# The Introduction of the Propargyl Group at a Ring Juncture

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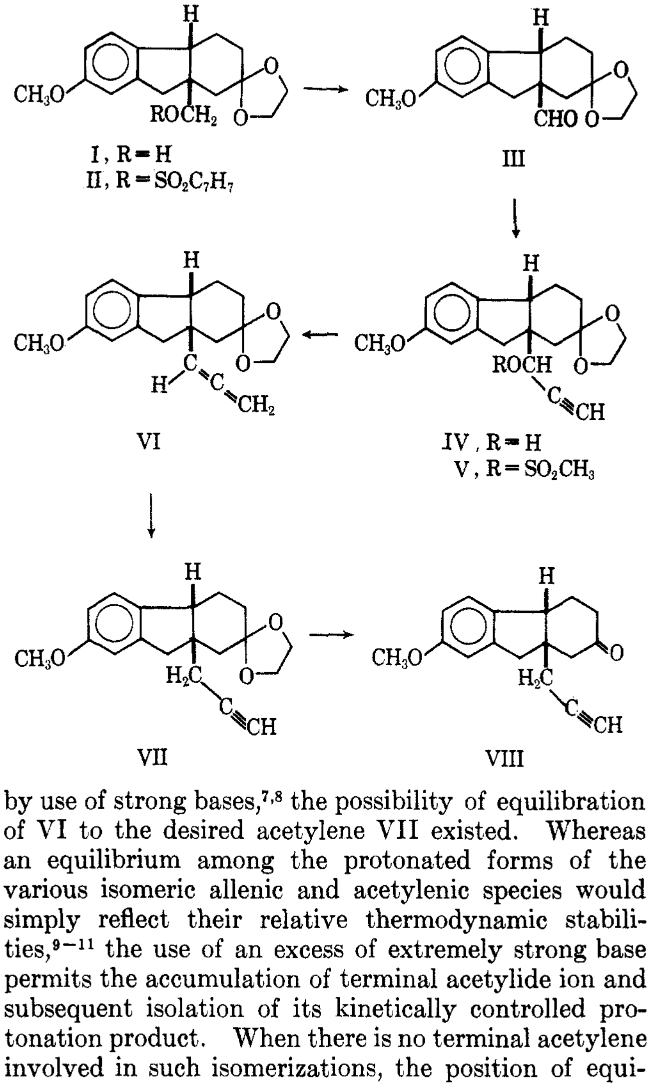
In the course of our work, we have had the occasion to wish to introduce synthetically a propargyl group at a ring juncture in a polycyclic system. This is a problem which presents some difficulties and, as we have devised a useful synthetic scheme leading to the introduction of the desired functionality, we wish to report our results.

Since our starting point was the neopentyl-type alcohol I,[1] an attempt at direct introduction, involving displacement by acetylide of the halide or alkyl- or arylsulfonate ester of I, seemed most desirable. To the best of our knowledge, such a direct displacement at an angular, neopentyl carbon atom by acetylide ion had never been successfully accomplished and our experience did not alter this situation.

Alcohol I was treated with *p*-toluenesulfonyl chloride in pyridine and tosylate II was isolated in 41% yield as a stable solid. Attempted reaction of II in dimethylformamide–dimethoxyethane solution[2] with freshly prepared potassium acetylide, however, failed to yield any material which had incorporated the desired acetylene function, as indicated by complete lack of the characteristic monosubstituted acetylene absorptions at 2100–2150 and 3300 cm$^{-1}$ in the infrared spectrum of the product.

Our alternative approach proceeded as follows: alcohol I was oxidized with chromium trioxide in pyridine solution[3] to the neopentyl aldehyde (III) in 62% yield; this compound, on treatment with lithium acetylide, was converted in high yield to the secondary, propargyl alcohol IV and thence, again in good yield, to V, the methanesulfonate ester of IV. Both IV and V were isolated only as liquids and, since each was assumed to exist as a mixture of diastereoisomers, no attempt was made to characterize them fully (Scheme I).

