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## Reaction of Copper(1) Acetylides with Halogeno-acetylenes

## By R. F. Curtis\* and J. A. Taylor, Department of Chemistry, University College of Swansea, Singleton Park, Swansea, Glamorgan

The reaction between the copper(I) derivatives of propyne, ethynylbenzene, 5-ethynyl-2,2'-bithienyl, 3-(tetrahydropyranyloxy)prop-1-yne, 3,3-diethoxyprop-1-yne, and but-1-yn-3-ol with 3-bromoprop-2-yn-1-ol in pyridine at 35—50° gave a simple synthesis of the corresponding diynols hexa-2,4-diyn-1-ol (III), 5-phenylpenta-2,4-diyn-1-ol (V), 6-(tetrahydropyranyloxy)hexa-2,4-diyn-1-ol, and 6,6-diethoxyhexa-2,4-diyn-1-ol, hepta-2,4-diyn-1,6-diol, and 5-(5-hyoroxypenta-1,3-diynyl)-2,2'-bithienyl, respectively. Oxidation of (III) and (V) with nickel peroxide in benzene followed by deformylation led to the terminal acetylenes penta-1,3-diyne (XIV) and 4-phenylbuta-1,3-diyne, and subsequent coupling of the corresponding copper(I) salt of, *e.g.*, (XIV) with the 3-bromopropynol produced a new homologation sequence for polyacetylenes exemplified by the synthesis of octa-2,4,6-triyn-1-ol.

THE Cadiot-Chodkiewicz coupling reaction <sup>1</sup> for the synthesis of disubstituted acetylenes (R<sup>1</sup>C:CR<sup>2</sup>) from terminal acetylenes (R<sup>1</sup>C:CH) and 1-bromoacetylenes (R<sup>2</sup>·C:CBr) under mild conditions is well known. The coupling reaction between copper(I) acetylides (R<sup>1</sup>C:C·Cu) and various aryl <sup>2</sup> and heterocyclic <sup>3</sup> iodo derivatives (R<sup>2</sup>I) in pyridine solution to give substituted acetylenes (R<sup>1</sup>C:CR<sup>2</sup>) is also useful.<sup>4,5</sup>

It appeared that these two reactions could be combined to produce coupling under conditions in which an unstable or labile acetylene could be easily handled as an insoluble copper(I) derivative; it had already been suggested <sup>1,6</sup> that a copper(I) acetylide is an intermediate in the Chodkiewicz coupling reaction. We have briefly reported <sup>7</sup> this approach and we now give details and describe an extension.

When the copper(I) derivatives of propyne (I), ethynylbenzene (IV), 5-ethynyl-2,2'-bithienyl (VI), and but-1-yn-3-ol (VIII) were treated with 3-bromoprop-2-yn-1-ol (II) at 35—50° in oxygen-free pyridine (Scheme 1) a vigorous exothermic reaction gave hexa-2,4-diyn-1-ol

 $RC:CH + Br \cdot C:C \cdot CH_2 \cdot OH \longrightarrow R \cdot [C:C]_2 \cdot CH_2 \cdot OH$ As Cu(1) derivative

(III), 5-phenylpenta-2,4-diyn-1-ol (V), 5-(5-hydroxypenta-1,3-diynyl)-2,2'-bithienyl (VII), and hepta-2,4-diyn-1,6-diol (IX), respectively, in good yields. Extensions of this included the reaction of the copper(I) salt of 3-(tetrahydropyranyloxy)prop-1-yne (X) with the same bromo-derivative to give the symmetrical diyndiol

<sup>1</sup> W. Chodkiewicz, J. S. Alhuwalia, P. Cadiot, and A. Willemart, *Compt. rend.*, 1957, **245**, 322.

<sup>2</sup> R. D. Stephens and C. É. Castro, J. Org. Chem., 1963, 28, 3313.

<sup>3</sup> R. E. Atkinson, R. F. Curtis, and G. T. Phillips, *Chem. and Ind.*, 1964, 2101.

derivative (XI), protected on only one of two identical functional groups, and the reaction of **3,3**-diethoxyprop-1-ynylcopper(I) (XII) to give the diethyl acetal (XIII) of the corresponding hydroxy-diynaldehyde.

