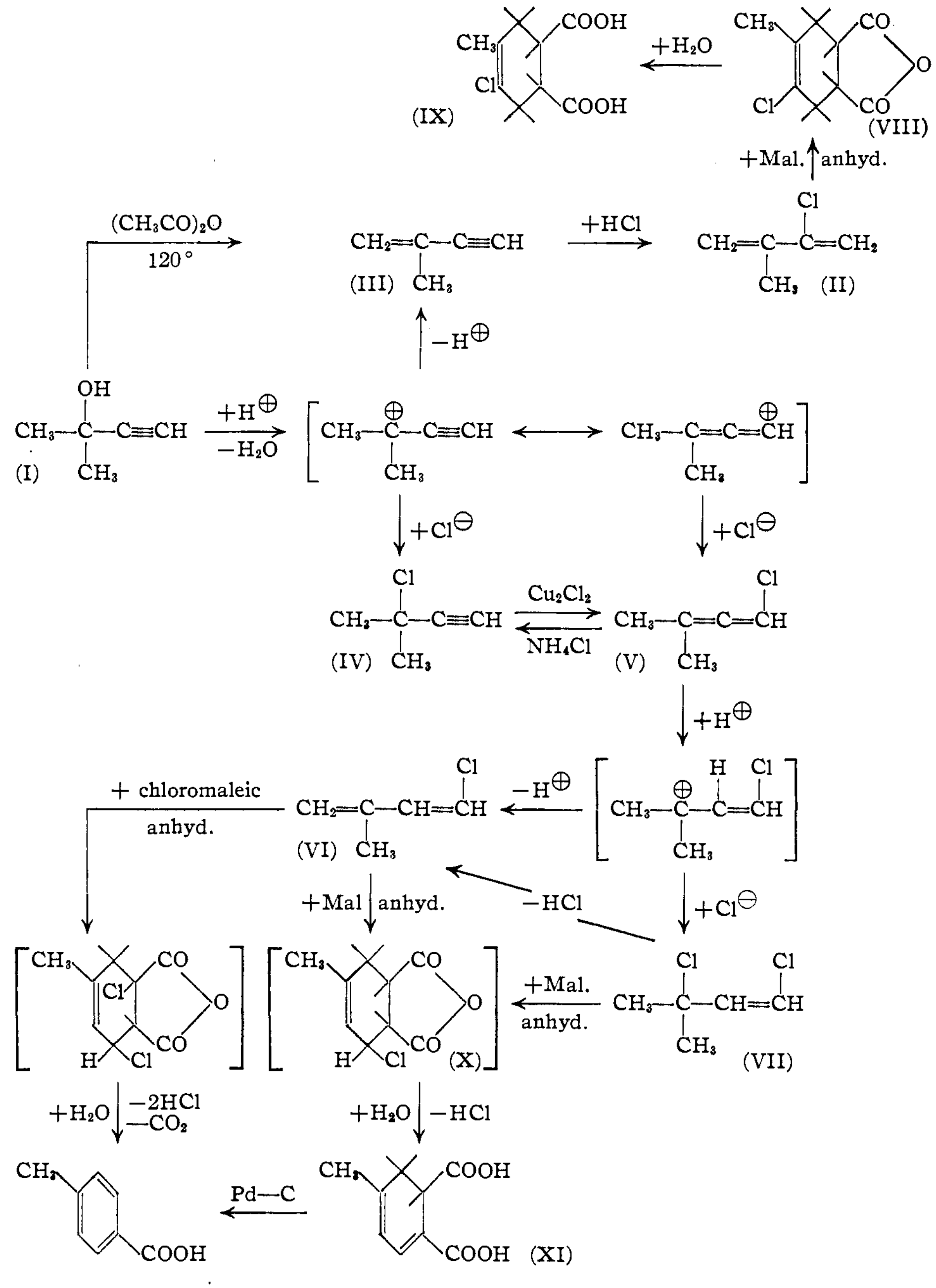
[3] Hurd and McPhee, THIS JOURNAL, **71**, 398 (1949).

