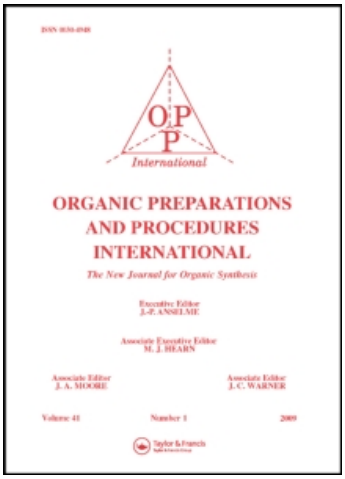


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# SIMPLE SYNTHESIS OF ALKYNES FROM 1,2-DIBROMOALKANES USING PTC CONDITIONS

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# SIMPLE SYNTHESIS OF ALKYNES FROM 1,2-DIBROMOALKANES USING PTC CONDITIONS

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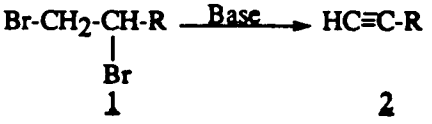
Terminal alkynes are useful starting materials or intermediates in the synthesis of natural products.[1] One of the possible synthesis of terminal alkynes is the double elimination of hydrogen bromide from 1,2-dibromoalkanes (1). Although sodium amide[2] and potassium hydroxide[3,4] are used most often as bases, these reagents have some disadvantages. Potassium hydroxide, for example, promotes the migration of acetylenic bond to the center of the chain.[4]

Even though sodium amide[2,5] catalyzes the reverse isomerisation,[6] impurities diminish the reactivity and can cause explosion.[2a] The migration of the C=C triple bond can be avoided by using PTC conditions (KOH[7] or KOBu$^t$ in petroleum ether[8] with 18-crown-6 or quaternary ammonium salts as phase-transfer catalysts.). In addition, the base-induced β-elimination to generate olefins from 2-haloalkanes by PTC conditions without solvent is known in the literature.[9]




1 2

a) R = $C_2H_5$; b) R = $C_3H_7$; c) R = $C_4H_9$; d) R = $C_5H_{11}$; e) R = $C_6H_{13}$; f) R = HOOC-$(CH_2)_8$

We now report the successful application of the elimination-without-solvent PTC method for the preparation or terminal acetylenic compounds. The conversion depends on the amount of base. Best results were achieved when four equivalent of base were used while the use of two equivalents led to products containing 2-40% vinyl and allyl bromides (Table 1). Migration of terminal C-C triple bond[10] was not observed. The extraction of base ($OH^{\ominus}$ ion) to the liquid phase is catalyzed by the Aliquat 336 (FLUKA)[11,12] as PTC catalyst. No reaction was observed upon stirring the mixture of potasium hydroxide (4 equiv.) and 1,2-dibromoalkane (1 equiv.) at 150°. However, a mixture of 1-alkyne, 1-bromo- and 2-bromo-alkene distilled from the reaction mixture with 40-70% conversion at a higher temperature (180°; Table 1).

10-Undecynoic acid[13] (2f), obtained from 10,11-dibromoundecanoic acid[14] (1f), via base-catalyzed HBr elimination, is an intermediate in the synthesis of 3,13- octadecadien-1-yl acetates,[14a] which are frequently occurring components of the pheromones of many pestiferous Synanthedon species.[15] The eliminations were carried out in refluxing solvents and those boiling above 80° gave the highest yields (Table 2). In hexane (bp. 69°), the yield dropped to 60%. Lower boiling solvents gave a mixture of vinyl bromides. The elimination process required only 3 hrs in toluene to yield 2f (90%). Aliquat 336 (FLUKA) is more effective phase-transfer catalyst than Adogen 464 (ALDRICH), as seen by higher yields in shorter reaction times (entries 5 and 6, 2 and 3). The use of solid potassium carbonate led to the formation of significant quantities of unidentified side-products, and the yield of 2f was 30% or less (entry 8). Increasing the reaction time resulted in only increasing the amount of side-products.

## EXPERIMENTAL SECTION

General Procedure.- A vigorously stirred mixture of 1,2-dibromoalkane (1.0 mol),[17] well-pulverized potassium hydroxide (4.0 mol) and Aliquat 336 (FLUKA) (7 ml) was fractionated slowly. The distillation of final products must be started immediately after mixing

the reagents. The crude products were purified by distillation after drying over $Na_2SO_4$. The pure products listed below were isolated as colorless liquids.

1-Butyne, bp. 14°C/760 mm, lit.[18] bp. 14°C/760 mm; yield: 90%; $^1$H-NMR($CDCl_3$): δ 2.19 (qd, $J_1$ = 7Hz, $J_2$ = 2Hz, 2H, $-CH_2-$), 1.93 (t, J = 2Hz, 1H, ≡CH), 1.15 (t, J = 7Hz, 3H, $-CH_3$).

