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UNEXPECTED REACTION OF 2-ACETYLTHIOPHENE WITH PHENAYLCETYLENE IN KOH/DMSO SUSPENSION

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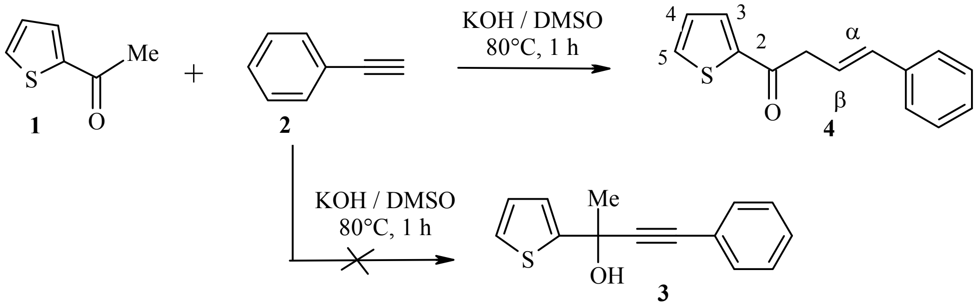
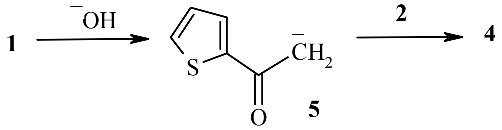
In a study of the Favorsky reaction [1, 2] between 2-acetylthiophene **1** and phenylacetylene **2** in the superbase system KOH/DMSO at 80ºC (higher than the 0-25ºC usually recommended [2]) we unexpectedly found that the styrylmethyl 2-thienyl ketone **4** is obtained in 56% yield rather than the acetylenic alcohol **3**.



The ketone **4** is the product of addition of the 2-acetylthiophene **1** as a CH acid (deprotonated through the action of superbase) to the phenylacetylene **2**:



The reaction is characterized by high chemoselectivity, the acetylenic alcohol **3** not being seen by ^{1}H NMR in the reaction mixture. Another important feature of this novel reaction is its regio- and stereoselectivity. Carbanion **5** adds exclusively to the β-carbon atom of the acetylene **2** to form the adduct with just the (*E*)-configuration (^{1}H NMR), this being untypical of nucleophilic addition to a triple bond (the (*Z*)-adducts generally being formed [3]).

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Attention was turned to the fact that the expected prototropic shift of the double bond towards the carbonyl group to give the isomeric α,β-ethylene ketone did not occur during the reaction. This points to a weaker conjugation of the double bond to the carbonyl group when compared with the styryl fragment.

It should be stressed that base-catalyzed addition of ketones to a carbon-carbon triple bond has not been reported in the literature at this time. There is good reason to believe that the reaction discovered and its development can lead to the creation of a novel, general methodology for the functionalization of heterocycles (i.e. their acylation and subsequent reaction with acetylenes).

IR spectra were taken on a Bruker ISF-25 instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 400 spectrometer (400 and 100 MHz respectively) using $CDCl_3$ and with HMDS as internal standard at $\delta = 0.05$ ppm.

A mixture of 2-acetylthiophene **1** (1.0 g, 8 mmol), phenylacetylene **2** (0.81 g, 8 mmol), and $KOH\cdot0.5H_2O$ (0.52 g, 8 mmol) in DMSO (20 ml) was heated with stirring for 1 h at 80ºC. After cooling to room temperature the reaction mixture was diluted with water (40 ml), neutralized with NH_4Cl, and extracted with ether (4×5 ml). The combined ether extract was washed with water (3×5 ml) and dried over K_2CO_3. Evaporation of the ether gave the raw product (1.47 g) which was column chromatographed on basic aluminium oxide (pH 8.25, eluent hexane) to give the pure ketone **4** (1.02 g, 56%).

***(E)*-4-Phenyl-1-(Thien-2-yl)- 3-buten-1-one (4)**. Beige colored crystals; mp 42ºC (hexane). IR spectrum (KBr), ν, cm^{-1}: 3436, 3026, 1660, 1516, 1495, 1353, 1299, 1208, 1053, 963, 945, 859, 839, 765, 726, 692, 583, 498, 463. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.77 (1H, dd, $^{3}J = 3.8$, $^{4}J = 1.3$, H-3); 7.63 (1H, dd, $^{3}J = 4.9$, $^{4}J = 1.2$, H-5); 7.36 (2H, m, H-*o*); 7.29 (2H, m, H-*m*); 7.21 (1H, m, H-*p*); 7.13 (1H, dd, $^{3}J = 3.8$, $^{4}J = 4.9$, H-4); 6.56 (1H, d, $^{3}J = 16.1$, H-α); 6.42 (1H, dt, $^{3}J = 16.1$, $^{3}J = 6.8$, H-β); 3.82 (2H, d, $^{3}J = 6.8$, CH_2). ^{13}C NMR spectrum, δ, ppm: 190.8 (C=O), 143.8 (C-2), 136.9 (C-*i*), 133.9 (C-α), 133.4 (C-5), 132.4 (C-3), 128.6 (C-*m*), 128.2 (C-4), 127.6 (C-*p*), 126.4 (C-*o*), 122.3 (C-β), 43.7 ($\underline{C}H_2$). Found, %: C 73.74; H 5.45; S 14.00. $C_{14}H_{12}OS$. Calculated, %: C 73.65; H 5.30; S 14.04.

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