[4] Carothers and Coffman, *ibid.*, **54**, 4071 (1932).

[5] Favorskii and Favorskaya, *Compt. rend.*, **200**, 839 (1935); Favorskaya, *J. Gen. Chem.* (*U. S. S. R.*), **9**, 386, 1237 (1939); Favorskaya and Zakharova, *ibid.*, **10**, 446 (1940).

study of the mechanisms of rearrangements in the acetylene series, it seemed imperative to examine this problem in view of the confusing literature.

CHART I



The Hurd–McPhee procedures have been repeated many times. Contrary to their statement,[4] we were consistently unable to separate a good yield of "light green-yellow oil" when the carbinol was shaken for ten to twenty minutes with three to four moles of concentrated hydrochloric acid. The mixture darkened rapidly and steam distillation was necessary to recover most of the product. In a typical experiment 84 g. of I yielded, after thirty minutes, only 9 g. of product by separation and an additional 45 g. by distillation. The separated oil did not react with maleic anhydride while the steam distilled portion did. The latter, however, gave the adduct (IX) in very small yield, indicating that the steam distilled oil contained, at best, only four or five per cent. of II. Careful fractional distillation of material recovered from maleic anhydride treatment disclosed that the chief product was IV contaminated with III and VI as well as II. It is estimated that IV accounts for about half the product, the other half being II, III, VI and unidentified. The 36% yield of formaldehyde[4] by ozonolysis is thus understandable.

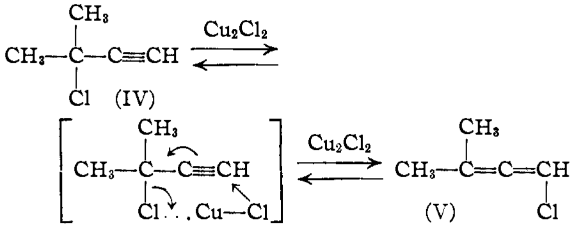
Since the maleic anhydride adduct of II was always recovered as the diacid (IX) rather than the anhydride (VIII), the latter was prepared independently from an authentic sample of II. The melting point of VIII proved to be 79–80°, rather than 124–126° as reported by Hurd and McPhee. Hydrolysis of VIII gave IX identical with that obtained from the carbinol reactions.

When the purified tertiary chloride (IV) was shaken for one hour with concentrated hydrochloric acid and steam distilled, IV was recovered in 90% yield with unchanged refractive index and gave only a trace of product with maleic anhydride. This would indicate that II originates in the carbinol reaction *via* III and not by a rearrangement or addition–elimination mechanism.

Seeking a procedure whereby steam distillation could be avoided, it was observed that reaction of the carbinol with five moles of hydrochloric acid and one mole of calcium chloride achieved this end. Good yields of oil separated directly at 20°. In this way the tertiary chloride (IV) was obtained in better than 50% yield and II and III were substantially absent. The chief by-product was the dichloride (VII) with good evidence for the formation of some VI also.

The presence of cuprous and ammonium chlorides had a notable effect on the course of the carbinol–hydrogen chloride reaction. An oily upper layer appeared within ten minutes and grew slowly during three to four hours. Though the mixture became very dark, the upper layer was discernible with the aid of a lamp and could be separated directly or by steam distillation. By either method the product consisted mostly of IV and V with evidence for the presence of VI and/or VIII.[6] The amount of VI was greater if the mixture was steam distilled; conversely, VII could be isolated if steam distillation was avoided. Both VI and VII reacted with maleic anhydride, yielding XI, no doubt *via* the unstable intermediate X. Furthermore, VI and VII reacted with chloromaleic anhydride to form *p*-toluic acid.