We have recently described <sup>5</sup> the preparation of terminal aryl and heterocyclic acetylenes through deformylation of acetylenic aldehydes and this method proved equally applicable in the aliphatic series to give a new route to di- and tri-acetylenes. For example, oxidation of the diynol (III) with nickel peroxide in benzene at 50° gave the corresponding aldehyde which was directly treated with methanolic 2N-sodium hydroxide at 50° to give penta-1,3-diyne (XIV) (Scheme 2). In the same way the phenyldiynol (V) gave the diacetylene (XV).

$$\begin{array}{ccc} \operatorname{R} \cdot [\operatorname{C}:\operatorname{C}]_{2} \cdot \operatorname{CH}_{2} \cdot \operatorname{OH} & \xrightarrow{\operatorname{NiO}_{2}} & (\operatorname{R} \cdot [\operatorname{C}:\operatorname{C}]_{2} \cdot \operatorname{CHO}) & \xrightarrow{\operatorname{NaOH}} & \operatorname{RC}:\operatorname{C} - \operatorname{C}:\operatorname{CH} \\ (\operatorname{III}; & \operatorname{R} = \operatorname{Me}) & (\operatorname{XVII}; & \operatorname{R} = \operatorname{Me}) & (\operatorname{XIV}; & \operatorname{R} = \operatorname{Me}) \\ (\operatorname{V}; & \operatorname{R} = \operatorname{Ph}) & (\operatorname{XVII}; & \operatorname{R} = \operatorname{Me}) & (\operatorname{XV}; & \operatorname{R} = \operatorname{Ph}) \\ & \operatorname{Scheme} 2 \end{array}$$

Such acetylenes can most easily be isolated as their characteristic and highly insoluble copper(I) derivatives; these can then be used directly for moving up the homologous series with further 3-bromoprop-2-yn-1-ol by the sequence already described.

The bromoacetylene (II) is thus used for substitution of terminal acetylenes by one further acetylene unit in a manner similar to that described by Bohlmann<sup>8</sup> using **3**-bromopropiolic acid. The sequence is exemplified by the conversion of hex-2,4-diyn-1-ol (III) prepared as in Scheme I, *via* the diynaldehyde (XVII) which was not isolated (Scheme 2) to penta-1,3-diyne (XIV) and thence through the copper(I) derivative of (XIV) *via* Scheme 1 again to octa-2,4,6-triynol (XVI).

The protection of terminal acetylenes by trialkylsilyl groups and the use of  $\alpha$ -bromo- $\omega$ -trialkylsilyl acetylenes for the stepwise construction of terminal phenylpoly-

<sup>4</sup> A. M. Sladkov and L. Yu. Ukhin, Uspekhi Khim., 1968, 37, 1750.
<sup>5</sup> R. E. Atkinson, R. F. Curtis, D. M. Jones, and J. A. Taylor,

 <sup>5</sup> R. E. Atkinson, R. F. Curtis, D. M. Jones, and J. A. Taylor, J. Chem. Soc. (C), 1969, 2173.
 <sup>6</sup> G. Eglinton and W. McCrae, Adv. Org. Chem., 1963, 4, 254.

<sup>6</sup> G. Eglinton and W. McCrae, Adv. Org. Chem., 1963, 4, 254.
 <sup>7</sup> R. F. Curtis and J. A. Taylor, Tetrahedron Letters, 1968, 2919.

<sup>8</sup> F. Bohlmann, W. Sucrow, and I. Queck, *Chem. Ber.*, 1964, 97, 2586.

acetylenes by Cadiot-Chodkiewicz coupling has also been described.<sup>9</sup> Difficulties were observed in the phenyl series when the substitution of the bromoacetylene and the terminal acetylene were reversed and also with monotrimethylsilyl derivatives rather than phenylacetylenes. These difficulties may be connected with the instability of some trialkylsilyl derivatives towards copper(I) ions.<sup>6</sup> These problems do not arise in the present method which also overcomes some of the other difficulties which may arise in the conventional Cadiot-Chodkiewicz coupling, e.g., conversion of the bromocomponent into an amidine, low solubility of the ethynyl component, or precipitation of an insoluble copper(I) acetylide.10

