An Improved Method for Preparing and Utilizing Alkali Metal Acetylenides

A. FISCHEL, J. M. COISNE**, H. P. FIGEYS*

Department of Organic Chemistry, Faculty of Sciences, Free University of Brussels, 50 Av. F. D. Roosevelt, B-1050 Brussels, Belgium

One of the fundamental synthetic methods in acetylenic chemistry is the preparation of alkali metal acetylenides (I). These can be made by two different procedures: either the direct reaction of acetylene with the metal itself (Method A), or an indirect way (Method B) in which an alkali derivative reacts with acetylene.

\[
\begin{align*}
M + HC \equiv CH & \rightarrow HC \equiv CM \quad \text{Method A} \\
\text{MNH}_2 \quad \text{or} \quad R^1M & \rightarrow HC \equiv CH \quad \text{Method B}
\end{align*}
\]

This second method (Method B) is by far the most commonly used in the laboratory and is recommended by the classical reference books on acetylenic chemistry.\(^5\) Refluxing ammonia appears to be the solvent of choice, sodium or lithium amide being the metalling agent.\(^6\) The preparation of this amide, even catalyzed, appears however to be rather tricky and slow.\(^7\) Furthermore, the endpoint of the exchange reaction between the amide and the acetylene is often indefinite (black-grey to black suspension) and is easily missed. As a consequence, results obtained by the indirect method are often hardly reproducible; for instance, ethynylation of benzaldehyde with sodium acetylide prepared by the indirect way gave 21%\(^7\) or 57%\(^8\) of 1-phenyl-2-propyn-1-ol, by-products being mainly resins\(^7\) or benzylic alcohol and benzoic acid.\(^4\)

The direct method (Method A) consists in the dissolution of the alkali metal in liquid ammonia, followed by the passage of an acetylene stream.\(^11\) The ethynylation of benzaldehyde (2; \(R^2 = H, R^3 = C_6H_5\)) using this procedure has been reported to be unsuccessful; benzylic benzoate (12%)\(^7\) or 1-phenyl-2-propyn-1-ol (22%)\(^6\) and cinnamic acid (17%)\(^6\) were the only products isolated. Furthermore, the dissolution of the metal is even more lengthy and cumbersome than the formation of the alkali metal amide. If acetylene is bubbled continuously while adding the alkali metal,\(^11\) a 45% yield of 1-phenyl-2-propyn-1-ol (3; \(R^2 = H, R^3 = C_6H_5\)) is however obtained.\(^12\) When the acetylene stream is maintained during the whole reaction course, side-reactions such as glycol formation\(^13\) are avoided and benzaldehyde can be ethynylated in 82% yield.\(^14\) “Continuous bubbling” procedures, however, are not entirely satisfactory, necessitating a severe control of the rate of alkali metal addition and inlet-tubes being easily obstructed; this results in time-consuming, cumbersome, risky, and, sometimes, even outright dangerous operations.

We now report a way to overcome the drawbacks of the direct method. We found that bubbling acetylene in liquid ammonia at \(-78^\circ C\) easily doubles the initial volume of solvent. When, after stopping the stream of acetylene gas, the alkali metal is added in small portions, the rate of reaction is high and the resulting acetylide precipitates out of the reaction phase as a finely divided white powder. In these conditions, where acetylene is in excess both for the acetylide formation and for the ethynylation itself, the most sensitive and unstable carbonyl compounds can be ethynylated in high yields and no traces of the corresponding glycols were found. Moreover, pure sodium acetylide \((\text{I}; M = Na)\) can easily be prepared by evaporation of the solvents and stored in an inert atmosphere for a long time without any apparent loss of activity.

A test-run of our method consisting in the ethynylation of benzaldehyde gave the expected ynoil with 84% yield. Similarly, \(\alpha\)-iodobenzaldehyde could be ethynylated in 72% yield, while both the indirect amide\(^13\) and the direct procedure described in Ref.\(^11\) completely failed to give the desired product. In the terpene field, the ethynylation of (\(\pm\)-trans-1,4afl-trimethyl-calam-5-one which had been realized\(^16\) by the indirect amide procedure with 79% yield (only one epimer detected), could be achieved in 93% yield with the method we propose, two epimers being isolated\(^17\).

The ease of manipulation, the absence of technical and chemical problems (in our hands, special safety problems due to the great concentration of dissolved acetylene were never encountered), the short reaction time required, and the high yields with even otherwise unstable carbonyl compounds, are the most striking features of this new procedure.