The effect of cuprous ammonium chloride appears due to its isomerizing action on IV. When pure IV was shaken with Cu_2Cl_2–NH_4Cl–HCl, V and VII were recovered with unchanged IV. The conversion of IV to V is an interesting 1,3-shift (Meyer–Schuster rearrangement[7]) and may be due to the intervention of a chelate-type intermediate.



The structures assigned[5] to IV and V appear well established. A copious white precipitate was obtained from IV with both alcoholic and ammoniacal silver nitrate solutions; V did not respond to these tests (turbidity only). Neither IV nor V undergo Diels–Alder reactions. Both are rapidly hydrolyzed by alkalies and it is noteworthy that V produces some I in this manner.[8] The infrared spectrum of V indicated that acetylenes and 1,3-dienes were substantially absent.[9] Like IV, V gives 3-methyl-1,2-butadiene by reduction with zinc–copper couple in alcohol.[10] Thus the only isolated product whose structure is not entirely certain is the dichloride (VII). Since it reacts with maleic anhydride in boiling benzene with evolution of hydrogen chloride and formation of XI and with chloromaleic anhydride in a similar manner to produce *p*-toluic acid, the assigned structure appears justified.

The various transformations of dimethylethynylcarbinol are diagrammed in Chart I and the properties of C_5H_7Cl isomers are given in Table I.

TABLE I

Compound	B. p., °C. 175 mm.	B. p., °C. Atm.	$n^{25}D$	d^{25}
$(CH_3)_2C(Cl)—C≡CH$	35	75–76	1.4155	0.9035
$(CH_3)_2C=C=CHCl$	62	100–103[a]	1.4738	.9435
$CH_2=C(CH_3)—C(Cl)=CH_2$	50–52	93[b]	1.4640	.9523

[a] With decomposition. [b] With polymerization.

Experimental

Dimethylethynylcarbinol (I) was prepared by the reaction of sodium acetylide with acetone.[11]

Isopropenylacetylene (III) was made from the carbinol by dehydration with acetic anhydride.[12]

2-Chloro-3-methyl-1,3-butadiene (II) was prepared from isopropenylacetylene (III) essentially as directed by Carothers and Coffman.[4] Thirty grams of III yielded 35 g. of steam distilled product. Fractional distillation through a helix-packed column gave a middle fraction, 10 g., b. p. 50–52° at 175 mm., $n^{25}D$ 1.4640, d^{25} 0.9523.

4-Methyl-5-chloro-1,2,3,6-tetrahydrophthalic Anhydride (VIII) and Acid (IX).—A 4.8-g. sample of 2-chloro-3-methyl-1,3-butadiene (II) was warmed with 2.3 g. of maleic anhydride at 50–60° for forty-five minutes. The mixture crystallized readily upon cooling. A portion of the product (VIII) was crystallized twice from a mixture of benzene and petroleum ether. The melting point was 79–80°, not altered by further crystallization.

Anal.[13] Calcd. for $C_9H_9ClO_3$: C, 53.88; H, 4.52; Cl, 17.65. Found: C, 53.75; H, 4.54; Cl, 17.74.

The remainder of the crude anhydride (VIII) was boiled with distilled water for conversion to the acid (IX). Recrystallization from water gave pure IX, m. p. 202–205°, uncor., dec. (sealed cap.). Neutral. equiv. calcd. for $C_9H_{11}ClO_4$, 109.3; found, 109.2.

Reaction of Dimethylethynylcarbinol with Hydrochloric Acid.—One mole of the carbinol (84 g.) was shaken with 3.5 moles (305 ml.) of C. P. concentrated hydrochloric acid containing 0.5 g. of hydroquinone while the temperature was controlled at 20°.[3] After thirty minutes the dark mixture was diluted with 100 ml. of water and steam distilled. The product was dried overnight (refrigerator) with 3 g. of anhydrous potassium carbonate; yield, 52.5 g. The entire sample was heated at 55° with 5 g. of maleic anhydride for thirty minutes, 20 ml. of water added and the mixture again steam distilled. The aqueous residue was filtered hot and allowed to cool, yielding 2.60 g. of crude 4-methyl-5-chloro-1,2,3,6-tetrahydrophthalic acid (IX). After several crystallizations from hot water containing "Nuchar-W," the m. p. was 202–205°, uncor., not depressed by the authentic sample.