SCHEME I



The next step in the sequence was reduction of the mesylate V by means of lithium aluminum hydride.[4,5] The case for direct displacement of mesylate from V by hydride or aluminohydride ion is undoubtedly at least as bad as the situation in II, since the steric factors involved are worse; however, the allene VI is produced in this reaction in 78% over-all yield from III. Whether the mechanism is a basic elimination of methanesulfonic acid[6] followed by reduction or simply an $S_N2'$ displacement[5] is still uncertain.

Since allenes and acetylenes can be interconverted by use of strong bases,[7,8] the possibility of equilibration of VI to the desired acetylene VII existed. Whereas an equilibrium among the protonated forms of the various isomeric allenic and acetylenic species would simply reflect their relative thermodynamic stabilities,[9–11] the use of an excess of extremely strong base permits the accumulation of terminal acetylide ion and subsequent isolation of its kinetically controlled protonation product. When there is no terminal acetylene involved in such isomerizations, the position of equilibrium may be governed by steric or other, more subtle factors.[9] However, in the present case, the irreversible formation of a relatively very stable acetylide anion could be expected to displace the equilibrium toward VII, the only accessible terminal acetylene.

In fact, when VI was treated with excess potassium amide in liquid ammonia, work-up resulted in the isolation of VII, a liquid ketal acetylene, which was characterized by hydrolysis with dilute acid to the corresponding solid keto acetylene VIII,[12] obtained in 82% yield from VI.

## Experimental Section[13]

***p*-Toluenesulfonate Ester of Compound I.**—Compound I (862 mg, 2.97 mmoles) was dissolved in 7.0 ml of dry pyridine and the solution was cooled with an ice bath prior to addition of 700 mg (3.67 mmoles) of *p*-toluenesulfonyl chloride. After standing

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[1] The synthesis and stereochemistry of this compound will be discussed elsewhere.

[2] T. F. Rutledge, *J. Org. Chem.*, **24**, 840 (1959).

[3] J. Schmidlin and A. Wettstein, *Helv. Chim. Acta*, **45**, 331 (1961).

[4] W. J. Bailey and C. R. Pfeifer, *J. Org. Chem.*, **20**, 95 (1955).

[5] T. L. Jacobs and R. D. Wilcox, *J. Am. Chem. Soc.*, **86**, 2240 (1964), and references cited therein.

[6] H. D. Hartzler, *ibid.*, **83**, 4997 (1961), and references cited therein.

[7] R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworth and Co., Ltd., London, 1955, pp 134–139.

[8] D. R. Taylor, *Chem. Rev.*, **67**, 317 (1967).

[9] W. R. Moore and H. R. Ward, *J. Am. Chem. Soc.*, **85**, 86 (1963).

[10] W. Smadja, *Ann. Chim.*, **10**, 105 (1965).

[11] J. H. Wotiz, W. E. Billups, and D. T. Christian, *J. Org. Chem.*, **31** 2069 (1966).

[12] G. Stork, S. Malhotra, H. Thompson, and M. Uchibayashi, *J. Am. Chem. Soc.*, **87**, 1148 (1965).

[13] Melting points were determined with a Kofler Micro hot-stage microscope and are uncorrected; infrared spectra of pure materials were taken using a Perkin-Elmer Model 421 spectrometer and those of uncharacterized intermediates with a Perkin-Elmer Model 137 spectrometer; ultraviolet spectra were determined using a Cary Model 14 spectrophotometer; nmr spectra were taken with a Varian A-60 spectrometer; microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill.

overnight in an ice bath, the solution was worked up by neutralization with aqueous hydrochloric acid and extraction with ether. Concentration of the dried extracts gave 535 mg (41%) of white crystals, mp 125–130°. Recrystallizations from ether produced material of mp 133.5–136° and having a characteristic tosylate absorption in its infrared spectrum at 1173 cm$^{-1}$, but no absorption in the hydroxyl or carbonyl regions; $\lambda_{max}^{EtOH}$ 226 mμ (ε 19,500), 282 (2800).

