

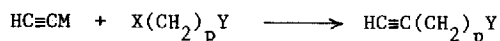
MULTIPOSITIONAL ISOMERISATION OF FUNCTIONALLY SUBSTITUTED
ALKYNES CATALYSED BY POTASSIUM 3-AMINOPROPYLAMIDE

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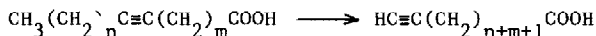
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Straightforward preparation of ω -monoynoic acids requires, in an essential step, coupling of an α,ω -disubstituted alkane with a metal acetylide:



It is general experience, however, that 1,12-dodecanediol is the longest obtainable α,ω -disubstituted alkane which can still be converted conveniently into an α,ω -disubstituted alkane with different substituents. Since, when $\text{Y} = \text{Cl}$, malonic ester synthesis can add only two carbon atoms, preparation of ω -monoynoic acids $\text{HC}\equiv\text{C}(\text{CH}_2)_{p+1}\text{COOH}$ in reasonable yields via this route is in practice limited to $p=12$. In consequence, synthesis of long-chain ω -monoynoic acids via isomerisation of the corresponding monoynoic acids with the triple bond in a more proximal position according to



would be a desirable method, since ω -monoynoic acids with $n+m+1 > 13$ would then become available conveniently and in reasonable yields.

Base-catalysed single-positional isomerisation of 2- and 3-monoynoic acids with potassium hydroxide^{1,2}, sodium hydroxide³ and sodium amide⁴ are reported to give equilibrium mixtures with the 3-monoynoic acid as the major constituent. This tendency to form equilibrium mixtures is generally encountered in base-catalysed isomerisation of functionally substituted alkynes⁵.

Only in a few instances has isomerisation involving a single migration found synthetic application. Thus Brandsma²⁾ describes the preparation of 2-butyne from 1-butyne in about 100% yield using potassium *tert*-butoxide in dimethyl sulfoxide, and the conversion of 1-methyl-2-*tert*-butyl acetylene into neopentyl acetylene in 88-95% yield using potassium amide in liquid ammonia.

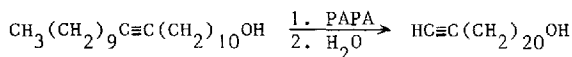
Although base-catalysed migration of triple bonds over more than two positions has been attained in low yields with sodium amide⁶⁾, Brown and Yamashita⁷⁾ reported high-yield multipositional isomerisation of various "internal" alkynes to 1-alkynes. When using potassium 3-aminopropyl amide (PAPA) in 1,3-diaminopropane (APA) as a solvent, in a 1.2-1.5 molar ratio to 7-tetradecyne, they could convert the 7-tetradecyne at 15-20°C in 1-2 min into 1-tetradecyne (pure by GLC) in 89% isolated yield.

We submitted 2-hexynoic acid, 4-decyloic acid and *tert*-butyl-4-decyloate to base-catalysed rearrangement with the PAPA/APA system using a 2.0-3.0 molar ratio of 0.6 mol/l PAPA in APA for the acids and a 1.2 molar ratio of 0.17 mol/l base for the ester. In these carboxylic derivatives isomerisation to the terminal position was not observed. The product of the reaction with 2-hexynoic acid consisted for the greater part of a dienic compound, most probably *trans*-3,5-hexadienoic acid, and isomerisation of the two other compounds led to a complicated mixture.

When, however, alkyn-1-ols with an internal triple bond were used, alkyn-1-ols with a terminal triple bond could be obtained in good yields. Thus 2- and 3-undecynol were both converted into 10-undecynol in > 80% yield using a 2.0-3.0 molar ratio of a 0.6 mol/l solution of PAPA in APA at room temperature. Only the reaction time (20 h at room temperature) for complete conversion as monitored by GLC was much longer than those reported by Brown for unsubstituted and methyl-substituted alkynes (2-10 min). (See Table 1).

With alkynols the internal triple bond could be shifted over as many as 10 positions; for example, 11-docosynol could be converted into 21-docosynol in 87% isolated yield. Again, allenes and dienes were not observed in the end product. Since alkynols with a terminal triple bond can easily be converted into ω -monoynoic acids (by oxidation or conversion of its halide by nitrile or malonic acid synthesis) multipositional migration of alkynols with an internal triple bond offers a convenient route to long-chain ω -monoynoic acids.

In a typical experiment, 2 ml KH-paraffin suspension (22.5%, ex Alfa Products, for safe handling cf. Ref. 7) was washed three times in an argon atmosphere with 10 ml ether, freshly distilled from LiAlH₄, to remove the paraffin. The 0.397 g KH (9.92 mmol) that was left after vacuum evaporation of the ether, was stirred for 1 h at room temperature with 20 ml dry APA (ex Aldrich, 98%, distilled from BaO, b.p. 43°C/16 mm Hg, kept on molecular sieve 0.3 nm). At 0°C 1.139 g 11-docosynol (3.53 mmol) was added; after 1 h at room temperature an 2½ h at 40-50°C the isomerisation was quantitative (GLC):



5 ml H₂O was added dropwise at 0°C and the mixture was extracted with ether. The ether layer was

Table 1

Isomerisation of functionally substituted alkynes with potassium 3-aminopropyl amide (PAPA) in 1,3-diaminopropane (APA)

Compound	Ratio ^a	Reaction time and temp	Product	Yield (%)
2-Hexynoic acid	2.0; 3.0	20 h 20 ^o + 2½ h 45 ^o	b	-
4-Decynoic acid	2.2	48 h 20 ^o	c	-
Butyl-4-decyanoate	1.2	1 h 20 ^o	c	-
2-Undecynol	3.0	20 h 20 ^o	10-undecynol	> 80 ^d
3-Undecynol	2.2; 2.8	20 h 20 ^o	10-undecynol	> 80 ^d
11-Docosynol	2.4	24 h 20 ^o	21-docosynol	~ 80 ^e
11-Docosynol	3.0	24 h 20 ^o	21-docosynol	> 90 ^d
11-Docosynol	3.0	1 h 20 ^o + 2½ h 45 ^o	21-docosynol	87 ^f

^aMolar ratio KH:Ynoic compound. ^bMixture probably with *trans*-3,5-hexadienoic acid as a major compound. ^cMixture. ^dAccording to PMR. ^eAccording to GLC. ^fIsolated yield.

acidified with 4 mol/l HCl, washed acid free with H₂O, dried on Na₂SO₄ and evaporated to leave 1.055 g solid. Recrystallisation from light petroleum (40-55^o) gave 991 mg (87%) 21-docosynol, m.p. 71-75^o, purity by GLC 91% (5% MER-2 on Chromosorb WAS-DMCS HP, 80-100 mesh, 2 m, 2 mm int. diam.); C 81.93% (calcd. 81.91), H 13.19% (13.12), O 4.89% (4.96); IR 1000-1070 and 3280 cm⁻¹ (-CH₂OH), 625, 2120 and 3280 cm⁻¹ (HC≡C-); PMR (300 MHz; TMS int., CCl₄) δ 1.1-1.6 (mult., 36 H, -(CH₂)_n-), 1.75 (trip., 1 H, J=2.7 Hz, HC≡C-), 2.13 (trip. of trip., 2 H, J=7.0 and 2.7 Hz, -C≡CCH₂-) and 3.53 ppm (trip., 2 H, J=6.5 Hz, -CH₂O-), -OH shifted by dilution; MS m/e 322 (calcd. 322).

At present we are exploring which other functional groups allow the desired multipositional migration.

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