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N.S. Zefirov on His 70th Anniversary

The Role of Potassium Cation in the Favorskii Ethynylation of Acetone: Effekt of Dibenzo-18-crown-6

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Abstract—Macrocyclic polyether dibenzo-18-crown-6 possessing a specific affinity for potassium cation inhibits ethynylation of acetone with acetylene in the presence of KOH according to Favorskii. The inhibition becomes stronger in the presence of the complex dibenzo-18-crown-6·KOH·MeOH as catalyst (both in excess acetone and in DMSO). The effect does not originate from deactivation of acetone, for its aldol-like condensation is accelerated in the presence of both dibenzo-18-crown-6 and its complex (the selectivity of ethynylation sharply falls down). Thus, apart from the high basicity of the medium, activation of acetylene due to complex formation with potassium cation plays an important role in the Favorskii ethynylation of ketones.

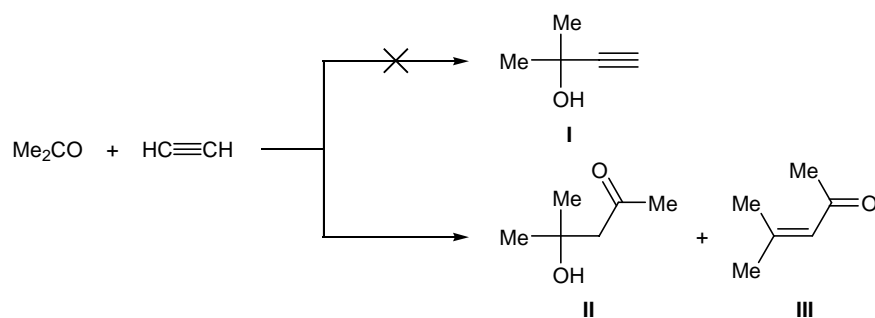
The Favorskii reaction has long become a common tool in practical organic chemistry. Its classical version implies condensation of ketones or aldehydes with acetylene in the presence of alkalis, mainly in the presence of potassium hydroxide [1, 2]. The reaction involves intermediate formation of acetylene complexes with alkali metal hydroxides, which were isolated and characterized (Tedeschi complexes) [3]. According to quantum-chemical calculations [4], these complexes have a T-shaped structure where the alkali metal cation interacts with π electrons of the triple bond, thus favoring deprotonation and addition of anions [2]. Favorskii reactions are strongly facilitated in superbasic suspensions of MOH (where M is an alkali metal) in hexamethylphosphoric triamide [5] and dimethyl sulfoxide [2, 6], which was rationalized in terms of separation of MOH ion pair and activation of hydroxide ion which abstracts proton from acetylene. On the basis of quantum-chemical calculations [4, 7] it was also presumed [2, 6] that acetylene may be activated within ligand environment (solvate shell) of alkali metal cation via replacement of one weak ligand. On the other hand, it might be expected that strong ligands, e.g., crown ethers, should hamper approach of acetylene to the cation; in this case, provided that the cation does play some role in the acetylene activation, the elimination reaction should be inhibited.

With the goal of elucidating the role of alkali metal cation in the Favorskii reaction, as well as in other acetylene reactions catalyzed by alkali metal hydroxides, we examined ethynylation of acetone in the presence of dibenzo-18-crown-6 (which is a macrocyclic polyether capable of specifically binding potassium cation) and its complex with KOH.

Complexes of macrocyclic polyethers with alkali metal hydroxides are known to catalyze a number of reactions involving anions, e.g., condensation of acetonitrile with aldehydes and ketones [8], hydrolysis of sterically hindered esters [9], condensation of cyclopentadiene with ketones [10], and Smiles rearrangement [11]. Sodium hydroxide in the presence of dibenzo-18-crown-6 accelerates cycloaddition of dichlorocarbene to styrene [12]. The complex KOH–18-crown-6 was used in the kinetic study of the reaction of propyl bromide with hydroxide ion [13]. According to the generally accepted views, crown ethers activate alkali metal hydroxides by improving their solubility in organic solvents (the complexes thus formed are more lipophilic) and increasing the basicity of the medium (ion pair separation effect).