Pyridine is an excellent solvent for copper(II) acetylides; this may be due to depolymerisation or co-ordination with the solvent.<sup>11</sup> In addition, self-coupling of the bromoacetylene under the influence of copper(II) bromide, which is known to be an important side reaction, is probably prevented by the rapid reaction and by complex formation between the copper(I) bromide and the solvent in which it is highly soluble.<sup>12</sup> Copper(I) chloride is known to form stable complexes with pyridine.13

However, yields are not necessarily higher in all cases; the method is complementary to the more usual process and has special advantages for the homologation sequence described.

## EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus, u.v. spectra were measured on a Unicam SP 800 spectrophotometer in methanol, and i.r. spectra were determined for potassium bromide discs or films with Perkin-Elmer spectrophotometers (models 257 and 457). <sup>1</sup>H N.m.r. spectra were determined at 60 MHz for deuteriochloroform solution with a Perkin-Elmer R10 spectrometer, or at 100 MHz with a Varian HA 100 spectrometer. System I of our earlier publication 14 was used for t.l.c. and plates were developed with aqueous potassium permanganate. Silica gel was 200-300 mesh (Koch-Light), and alumina was Spence H, acid-washed to neutrality and activated at 100° for 10 h.

WARNING: Copper(I) acetylides can explode and one detonation occurred during this investigation. Copper(1) derivatives of acetylenic hydrocarbons are much less stable than those of acetylenic alcohols but in all cases the hazard can be reduced by keeping and using the acetylides in a slightly damp state.

Hexa-2,4-diyn-1-ol (III).--The following procedure is typical of all later couplings. The copper(I) derivative (20.4 g) of propyne (I), in pyridine (250 ml) was thoroughly purged with nitrogen and then 3-bromoprop-2-yn-1-ol<sup>15</sup> (27.0 g) was added dropwise with stirring under nitrogen so as to maintain the temperature at  $35-40^{\circ}$ . The dark

9 R. Eastmond and D. R. M. Walton, Chem. Comm., 1968,

204. <sup>10</sup> G. Eglinton and W. McCrae, Adv. Org. Chem., 1963, 4, 256, 257.

<sup>11</sup> G. E. Coates, M. L. H. Green, and K. Wade, 'Organo-metallic Compounds,' Methuen, London, 3rd edn., vol. 2, p. 274.
 <sup>12</sup> A. Naumann, Ber., 1904, **37**, 4609.

13 W. Lang, Ber., 1888, 21, 1578.

solution was poured into 4N-hydrochloric acid (1 l) and extracted with ether (4  $\times$  300 ml.), which was washed with 4N-hydrochloric acid, saturated sodium hydrogen carbonate, and water and then dried (MgSO<sub>4</sub>). Evaporation gave a dark oil which was passed through silica gel (1 kg); elution with chloroform gave hexa-2,4-diyn-1-ol (III) (11.1 g) as very pale yellow needles (from pentane), m.p. 47° (lit.,<sup>16</sup> 47°) (Found: C, 76.6; H, 6.5. Calc. for C<sub>6</sub>H<sub>6</sub>O: C, 76.6; H,  $6\cdot4\%$ ;  $\lambda_{max}$  230, 241, and 255 nm (log  $\varepsilon$  2.75, 2.73, and 2.58);  $\nu_{max}$  3250, 1030 (OH), and 2260 cm<sup>-1</sup> (C:C);  $\tau$  5.68 (2H, s, CH<sub>2</sub>), 7.35 (1H, s, OH), and 8.03 (3H, s, -Me).