1-Pentyne, bp. 40°C/760 mm, lit.[19] bp. 40.2°C/760 mm; yield: 98%; IR(film): 3300 cm$^{-1}$ (sharp, -C≡CH), 2120 cm$^{-1}$ (C≡C), 630 cm$^{-1}$(≡CH); $^1$H-NMR($CDCl_3$): δ 2.16(td, $J_1$ = 7Hz, $J_2$ = 2Hz, 2H, $-CH_2-C\equiv C$), 1.92 (t, J = 2Hz, 1H, ≡CH), 1.55 (m, J = 7Hz, 2H, $-CH_2-CH_3$), 0.99 (t, J = 7Hz, 3H, $-CH_3$).

1-Hexyne, bp. 73°C/760 mm, lit.[8,20] bp. 71.3°C/720 mm; yield: 98%; IR(film): 3300 cm$^{-1}$ (sharp, -C≡CH), 2120 cm$^{-1}$ (C≡C), 630 cm$^{-1}$ (≡CH); $^1$H-NMR($CDCl_3$):δ 2.05- 2.25 (m, 2H,$-CH_2-C\equiv C$), 1.9 (t, J = 3Hz, 1H, ≡CH), 1.2-1.6 (m, 4H,$-(CH_2)_2-$), 0.9 (t, J = 7Hz, 3H, $-CH_3$).

TABLE 1. Formation of 1-Alkynes From 1,2-Dibromoalkanes (1) by Elimination

| R | KOH (equiv) | Conditions[a] | Yield of 2 (%) | Olefinic impurities (%) |
|---|---|---|---|---|
| $C_2H_5$ | 4 | A | 90 | 10[b] |
| | 4 | B | 85 | 15[b] |
| | 2 | A | 50 | 40[b] |
| | 2 | B | 60 | 30[b] |
| $C_3H_7$ | 4 | A | 98 | 0 |
| | 4 | B | 98 | 0 |
| | 2 | A | 90 | 3 |
| | 2 | B | 95 | 0 |
| | 4 | C | 10 | 30 |
| $C_4H_9$ | 4 | A | 98 | 0 |
| | 2 | A | 70 | 5 |
| | 2 | B | 90 | 1 |
| | 4 | C | 20 | 40 |
| $C_5H_{11}$ | 4 | A | 97 | 0 |
| | 2 | A | 50 | 20 |
| | 2 | B | 85 | 5 |
| | 4 | C | 30 | 40 |
| $C_6H_{13}$ | 4 | A | 99 | 0 |
| | 4 | C | 20 | 5 |

a) A: Distillation of the final products starts immediatelly after mixing the reagents.
B: The reaction mixture was stirred vigorously at 25°C for 1 hr before distillation.
C: 1,2-Dibromoalkane (1.0 mol) and potassium hydroxide (4.0 mol) was stirred at 150°C for1 hr then 180° C for 30 min. The end-products were distilled from the mixture.

b) The olefinic side products (1-bromo-1-butene and 2-bromo-1butene) are too volatile and were distilled from the reaction mixture before the elimination of a second mole of hydrogen bromide.

Table 2. Elimination of Hydrogen Bromide from 10, 11-Dibromoundecanoic Acid

| Entry | Base | Solvent bp(°C) | Catalyst | Reaction time under reflux (hr) | Yield of 2f (%) |
|---|---|---|---|---|---|
| 1. | NaOH | DME (85) | Aliquat 336 | 12 | 81[16] |
| 2. | KOH | Hexane (69) | Aliquat 336 | 12 | 65[16] |
| 3. | KOH | Hexane (69) | Adogen 464 | 24 | 60 |
| 4. | KOH | Petrol ether (40-70) | Adogen 464 | 24 | —* |
| 5. | KOH | Cyclohexane (81) | Adogen 464 | 24 | 75[14] |
| 6. | KOH | Cyclohexane (81) | Aliquat 336 | 12 | 90 |
| 7. | KOH | Toluene (111) | Aliquat 336 | 3 | 90 |
| 8. | $K_2CO_3$ | Toluene (111) | Aliquat 336 | 3 | 30 |

* A reddish brown oil was obtaind which was converted to 2f by KOH (Adogen 464, reflux in cyclohexane for 20 hrs) or KOBu$^t$ (18-crown-6, reflux in cyclohexane for 20 hrs), and to 10-undecen-1-ol by reduction with $LiAlH_4$ in ether at 25°C for 24 hrs.