While attempting to develop a procedure for the preparation of a complex of KOH with dibenzo-18-crown-6 we came to the conclusion that such complex

Scheme 1.



was unlikely to be isolated as individual substance. The formation of KOH–dibenzo-18-crown-6 complex was presumed for the first time by Pedersen [14] on the basis of the fact that the electric conductivity of a solution of potassium hydroxide in methanol decreased in the presence of dibenzo-18-crown-6. Lutz *et al.* [15] reported on the formation of such complex containing methanol, but only the IR spectra were given. We succeeded in isolating the complex dibenzo-18-crown-6·KOH·MeOH (from methanol) and characterizing it by the ^1H NMR, UV, and IR spectra [16]. Just that complex was used in the ethynylation of acetone. For comparison, we used as catalyst calcined potassium hydroxide and its mixture with dibenzo-18-crown-6.

The results are summarized in Table 1. It is seen that no expected acetone ethynylation product, 2-methyl-3-butyn-2-ol (**I**), is formed in the presence of dibenzo-18-crown-6·KOH·MeOH (even traces of **I** were not detected in the reaction mixture). The reaction mixture contained only 4-hydroxy-4-methylpentan-2-one (**II**) and 4-methyl-3-penten-2-one (**III**), i.e., products of aldol-like condensation of acetone. Compounds

II and **III** accumulate in the reaction mixture over a period of 1 h, and their concentrations then remain almost constant (a slight tendency to decrease is observed, presumably as a result of further condensation). Under analogous conditions, but in the presence of KOH, the reaction mixture after 30 min contained ketone **III** and 2.2% of acetylenic alcohol **I** whose concentration increased with time (Table 1). These data indicate that dibenzo-18-crown-6·KOH·MeOH does not catalyze the ethynylation reaction, though it is as active as KOH in the aldol condensation of acetone.

Our results are consistent with the formation of complexes by acetylenic alcohols and alkali metal hydroxides [3] as intermediates in the reverse Favorskii reaction. Binding of potassium cation by crown ethers hampers formation of such complexes, thus inhibiting decomposition of tertiary acetylenic alcohols.

It is known [2, 17] that acetylenic alcohols can be obtained in nearly quantitative yield from ketones and acetylene in the superbasic system KOH–DMSO (20–25°C, atmospheric pressure). We examined the effect of dibenzo-18-crown-6·KOH·MeOH on the ethynylation

Table 1. Ethynylation of acetone without a solvent (20–22°C, atmospheric pressure)

Catalyst, wt % (concentration of KOH, wt %)	Reaction time, min	Composition of the reaction mixture, ^a %		
		I	II	III
KOH, 3.4 (3.4)	30	2.2	ND	1.4
	60	3.1	ND	1.5
	90	4.9	ND	2.3
Dibenzo-18-crown-6·KOH·MeOH, 19.3 (1.7)	60	ND	1.5	0.9
	120	ND	1.0	0.6
Dibenzo-18-crown-6·KOH·MeOH, 38.6 (3.4)	10	ND	ND	Traces
	20	ND	0.4	0.3
	30	ND	ND	0.9
	60	ND	ND	1.7
	90	ND	ND	2.1

^a ND stands for not detected.

Table 2. Ethynylation of acetone in DMSO^a

Run no.	Catalyst (g)	Temperature, °C	Reaction time, h	Yield of I , g (%)	Conversion of acetone, %
1 ^b	KOH (0.98)	11–13	9	14.25 (62)	86
2 ^b	KOH (0.98)	20–22	4	3.13 (13)	24
3 ^c	KOH (0.86)	20–22	4	7.06 (30)	63
4 ^c	Dibenzo-18-crown-6 (5.4), KOH (0.86)	11–13	9	11.77 (51)	60
5 ^c	Dibenzo-18-crown-6 (5.4), KOH (0.86)	20–22	4	1.58 (7)	24
6 ^{c,d}	Dibenzo-18-crown-6 (16.4), KOH (0.86)	20–22	4	1.28 (5)	39
7	Dibenzo-18-crown-6·KOH·MeOH (7.01)	11–13	9	1.38 (6)	56
8	Dibenzo-18-crown-6·KOH·MeOH (6.97)	20–22	4	0.63 (3)	41

^a DMSO, 50 ml; acetone, 16 g (276 mmol).

^b Moist KOH (15% of H₂O).

^c Calcined KOH.

^d DMSO, 100 ml.

tion of acetone under these conditions. For comparison, KOH and its mixture with dibenzo-18-crown-6 were used as catalysts, and the reaction temperature and time were varied. Taking into account poor solubility of dibenzo-18-crown-6 in DMSO (0.048 M at 26°C) [14, 18], the molar ratio catalyst–acetone was taken equal to 1:20 which is far from the optimal value [17].