Anal. Calcd. for $C_9H_{11}ClO_4$: C, 49.44; H, 5.07; Cl, 16.22. Found: C, 50.10; H, 5.18; Cl, 15.73.

The recovered oil was dried again (K_2CO_3); yield, 41 g., $n^{25}D$ 1.4278, and fractionally distilled at 175 mm. through a helix-packed column, packed section 0.9 × 70 cm.

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[6] Compound VI could not be isolated since it codistilled with V. Treatment of the mixture with maleic anhydride permitted distillation of V in pure condition and extraction of XI from the residue.

[7] Meyer and Schuster, *Ber.*, **55B**, 819 (1922); Hennion, Davis and Maloney, THIS JOURNAL, **71**, 2813 (1949).

[8] We hope to report later our studies on the hydrolysis of these compounds.

[9] Grateful acknowledgment is made to Drs. A. S. Carter and Madison Hunt, Jackson Laboratory, du Pont Company, for the infrared examination.

[10] Ginzburg, *J. Gen. Chem.* (*U. S. S. R.*), **10**, 513 (1940); *C. A.*, **34**, 7843 (1940); Hennion and Sheehan, THIS JOURNAL, **71**, 1964 (1949).

[11] Hennion and Froning, *ibid.*, **62**, 654 (1940).

[12] Thompson, Milas and Rovno, *ibid.*, **63**, 754 (1941).

[13] Analyses by Micro-Tech Labs, Skokie, Illinois.

Six fractions were collected: (1) 4.78 g., b. p. 23–33°, $n^{25}_{\rm D}$ 1.4123; (2) 7.26 g., b. p. 33–35°, $n^{25}_{\rm D}$ 1.4130; (3) 8.92 g., b. p. 35–36°, $n^{25}_{\rm D}$ 1.4154; (4) 3.18 g., b. p. 36–50°, $n^{25}_{\rm D}$ 1.4371; (5) 3.70 g., b. p. 50–55°, $n^{25}_{\rm D}$ 1.4572; (6) 2.35 g., b. p. 55–57°, $n^{25}_{\rm D}$ 1.4595. The cold trap contained 5.26 g., $n^{25}_{\rm D}$ 1.4102, and the still residue weighed 2.33 g.

Fractions (5) and (6) began to darken immediately. They were combined and treated with 3 g. of maleic anhydride as described above. The yield of crude adduct was 1.30 g. Two recrystallizations from dilute alcohol containing "Nuchar-W" gave a chlorine-free product, m. p. 205–210°, uncor., neutral. equiv., 91.5, identified as 4-methyl-2,3-dihydrophthalic acid (*vide sub*).

Fractions (1–4) and cold trap condensate were combined and refractionated through a 0.5 × 100 cm. column at atmospheric pressure. There was 2.8 g. volatile forerun, isopropenylacetylene (III), and 17.1 g. of dimethylethynylcarbinyl chloride (IV), b. p. 74–76°.

