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LETTERS TO THE EDITOR

Superbasic System CsOH/DMSO as a Catalyst of Nucleophilic Addition of Acetophenone to Phenylacethylene

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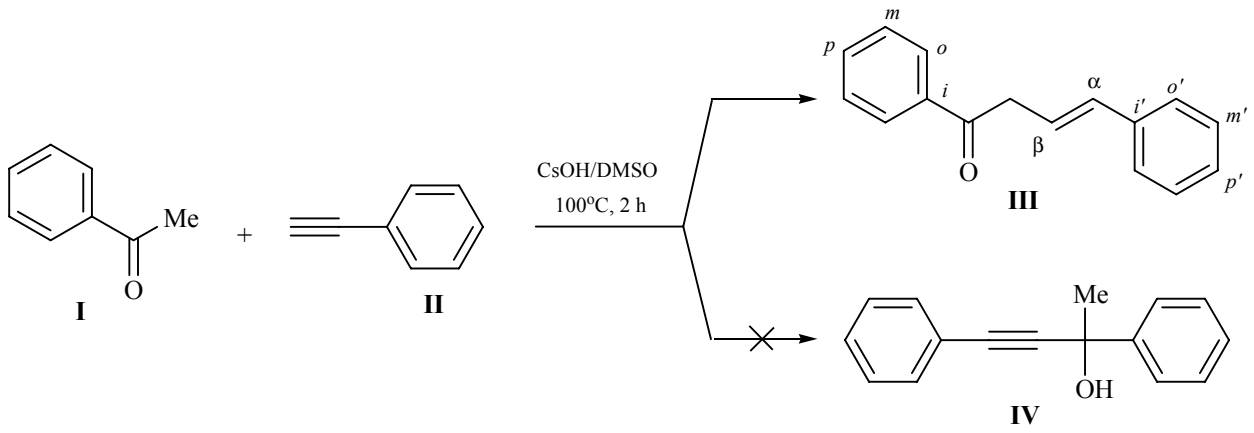
So far, the base-catalyzed addition of ketones to acetylenes was unknown. The reason, apparently, is the assumption that acetylenes, as a rather strong CH-acids under the action of strong bases would be deprotonated into acetylenide anions, which are inert with respect to other nucleophiles. Moreover, acetylenide anions readily (at room and lower temperatures) add to the carbonyl group of ketones (the Favorsky reaction [1, 2]).Yet, however, the fact that upon heating above 60°C tertiary acetylenic alcohols decompose into the starting components, ketones and acetylenes (the reverse Favorsky reaction [3]) is disregarded. It can be assumed, therefore, that at elevated temperature carbanions of ketones will add to non-ionized molecules of acetylenes existing in equilibrium with acetylenide anions. Such an addition is the more probable since ketones are stronger CH-acids than acetylenes (pKa in DMSO for acetophenone is ~22–24, for phenylacetylene ~26–29 [4]).

Following this logic, we have studied the reaction of acetophenone **I** with phenylacetylene **II** in the superbasic system CsOH/DMSO at 100°C. Indeed, it turned out that ketone **I** adds to acetylene **II** to afford styrylmethyl phenyl ketone **III** in up to 70% yield. The reaction is characterized by high chemoselectivity: the product of the Favorsky reaction, acetylenic alcohol **IV**, cannot be even detected in the reaction mixture by the ^{1}H NMR spectroscopy (Scheme 1).

An important preparative advantage of the new reaction is its stereospecificity: Adduct **III** is obtained exclusively as the *E*-isomer. However, this stereospecificity is not a result of the kinetic control, since if the reaction is stopped after 1 h the ratio of the *E*- and *Z*-isomers is 1:1. Therefore, it is evident that first the *Z*-isomer is formed (in accordance with the rule of the *trans*-nucleophilic addition to mono-substituted acetylenes [5]) which upon further heating

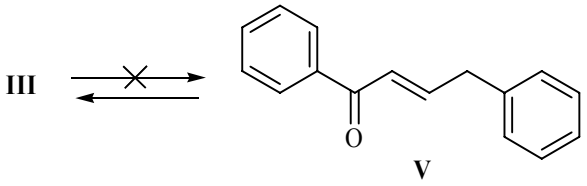
Scheme 1.



completely isomerizes into the *E*-isomer, that is, the stereochemistry is thermodynamically controlled.

Noteworthy is also the regiospecificity of the reaction: The carbanion of acetophenone adds only to the terminal acetylenic carbon atom. We also failed to detect in the reaction mixture chalcone **V**, which could be formed due to prototropic migration of the double bond towards the carbonyl group. This is indicative of a stronger conjugation in the *E*-styryl fragment as compared to that in chalcone **V** (Scheme 2).

Scheme 2.



V

***(E)*-1,4-Diphenyl-3-buten-1-one (III).** The mixture of acetophenone **I** (0.50 g, 4 mmol), phenylacetylene **II** (0.43 g, 4 mmol), and $CsOH \cdot H_2O$ (0.70 g, 4 mmol) in 15 ml of DMSO was heated for 2 h at 100°C with stirring on a magnetic stirrer. The reaction mixture was diluted with water (40 ml), neutralized with NH_4Cl, and extracted with ether (4 × 5 ml). The ether extract was washed with water (3 × 5 ml), dried over potassium carbonate, ether was removed. From the residue (0.81 g), pure ketone **III** was isolated by column chromatography (Al_2O_3, hexane). Yield 0.64 g (69%). White crystals, mp 92–94°C. IR spectrum, ν, cm^{-1}: 3082, 3061, 3023, 1683, 1597, 1496, 1449, 1399, 1356, 1334, 1296, 1277, 1208, 1071, 983, 908, 749, 732, 688, 566, 501. ^{1}H NMR spectrum, δ, ppm: 7.99 m (2H, H_o), 7.56 m (1H, H_p), 7.46 m (2H, H_m), 7.36 m (2H, $H_{o'}$), 7.28 m (2H, $H_{m'}$), 7.20 m (1H, $H_{p'}$), 6.53 d (1H, H_α, ^3J 16.1 Hz), 6.45 d.t (1H, H_b, ^3J 16.1 Hz, ^3J 6.1 Hz), 3.90 d (2H, CH_2, ^3J 6.1 Hz). ^{13}C NMR spectrum, δ, ppm: 197.9 (C=O), 137.0 ($C_{i'}$), 136.5 (C_i), 133.5 (C_α), 133.1 (C_p), 128.6 (C_m), 128.4 ($C_{m'}$), 128.3 (C_o), 127.3 ($C_{p'}$), 126.2 ($C_{o'}$), 122.5 (C_b), 42.7 (CH_2). Found, %: C, 86.67; H 6.57. Calculated, %: C, 86.45; H, 6.35. (222.28).

Apparently, there are no principal restrictions to expand this reaction to other ketones, acetylenes, and superbasic media. We continue investigations in this direction.

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