\((\pm\)-trans-5a-Ethynyl-1,1,4afl-trimethyldecachlorophthalalene-5f-ol and (\(\pm\)-trans-5f-Ethynyl-1,1,4afl-trimethyldecachlorophthalalene-5a-ol: An apparatus consisting of a three-necked flask, a Dry ice condenser, and a pressure equalizing dropping funnel is assembled and fitted with a magnetic stirrer and a nitrogen bubbler. Liquid ammonia (200 mL) is distilled from lithium into the flask, well immersed in a Dry Ice/acetone bath. Pure acetylene (technical quality acetylene should be purified by bubbling successively through an alkaline solution of pyrogallol and through sulfuric acid) is let in and is immediately dissolved in the ammonia. No significant bubbling of acetylene should occur before the original volume has doubled (~2 h); this could happen when the cooling is insufficient. The acetylene stream is interrupted and metallic sodium (2.33 g, 110 mmol) is added as little clean fresh-cut bits.\(^18\) The reaction is fairly rapid. When all the sodium has disappeared, a solution of (\(\pm\)-1,1,4afl-trimethyl-1,2,3,4a,4a,7,8,8a-octahydrodichlorophthalalene-5Hf-one (1.0 g, 5.2 mmol)\(^19\) in anhydrous diethyl ether (50 mL) is added dropwise over 0.5 h and the stirring is continued for 4 h. Solid ammonium chloride (20 g) and diethyl ether (50 mL) are added and the cooling bath as well as the Dry Ice condenser removed. After evaporation of the ammonia and excess acetylene, water (80 mL) is added, the organic layer decanted, washed with 5% hydrochloric acid, and the acid washings extracted with ether. The combined organic solutions are washed with 5% sodium hydroxide carbonated and saturated brine, dried with magnesium sulphate, and evaporated to give, after alumina column chromatography (eluens: benzene:diethyl ether mixture, gradient from 9:1 to 1:1) the two epimers.

\((\pm\)-trans-5a-Ethynyl-1,1,4afl-trimethyldecachlorophthalalene-5f-ol: yield: 0.91 g (80%); m.p. 60-70°C (pentane) (Lit.\(^10\), m.p. 68-70°C). M.S.: \(m/e\) (relative intensity) = 220 (M\(^+\), 8), 149 (22), 135 (22), 123 (100), 109 (27), 96 (25), 85 (26), 81 (33), 69 (38), 55 (35). I.R. (KBr): v\(_\text{max}\) = 3400 3500 (OH), 3290 cm\(^{-1}\) (\(\equiv\text{CC}-\text{H}\)).

\((\pm\)-trans-5f-Ethynyl-1,1,4afl-trimethyldecachlorophthalalene-5a-ol: yield: 0.148 g (13%); oily liquid. M.S.: \(m/e\) (relative intensity) = 220 (M\(^+\), 5), 149 (25), 135 (24), 123 (100), 109 (29), 96 (29), 95 (36), 82 (27), 81 (38), 69 (38), 55 (39).
I.R. (film): \nu = 3400-3500 (OH), 3290 cm\(^{-1}\) (\(\equiv C\equiv H\)).

\(^1\)H-N.M.R. (CDCl\(_3\)): \(\delta = 0.82\) (s, 3 H, methyl); 0.87 (s, 3 H, methyl); 1.13 (s, 3 H, angular methyl); 2.37 ppm (s, 1 H, \(\equiv C\equiv H\)).

1-(\textit{o}-Iodoethyl)-2-propyn-1-ol:
Prepared in essentially the same manner from sodium (5.52 g, 0.24 mol) and \(o\)-iodobenzaldehyde (26.4 g, 0.114 mol) in a mixture of acetylene and ammonia (400 ml), giving after similar work-up and filtration on a small column (silica gel/chloroform) followed by preparative T.L.C. (silica gel, benzene) the desired ynlol as a yellowish solid; yield: 21.59 g (73\%); m.p. 30-32\°C.

\(\text{C}_3\text{H}_6\text{NO}\) calc. C 41.89 H 2.73 I 49.18

(258.1) found 41.77 2.76 49.22

M.S.: m/e (relative intensity) 258 (M\(^+\), 100), 240 (32), 131 (84), 103 (55), 102 (53), 77 (65), 63 (45).

I.R. (film): \(\nu = 3350\) (OH), 3290 (\(\equiv C\equiv H\)), 2120 cm\(^{-1}\) (\(\equiv C\equiv C\)).