5-Phenylpenta-2,4-diyn-1-ol (V).—The copper(I) derivative (24.6 g) of ethynylbenzene in pyridine (200 ml), with the bromopropynol (II) (20.3 g) in pyridine (50 ml) gave, on work-up as before, the diynol (V) (15.5 g) as pale yellow needles (from pentane), m.p. 38-39° (lit.,<sup>17</sup> 39-40°) [Found: M (mass spectrometry) 156.0574  $\pm$  0.0004. Calc. for  $C_{11}H_8O$ : 156.0575];  $\lambda_{max}$  244, 257, 271, and 288 nm (log  $\varepsilon$  4.10, 4.44, 4.59, and 4.52);  $\nu_{max}$  3300, 1020 (OH), 2260 (CiC), 760, and 690 cm<sup>-1</sup> (monosubstituted phenyl); τ (CS<sub>2</sub>) 2·80 (5H, m, phenyl), 5·72 (2H, s, CH<sub>2</sub>), 6·40 (1H, s, OH)

5-(5-Hydroxypenta-1,3-diynyl)-2,2'-bithienyl (VII).—The copper(1) derivative (369 mg) of 5-ethynyl-2,2'-bithienyl<sup>5</sup> in pyridine (10 ml) with the bromopropynol (II) (198 mg) gave, after chromatography over silica gel and elution with pentane-ether (10:1), the 2,2'-bithienyl derivative (VII) (198 mg) as pale yellow needles (from ether), m.p. 92-93° M (mass spectrometry) 244.0007  $\pm$  0.0012. [Found:  $C_{13}H_8OS_2$  requires 244.0017];  $\lambda_{max}$  228, 258, and 354 nm (log  $\epsilon$  4.17, 4.00, and 4.66);  $\nu_{max}$  3260, 1015 (OH), 2220 (C:C), 840, 685 (2-thienyl), and 795 cm<sup>-1</sup> (thiophen-2,5-diyl); τ 2·75-3·05 (5H, m, 2,2'-bithienyl protons), 5·60 (2H, s, CH<sub>2</sub>), and 8.20 (1H, s, OH).

Hepta-2,4-diyn-1,6-diol (IX).-The copper(I) derivative (37.5 g) of but-1-yn-3-ol (VIII) in pyridine (200 ml) was treated with the bromopropynol (II) (38.0 g). Work-up by chromatography over silica gel and elution first with chloroform and then with chloroform-methanol (95:5) gave the dividiol (IX) (9.7 g.) as plates from ether-pentane, m.p. 50-51° (lit., 18 50-53°) (Found: C, 68.0; H, 6.3. Calc. for  $C_7H_8O_2$ : C, 67.7; H, 6.5%);  $\lambda_{max}$  221, 232, 244, and 257 nm (log  $\varepsilon$  2.45, 2.58, 2.60, and 2.39);  $\nu_{max}$  3320, 1100, 1015 (CH-OH and CH<sub>2</sub>·OH), and 2170 cm<sup>-1</sup> (CC);  $\tau$  5.44 (1H, q, CH•OH), 5·69 (2H, s, uH<sub>2</sub>•OH), 7·94—8·25br (2H, s,  $2 \times OH$ ), and 8.54 (3H, d, J 8 Hz, Me)).

6-(Tetrahydropyranyloxy)hexa-2,4-diyn-1-ol (XI).—The copper(I) derivative (4.04 g) of 3-(tetrahydropyranyloxy)prop-1-yne (X) in pyridine (40 ml) was treated with the bromopropynol (II) (2.70 g) and worked up without the acid-wash. After removal of ether residual pyridine was removed under reduced pressure and the residue was purified by chromatography over silica gel. Elution with pentane-ether (5:1) gave the divided derivative (XI) (1.40)g) as an oil, b.p. 122—124° at 0.05 mmHg,  $n_{\rm D}^{26}$  1.5230 [Found: M (mass spectrometry)  $194.0943 \pm 0.0009$ .  $C_{11}H_{14}O_3$  requires 194.09429];  $\lambda_{max}$ , 222, 232, 244, and 258

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   <sup>18</sup> E. R. H. Jones, J. M. Thompson, and M. C. Whiting, J. Chem. Soc., 1957, 2012.

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nm (log  $\varepsilon$  2·70, 2·89, 2·86, and 2·74);  $v_{max}$  3300, 1030 (OH), and 2120 cm<sup>-1</sup> (C:C);  $\tau$  5·24 (1H, s, O·CH·O), 5·73 (4H, s, CH<sub>2</sub>·[C:C]<sub>2</sub>·CH<sub>2</sub>), 6·35 (2H, m, O·CH<sub>2</sub>), 7·0 (1H, s, OH), and 8·38br [6H, s, CH<sub>2</sub> (ring)].