*Anal.* Calcd for $C_{24}H_{28}O_6S$: C, 64.84; H, 6.35. Found: C, 64.81; H, 6.53.

**Oxidation of Compound I to the Neopentyl Aldehyde III.**—Compound I (16.2 g, 56 mmoles) was dissolved in 250 ml of pyridine containing 1% water and to this was added 750 ml of a saturated solution of chromium trioxide in pyridine containing 1% water. The flask, flushed with nitrogen and stoppered, was allowed to stand at room temperature with gentle stirring. After 24 hr another 500 ml of the above solution of chromium trioxide in pyridine was added. The mixture was worked up after a total of 48 hr by addition of ether, filtration, concentration, and chromatography on a column of Florisil. Concentration of fractions eluted with 25–50% ether in hexane and recrystallization of the resulting solid from hexane yielded 9.94 g (62%) of aldehyde: mp 66–71°, further recrystallization raised the melting point to 69.5–72°; $\nu_{max}^{CCl_4}$ 2710, 1720 cm$^{-1}$; $\lambda_{max}^{EtOH}$ 283 mμ (ε 2700); nmr ($CH_2Cl_2$), 1 H singlet at τ 0.1, 3 H complex at 2.8–3.4, 4 H singlet at 6.2, 3 H singlet at 6.3, 1 H triplet at 6.5 ($J$ = 4 cps), pair of 1 H doublets at 7.1 and 7.3 ($J$ = 15 cps), 6 H complex at 7.8–8.7.

*Anal.* Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.76; H, 7.01.

**Reaction of Aldehyde III with Lithium Acetylide.**—In a flask fitted with a Dry Ice condenser a solution was prepared of 1.260 g (180 mg-atoms) of lithium in 250 ml of dry ammonia; dry acetylene was then passed into the solution until discharge of the blue color. To the stirred suspension of lithium acetylide was then added 5.00 g (17.5 mmoles) of aldehyde III in 60 ml of dry tetrahydrofuran. The mixture was stirred for 1 hr and the ammonia was allowed to evaporate overnight. Work-up by addition of water, extraction with ether, and concentration of the dried extracts gave IV as a pale yellow viscous oil lacking infrared absorption attributable to carbonyl, but having absorption at *ca.* 3630, 3420, and 3320 cm$^{-1}$. The nmr spectrum ($CCl_4$), although somewhat messy, was consistent with structure IV: 3 H complex at τ 2.8–3.5, 1 H doublet at 5.4 ($J$ = 14 cps), 18 H complex at 5.9–9.0, including a broad singlet at 6.15 and a sharp singlet at 6.3.

**Preparation of the Methanesulfonate Ester of IV.**—The crude propargyl alcohol IV from the previous step was dissolved in 133 ml of dry pyridine and the solution cooled with an ice bath. Freshly distilled methanesulfonyl chloride (2.22 ml; 3.28 g, 28.9 mmoles) was added and the flask, flushed with nitrogen and stoppered, was kept in an ice bath for 24 hr. Work-up by addition of cold aqueous hydrochloric acid to slight acidity and extraction with ether, followed by concentration of the dried extracts, produced a yellowish oil lacking infrared absorption attributable to hydroxyl, but having bands at *ca.* 3330 and 2120 cm$^{-1}$.