\(^1\)H-N.M.R. (CDCl\(_3\)): \(\delta = 2.66\) (d, \(J = 2.0\) Hz, 1 H, \(\equiv C\equiv H\)); 4.46 (s, 1 H, OH); 5.66 ppm (d, \(J = 2.0\) Hz, 1 H, CHO).

U.V. (methanol): \(\lambda_{\text{max}} = 229\) nm (e = 9500); 260 nm (shoulder).

\(1,3\)-Bis-[\(\beta\)-hydroxy-2-propynyl]benzene:
Prepared in essentially the same manner from sodium (6.0 g, 0.261 mol) and isophthalaldehyde (5.0 g, 0.037 mol) in a mixture of acetylene and ammonia (400 ml), giving after similar work-up and filtration on a small silica column (chloroform/methanol; 100:2 v/v) a yellow liquid; yield: 5.39 g (78\%).

\(\text{C}_9\text{H}_{12}\text{O}_2\) calc. C 77.41 H 5.41

(156.2) found 77.27 5.50

M.S.: m/e (relative intensity) 186 (M\(^+\), 9), 168 (21), 139 (19), 131 (100), 115 (48), 77 (30), 57 (72), 51 (19).

I.R. (film): \(\nu = 3300\) (OH), 3270 (\(\equiv C\equiv H\)), 2120 cm\(^{-1}\) (\(\equiv C\equiv C\)).

\(^1\)H-N.M.R. (CDCl\(_3\)): \(\delta = 2.63\) (d, \(J = 2.3\) Hz, 2 H, \(\equiv C\equiv H\)); 4.25 ppm (s, 2 H, OH); 5.37 ppm (d, \(J = 2.3\) Hz, 2 H, CHO).

U.V. (CHCl\(_3\)): \(\lambda_{\text{max}} = 253\) nm (e = 1800), 270 nm (shoulder).

\((\pm)-1,4\alpha\)-Dimethyl-5-\(\alpha\)-ethylnyl-5\(\beta\)-hydroxy-4,4a,5,6,7,8-hexahydronaphthalene-2(3H)-one:
Prepared in essentially the same manner from lithium (0.15 g, 21.6 mmol) and \((\pm)-1,4\alpha\)-dimethyl-4,4a,5,7,8-tetrahydronaphthalene-2(3H)(5\(\alpha\)-H)-dione (2.00 g, 10.4 mmol) in a 1/1 mixture of acetylene and ammonia (150 ml), giving after similar work-up and chromatography (silica, benzene/ether; 9:1 to 7:3) \((\pm)-1,4\alpha\)-dimethyl-5-\(\alpha\)-ethylnyl-5\(\beta\)-hydroxy-4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one\(^{13}\); yield: 1.878 g (83\%); m.p. 148-150\°C (benzene).

M.S.: m/e (relative intensity) 218 \((\pm)-1,4\alpha\)-dimethyl-4,4a,5,7,8-tetrahydronaphthalene-2(3H)(5\(\alpha\)-H)-dione, 203 (24), 190 (23), 175 (39), 162 (46), 161 (28), 148 (43), 147 (41), 135 (57), 135 (41), 123 (68), 109 (30), 95 (28), 93 (40), 91 (45), 81 (45), 79 (32), 77 (39), 67 (26), 65 (21), 55 (27).

I.R. (KBr): \(\nu = 3300-3400\) (OH), 3230 (\(\equiv C\equiv H\)), 1645, 1605 cm\(^{-1}\).

\(^1\)H-N.M.R. (CDCl\(_3\)): \(\delta = 1.38\) (s, 3 H, angular methyl); 1.79 ppm (s, 3 H, vinylmethyl).

\(J.\ M.\ C.\) is indebted to the "Institut pour l’Encouragement de la Recherche dans l’Industrie et l’Agriculture" (I.R.S.I.A.) for a predoctoral fellowship.

Received: August 6, 1981
(Revised form: October 14, 1981)

---

* Author to whom correspondence should be addressed.

** Predoctoral I.R.S.I.A.-fellow.

14. C.f. also Ref.10.
21. The large excess of acetylene used here can be reduced: e.g., in larger scale preparations, up to 0.5 mol of benzaldehyde could be ethynylated with 1 mol of sodium in a volume as small as 500 ml of a 1/1 mixture of liquid ammonia and acetylene.
22. For sake of comparison with previous results, the same ratio of sodium to carboxylic compound was taken as described in Ref.19.