Experiments showed that in the presence of KOH, depending on the reaction conditions, acetylenic alcohol **I** was formed in a yield of 13 to 62%, the conversion of acetone being 24 to 86% (Table 2, run nos. 1–3). In the reaction performed with equimolar amounts of dibenzo-18-crown-6 and calcined KOH without preliminary preparation of the complex, the conversion of acetone (24 to 60%) and the yield of alcohol **I** (7 to 51%) were lower (Table 2; run nos. 4, 5). Insignificant decrease in these values in run no. 4 (Table 2) is likely to result from only partial binding of potassium hydroxide by the crown ether.

In fact, when the reaction mixture was preliminarily heated for 1 h at 130°C to ensure greater yield of the complex (Table 2, run no. 5) or when 3 equiv of dibenzo-18-crown-6 was used (Table 2, run no. 6), other conditions being equal, the conversion of acetone (24, 39%) and the yield of alcohol **I** (7, 5%) sharply decreased. Analogous decrease in the yield of **I** (6, 3%) and selectivity of the process (conversion 41 and 56%) was observed in the presence of the preliminarily prepared dibenzo-18-crown-6·KOH·MeOH complex (Table 2; run nos. 7, 8).

Therefore, dibenzo-18-crown-6 and its complex with potassium hydroxide and methanol (dibenzo-18-crown-6·KOH·MeOH) inhibit ethynylation of acetone even in DMSO, while the rate of aldol-like condensation of acetone (i.e., conversion) remains fairly high. This means that binding of potassium cation by crown ether affects primarily activation of acetylene. An analogous effect was observed previously in the reverse Favorskii reaction with tertiary arylacetylenic alcohols having polyether fragments as the aryl substituents (benzo-15-crown-5 and benzo-18-crown-6) [19, 20]. Common tertiary arylacetylenic alcohols decompose into the corresponding ketone and acetylene in the presence of a catalytic amount of calcined KOH (on heating in boiling benzene or toluene) [21], while acetylenic alcohols having a polyether fragment undergo reverse Favorskii reaction only in the presence of excess KOH [20].

EXPERIMENTAL

The progress of reactions was monitored by GLC on an LKhM-80 chromatograph equipped with a thermal conductivity detector and a 3000×3-mm column packed with 15 wt % of Carbowax 20M on Chromaton N-AW-HMDS (0.25–0.315 mm); carrier gas helium, oven temperature programming from 70 to 130°C; the components were quantitated using toluene as internal standard.

Dibenzo-18-crown-6 (TU 6-09-20-19-83; from Cherkassy Plant of Chemicals) was recrystallized from

benzene (mp 164°C). Potassium hydroxide (from Merck) was calcined at 400–450°C; it contained 97.4% of the main substance (according to the potentiometric titration data). Dimethyl sulfoxide was purchased from Merck. Acetylene (from Angarsk Petrochemical Company) was passed through a bottle charged with askarite (NaOH on asbestos).

The complex dibenzo-18-crown-6·KOH·MeOH was prepared according to the procedure described in [16]. The concentration of KOH in the complex was determined by titration in methanol with 0.1 N HClO₄ using an EV-74 potentiometer.

Ethynylation of acetone without a solvent. A reactor equipped with a temperature-control unit was charged with 7.76 g (134 mmol) of acetone which was saturated with acetylene under vigorous stirring until acetylene no longer absorbed. The required catalyst and 0.405 g (4.4 mmol) of toluene (as internal standard for GLC) were added under continuous supply of acetylene, and the mixture was stirred at 20–22°C. Samples for GLC analysis were withdrawn at definite time intervals (Table 1).