Preparation of Dimethylethynylcarbinyl Chloride (IV).—One mole of carbinol (I) was shaken at 20°, forty-five minutes, with one mole (111 g.) of calcium chloride, 1 g. of hydroquinone and five moles (420 ml.) of hydrochloric acid. The product was separated directly and dried over anhydrous potassium carbonate; yield, 96 g. Fractional distillation at 175 mm. through the 0.9 × 70 cm. helix-packed column gave 12 fractions: (1–7) 57.5 g., b. p. 28–38°, $n^{25}_{\rm D}$ 1.4148–1.4168; (8) 1.86 g., b. p. 38–50°, $n^{25}_{\rm D}$ 1.4488; (9) 2.97 g., b. p. 50–53°, $n^{25}_{\rm D}$ 1.4610; (10) 4.18 g., b. p. 53° (175 mm.)–46° (30 mm.), $n^{25}_{\rm D}$ 1.4653; (11–12) 19.0 g., b. p. 46–47° (30 mm.), $n^{25}_{\rm D}$ 1.4608–1.4610; cold trap, 2.29 g., $n^{25}_{\rm D}$ 1.4182; residue, 4 g.

Refractionation of cold trap condensate combined with fractions (1–7) gave 51.3 g. (50% yield) of tertiary chloride (IV), b. p. 72.6–75.8° (atm. press.), $n^{25}_{\rm D}$ 1.4152–1.4160.

Treatment of fraction (9) with 2.0 g. of maleic anhydride yielded 1.10 g. of impure XI. After recrystallization the m. p. was 204–207°, uncor.; neutral. equiv., 89.7; chlorine test negative; mixed m. p. without depression.

Redistillation of fractions (11–12) gave 12.0 g. (8.6% yield) of dichloride (VII), b. p. 49–50° (30 mm.), $n^{25}_{\rm D}$ 1.4611, d^{25} 1.0885. An earlier sample, $n^{25}_{\rm D}$ 1.4611, d^{25} 1.0761, was analyzed.

Anal. Calcd. of $C_5H_8Cl_2$: Cl, 51.01. Found: Cl, 46.8.

Reaction of Dimethylethynylcarbinol with Hydrochloric Acid in the Presence of Cuprous and Ammonium Chlorides.—One mole of carbinol (I) was shaken with 2 moles (170 ml.) of concentrated hydrochloric acid containing 10 g. of freshly prepared cuprous chloride, 5 g. of ammonium chloride and 0.3 g. of copper–bronze powder. After four hours the product was separated (upper layer), washed with 50 ml. of 1:1 hydrochloric acid, then with 50 ml. of water and dried with potassium carbonate; yield, 81 g. Fractional distillation under gradually diminishing pressure (to avoid decomposition) gave 9 fractions: (1–4) 32 g., b. p. 32° (175 mm.)–40° (125 mm.), $n^{25}_{\rm D}$ 1.4160–1.4265; (5) 7.25 g., b. p. 40° (125 mm.)–45° (100 mm.), $n^{25}_{\rm D}$ 1.4470; (6–8) 25.6 g., b. p. 45° (100 mm.)–47° (35 mm.), $n^{25}_{\rm D}$ 1.4672–1.4721; (9) 4.4 g., b. p. 47° (35 mm.)–46° (25 mm.), $n^{25}_{\rm D}$ 1.4622. Refractionation of fractions (1–4) gave 23 g. of dimethylethynylcarbinyl chloride (IV), b. p. 74–75° (atm. press.), $n^{25}_{\rm D}$ 1.4156. Similarly, fractions (6–8) distilled from 3 g. of maleic anhydride yielded 16.1 g. of 1-chloro-3-methyl-1,2-butadiene (V), b. p. 60–63° (175 mm.), $n^{25}_{\rm D}$ 1.4740.

Fraction (5) was refluxed for one hour with 3 ml. of chloromaleic anhydride and 3 ml. of benzene. Removal of the benzene and treatment of the residue with boiling water yielded 0.21 g. of crude *p*-toluic acid. After recrystallization from water the m. p. was 175–177°, not depressed by an authentic sample.

Fraction (9) was redistilled and gave 3.76 g. of impure dichloride (VII), b. p. 45–47° (25 mm.), $n^{25}_{\rm D}$ 1.4620, d^{25} 1.0265. Treatment of 2 ml. of this material with 2.0 g. of maleic anhydride yielded finally 0.46 g. of 4-methyl-2,3-dihydrophthalic acid (XI).