**Conversion of V to the Allene VI.**—The crude methanesulfonate ester V from the previous step, as a viscous liquid, was dissolved in 250 ml of dry ether and treated with excess lithium aluminum hydride by refluxing for 2.5 hr. Work-up by dropwise addition with stirring of saturated aqueous sodium sulfate and decantation of the organic liquors (and washing of the inorganic precipitate with ether) gave, on concentration, a yellow oil which was dissolved in hexane and chromatographed on Merck basic alumina. Reconcentration of appropriate fractions gave 4.06 g (78.5% from III) of crystalline allene which, when recrystallized from hexane, melted at 66–68°: $\nu_{max}^{CCl_4}$ 1960 cm$^{-1}$; $\lambda_{max}^{EtOH}$ 228 mμ (ε 7200), 282 (2700); nmr ($CCl_4$), 3 H complex at τ 2.8–3.5, 1 H triplet at 4.3 ($J$ = 7 cps), 2 H doublet at 5.25 ($J$ = 7 cps), complex absorption at 6.0–9.0, including a 4 H singlet at 6.2 and a 3 H singlet at 6.3.

*Anal.* Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.48; H, 7.18.

**Conversion of VI to Keto Acetylene VIII.**—The ketal allene VI (3.0 g, 10 mmoles) was dissolved in 15 ml of dry tetrahydrofuran and added with stirring to a solution of potassium amide prepared from 725 mg of potassium (18.5 mg-atom), 150 ml of dry ammonia, and a trace of ferric chloride. The mixture was stirred at reflux temperature for 1 hr and worked up by addition of solid ammonium chloride, evaporation of ammonia, addition of water, and extraction with ether and pentane. Concentration of the dried extracts gave about 2.8 g of a colorless oil exhibiting infrared absorption at *ca.* 3340 and 2130 cm$^{-1}$, attributable to terminal acetylene. Since the product could not be induced to crystallize and since the ketal was no longer required for our purposes,[12] the entire product was deketalized by stirring at room temperature for 1.5 hr in a mixture of 100 ml of methanol, 20 ml of water, and 3 ml of hydrochloric acid. Work-up by neutralization with aqueous sodium bicarbonate and extraction with ether yielded, on concentration, 2.1 g (82%) of crude crystalline VIII. Recrystallization from hexane–ether gave material melting at 71–72°: $\nu_{max}^{CCl_4}$ 3310, 1710 cm$^{-1}$; $\lambda_{max}^{EtOH}$ 282 mμ (ε 2700); nmr ($CCl_4$), 3 H complex at τ 2.8–3.5, 3 H singlet at 6.3, 1 H triplet at 6.8 ($J$ = 4 cps), pair of 1 H doublets at 7.1 and 7.4 ($J$ = 16 cps), 8 H complex at 7.5–8.0, 1 H triplet at 8.1 ($J$ = 2.5 cps).

*Anal.* Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.30; H, 7.25.

**Registry No.**—II, 13758-72-0; III, 13673-64-8; IV, 13673-65-9; VI, 13673-66-0; VIII, 1149-97-9.

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## Pyrolysis of Tetrakis(dimethylamino)methane

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The recently reported tetrakis(dimethylamino)methane[1] was observed to decompose slowly at temperatures slightly above its melting point (122.5–124.5°) and it was of interest to examine this decomposition in some detail.

When tetrakis(dimethylamino)methane is kept at 150°, it gradually loses dimethylamine (identified by mass spectral and nmr analyses) and the resulting residue is a mixture of an unknown, distillable liquid and a polymeric tar. The nuclear magnetic resonance (nmr) spectrum of the distillable liquid is relatively simple, being composed of a doublet centered at τ 5.34 ($J$ = 10.6 cps), a singlet at 7.42, a broadened singlet at 7.52, and another singlet at 7.70 in the ratio 1:6:3:6 (in benzene solvent, tetramethylsilane internal standard). On the basis of this spectrum and other data presented below, structure I was assigned to this compound. Additional nmr evidence is obtained from a sample to which dimethylamine was added as a source of exchangeable protons. The doublet at τ 5.34 becomes a singlet and the broad peak at τ 7.52 also becomes a sharp singlet, while the peaks at τ 7.42 and 7.70 remain unchanged. This corroborates the $=CHNHCH_3$ arrangement of structure I. The infra-

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[1] H. Weingarten and W. A. White, *J. Am. Chem. Soc.*, **88**, 2885 (1966).