6,6-Diethoxyhexa-2,4-diyn-1-ol (XIII).—The copper(1) derivative (1.74 g) of 3,3-diethoxyprop-1-yne (XII) in pyridine (30 ml) was treated with the bromo-derivative (II) (1.35 g), worked up as in the foregoing case and purified by chromatography over basic alumina (100 g). Elution with n-pentane–ether (10:1) gave the diynol (XIII) (1.60 g) as a colourless oil, b.p. 100° (block temp.) at 0.03 mmHg,  $n_{\rm D}^{27}$  1.4925 (Found: C, 65.3; H, 7.8. C<sub>10</sub>H<sub>14</sub>O<sub>3</sub> requires C, 65.9; H, 7.7%);  $\nu_{\rm max}$  3400, 1020 (OH), and 2150 cm<sup>-1</sup> (CiC);  $\tau$  4.61 [1H, s, CH(OEt)<sub>2</sub>], 5.6 (1H, s, CH<sub>2</sub>·OH), 6.37 (4H, complex m of ABX<sub>3</sub> system, CH<sub>2</sub>Me), 7.40 (1H, s, OH), and 8.74 (6H, t, Me).

Penta-1,3-diyne (XIV).—The diynol (III)  $(1\cdot 2 \text{ g})$  in benzene (30 ml) was stirred with nickel peroxide (10 g) at 50° for 30 min with control by t.l.c. Nickel peroxide was removed and the filtrate was quickly evaporated under reduced pressure to give an unstable oil which was dissolved in methanol (25 ml). 2N-Sodium hydroxide (40 ml) was added and the mixture was stirred at 50° for 1 h. Workup gave an ether extract which after evaporation was dissolved in methanol (30 ml) and added to a large excess of cuprammonium chloride-sodium acetate solution <sup>14</sup> at pH 6 to give penta-1,3-diynylcopper(I) (850 mg). An aliquot portion of the methanolic solution gave a mercury derivative as colourless microcrystals (from ethanol), m.p. 130° (decomp.) [lit.,<sup>19</sup> 130° (decomp.)] (Found: C, 36.5; H, 1.9. Calc. for  $C_{10}H_{g}Hg$ : C, 36.8; H, 1.9%);  $\nu_{max}$  2230 and 2110 cm<sup>-1</sup> (C:C).

4-Phenylbuta-1,3-diyne (XV).—In the same way the diynol (V) (3·12 g) in benzene (50 ml) with nickel peroxide (10 g.) gave the mercury derivative of the diyne (XV) (2·0 g) as cream needles, m.p. 196° (lit.,<sup>19</sup> 203-205°) (Found: C, 52·1; H, 2·3. Calc. for  $C_{20}H_{10}Hg$ : C, 52·6; H, 2·1%);  $\nu_{max}$ . 2220, 2100 (C:C), 760, and 695 cm<sup>-1</sup> (phenyl).

Octa-2,4,6-triyn-1-ol (XVI).—The copper(I) derivative (2.52 g) of penta-1,3-diyne (XIV) (see before) in pyridine (50 ml) with the bromopropynol (II) (2.7 g) gave the triynol (XVI) (1.56 g) as pale cream needles (from pentane), m.p. 93° (lit., <sup>16</sup> 93°) [Found: *M* (mass spectrometry), 118.0416  $\pm$  0.0006. Calc. for C<sub>8</sub>H<sub>6</sub>O: 118.0419];  $\lambda_{max}$  242, 254, 269, 275, 292, and 312 nm (log  $\epsilon$  2.52, 2.54, 2.48, 2.48, 2.50, and 2.37);  $v_{max}$  3300, 1020 (OH), and 2240 cm<sup>-1</sup> (CiC);  $\tau$  5.69 (2H, s, CH<sub>2</sub>), 6.25 (1H, s, OH), and 8.04 (3H, s, Me).

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