1-Heptyne, bp. 99°C/760 mm, lit. [8,20] bp. 99.7°C/760 mm; yield: 97%; IR(film): 3300 $cm^{-1}$ (sharp, -C≡CH), 2120 $cm^{-1}$ (C≡C), 630 $cm^{-1}$ (≡CH); $^1$H- NMR ($CDCl_3$): δ 2.05- 2.20 (m, 2H, -$CH_2$-C≡C), 1.92 (t, J = 3Hz, 1H, ≡CH), 1.3-1.65 (m, 6H, -$(CH_2)_3$-), 0.85 (t, J = 7Hz, 3H, -$CH_3$).

1-Octyne, bp. 125°C/760 mm, lit.[8,20] bp. 126.2°C/760 mm; yield: 99%; IR(film): 3300 $cm^{-1}$ (sharp, -C≡CH), 2120 $cm^{-1}$ (C≡C), 630 $cm^{-1}$(≡CH); $^1$H-NMR($CDCl_3$): δ 2.07-2.21 (m, 2H, -$CH_2$-C≡C), 1.91 (t, J = 3Hz, 1H, ≡CH), 1.2-1.65 (m, 8H, -$(CH_2)_4$-), 0.85 (t, J = 7Hz, 3H, -$CH_3$).

10-Undecynoic acid (2f).- 10,11-Dibromoundecanoic acid (100 g, 0.29 mol) which is made by standard procedures from readily available 10-undecenoic acid,[14] is combined with toluene (500 ml) in a vigorously stirred solution to which well-pulverized potassium hydroxide (74 g, 1.32 mol) and Aliquat 336 PTC catalyst (2 ml) were added. The resulting mixture was stirred under reflux for 3 hrs and allowed to cool. Then 300 mL of water was added and the mixture was acidified with concentrated HCl (50-80 ml). After separation of the organic layer, the water-layer was extracted with ether (2 X 200 ml) and then the combined organic solutions were washed successively with 1N HCl (2 x 100 ml), 5% $NaHCO_3$ (2 X 100 ml) and brine (2 X 100 ml). After drying over $MgSO_4$ the solution was concentrated in vacuo. The residue was purified by distillation in vacuo to yield 2f (47.6 g; 90%) as a colorless oil, bp. 144°C/0.4 mm, which on standing solidified, mp. 42°C, lit.[16] 42°C. IR(film): 3300 $cm^{-1}$(C≡CH), 3000-3200 $cm^{-1}$(COOH), 2100 $cm^{-1}$(C≡C),1700 $cm^{-1}$ (C=O), 650 $cm^{-1}$ (≡CH).

$^1$H-NMR($CDCl_3$): δ 12.1(s, 1H, -COOH), 2.2 (m, 4H, ≡C-$CH_2$- and -$CH_2$CO), 1.76(t, J = 3Hz, 1H, ≡CH), 1.1-1.7(m, 12H, -$(CH_2)_6$)ppm.

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## REDUCTION OF 1,3,5-TRISUBSTITUTED 2-ALKYLPYRAZOLIUM SALTS WITH COMPLEX METAL HYDRIDES. SYNTHESIS OF 3-PYRAZOLINES

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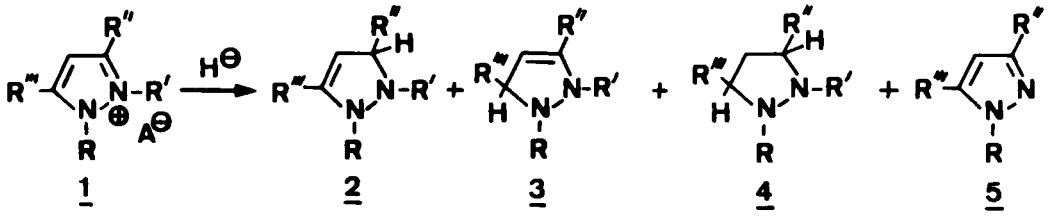
Although it has been reported that complex metal hydrides do not affect the azole ring,[1] we reported in previous papers that the reduction of activated isoxazole compounds by complex metal hydrides provides a good method for the regioselective synthesis of 2-, 3- and 4-isoxazolines.[2] The isoxazoline obtained depends on the kind of activation of the isoxazole nucleus. Thus, 3,5-dialkylisoxazoles with electron-withdrawing groups at C-4 are reduced to 2-isoxazolines regioselectively, whereas isoxazolium salts react with the same hydrides to give 4-isoxazolines.

This paper extends the scope of the process to pyrazoles and we now report a highly selective method for the synthesis of 3-pyrazolines (2, 3) by reduction of 1,3,5- trisubstituted 2-alkylpyrazolium salts (1) with either lithium aluminium hydride, sodium borohydride, or lithium tri-t-butoxy aluminium hydride. Some of these procedures also afforded pyrazolidines (4) and pyrazoles (5), the latter resulting from the hydrogenolysis of the N-R' bond. The results obtained in all these reactions are summarized in Table 1.



1 2 3 4 5

The results indicate that the reduction of 1 with lithium aluminium hydride or lithium