In another experiment one mole of I was treated as described above, except that the mixture was steam distilled. The dried product weighed 80 g. This was split into 8 fractions by distillation as described above. Those boiling between 32 and 50° at 175 mm. proved to contain mostly the tertiary chloride (IV); 15.8 g. recovered, $n^{25}_{\rm D}$ 1.4130–1.4182. Fractions boiling from 55 to 65° at 175 mm. (35.3 g.) were combined and refractionated from 5 g. of maleic anhydride, yielding 20.5 g. of 1-chloro-3-methyl-1,2-butadiene (V), b. p. 60–63° at 175 mm., $n^{25}_{\rm D}$ 1.4701–1.4739. The distillation residue was extracted three times with boiling water thus yielding 2.54 g. of crude 4-methyl-2,3-dihydrophthalic acid (XI). After several recrystallizations the m. p. was 202–205°, uncor. Mixed with a sample of IX, also melting at 202–205°, the m. p. was 188–193°.

Isomerization of Dimethylethynylcarbinyl Chloride.—Fifty-one grams of dimethylethynylcarbinyl chloride (IV), $n^{25}_{\rm D}$ 1.4152, and 0.3 g. of copper bronze powder were added to a solution of 10 g. cuprous chloride, 8 g. ammonium chloride and 5 ml. of concentrated hydrochloric acid in 25 ml. of water. The mixture was shaken mechanically for two hours with occasional cooling. The oil was then separated and dried (K_2CO_3); yield 32 g. Fractional distillation through the 0.9 × 70 cm. helix-packed column at 175 mm. gave 4.1 g. of recovered (IV), $n^{25}_{\rm D}$ 1.4150–1.4182, and 17 g. of 1-chloro-3-methyl-1,2-butadiene (V), b. p. 61–62° (175 mm.), $n^{25}_{\rm D}$ 1.4732–1.4742. The intermediate fractions weighed 6.2 g., $n^{25}_{\rm D}$ 1.4418–1.4561, and the still residue amounted to 3.2 g.

4-Methyl-2,3-dihydrophthalic acid (XI) was previously described[5] and reported to melt at 210–211°. In agreement with the assigned structure, our samples contained no chlorine; neutral. equivalent, calcd. for $C_9H_{10}O_4$: 91.1; found, three samples, 89.7, 91.5, 91.8. Heating with resorcinol and sulfuric acid in the usual way gave a pronounced fluorescein color test. The ultraviolet absorption spectrum of the acid indicated considerable conjugate unsaturation: $\lambda_{\max}$ 296 mμ and $\epsilon = 8750$ ($c = 3.32 \times 10^{-5}$ mole/liter in alcohol). A sample weighing 0.75 g. was boiled for one day with 10 ml. of water, 10 ml. of alcohol and 30 mg. of 10% palladium-carbon. *p*-Toluic acid crystallized from the hot solution after filtration of the catalyst; m. p. 174–176.5°, not depressed by an authentic sample.

Summary

1. The reaction of dimethylethynylcarbinol with three to four moles of concentrated hydrochloric acid at 20° consistently gave poor yields of the corresponding tertiary chloride and smaller amounts of several other products. One of these was 2-chloro-3-methyl-1,3-butadiene. Previous reports that the latter is formed to a large extent could not be confirmed.

2. When the reaction was accomplished with five moles of hydrochloric acid and one mole of calcium chloride the yield of tertiary chloride was notably improved, the chief by-product being a dichloride.

3. When the reaction was carried out in the presence of cuprous and ammonium chlorides the tertiary chloride was appreciably isomerized to 1-chloro-3-methyl-1,2-butadiene, which was readily isolated, and to 1-chloro-3-methyl-1,3-butadiene identified by its adduct with maleic anhydride.

4. Reasonable mechanisms are offered for the various reactions.

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