Ethynylation of acetone in the presence of KOH in DMSO. *a.* A suspension of 0.98 g (15 mmol) of KOH·0.5H₂O (15% of H₂O) in 50 ml of DMSO was cooled to 11–13°C and saturated with acetylene under vigorous stirring over a period of 7 h. Acetone, 16 g (276 mmol), was added over a period of 7 h at that temperature, and the mixture was stirred for 2 h under continuous supply of acetylene. The mixture was neutralized with carbon dioxide and filtered. The filtrate was distilled to isolate a fraction boiling in the temperature range from 50 to 150°C (720 mm), 38.4 g, which contained 5.8% (2.23 g, 38 mmol) of acetone (conversion 86%), 37.1% (14.25 g, 170 mmol) of 2-methyl-3-butyn-2-ol (yield 62%), and DMSO (Table 2, run no. 1).

b. A suspension of 0.98 g (15 mmol) of KOH·0.5H₂O in 50 ml of DMSO was vigorously stirred, heated to 130°C, slowly cooled to 20–22°C, and saturated with acetylene over a period of 1.5 h. Acetone, 16 g (276 mmol), was added over a period of 40 min at 20–22°C under stirring, acetylene being continuously supplied to the reactor. The mixture was stirred for an additional 3 h 20 min, neutralized with carbon dioxide, and filtered. The filtrate was distilled to isolate a fraction boiling in the temperature range from 50 to 150°C (715 mm), 24.11 g, which contained 50.6% (12.20 g, 210 mmol) of acetone (conversion 24%),

13% (3.13 g, 37 mmol) of 2-methyl-3-butyn-2-ol (yield 13%), and DMSO (Table 2, run no. 2).

c. Likewise, from 16 g (276 mmol) of acetone, 0.86 g (15 mmol) of calcined KOH (97.4%), and 50 ml of DMSO (the mixture was treated as described above), we obtained a fraction boiling in the temperature range from 50 to 150°C (720 mm), 18.20 g, which contained 32.9% (5.98 g, 103 mmol) of acetone (conversion 63%), 38.8% (7.06 g, 84 mmol) of 2-methyl-3-butyn-2-ol (yield 30%), and DMSO (Table 2, run no. 3).

Ethynylation of acetone in the presence of KOH

and dibenzo-18-crown-6 in DMSO. *a.* A suspension of 5.4 g (15 mmol) of dibenzo-18-crown-6 and 0.86 g (15 mmol) of calcined KOH in 50 ml of DMSO was cooled to 11–13°C and saturated with acetylene over a period of 7 h under vigorous stirring. Acetone, 16 g (276 mmol), was added over a period of 7 h at that temperature, and the mixture was stirred for 2 h under continuous supply of acetylene. The mixture was treated as described above, and the filtrate was distilled under reduced pressure to isolate (using a trap cooled to –60 to –70°C) a fraction (6.50 g) containing 95% (6.17 g, 106 mmol) of acetone and 5% (0.33 g, 4 mmol) of 2-methyl-3-butyn-2-ol and a fraction boiling in the temperature range from 20 to 84°C (25 mm), 58.38 g, which contained 0.5% (0.29 g, 5 mmol) of acetone, 19.6% (11.44 g, 136 mmol) of 2-methyl-3-butyn-2-ol (overall yield 11.77 g, 140 mmol, 51%), and DMSO. Conversion of acetone 60% (Table 2, run no. 4).

b. A suspension of 5.4 g (15 mmol) of dibenzo-18-crown-6 and 0.86 g (15 mmol) of calcined KOH in 50 ml of DMSO was vigorously stirred and heated to 130°C over a period of 1 h until a dark brown transparent solution was obtained. The mixture was slowly cooled to 20–22°C. When the temperature fell down to 40–45°C, the solution became viscous, and a thick homogeneous material was formed. The mixture was saturated with acetylene over a period of 1.5 h, 16 g (276 mmol) of acetone was added over a period of 40 min, and the mixture was stirred for 3 h 20 min under continuous supply of acetylene. The mixture was neutralized with carbon dioxide and filtered, and the filtrate was distilled to isolate a fraction boiling in the temperature range from 50 to 140°C (719 mm), 28.75 g, which contained 42% (12.1 g, 209 mmol) of acetone (conversion 24%), 5.5% (1.58 g, 19 mmol) of 2-methyl-3-butyn-2-ol (yield 7%), and DMSO (Table 2, run no. 5).

Likewise, from 16 g (276 mmol) of acetone, 16.4 g (45 mmol) of dibenzo-18-crown-6, and 0.86 g (15 mmol) of calcined KOH in 100 ml of DMSO, after appropriate treatment, we isolated a fraction boiling in the temperature range from 50 to 140°C (720 mm), 18.61 g, which contained 52.3% (9.73 g, 168 mmol) of acetone (conversion 39%), 6.9% (1.28 g, 15 mmol) of 2-methyl-3-butyn-2-ol (yield 5%), and DMSO (Table 2, run no. 6).

Ethynylation of acetone in the presence of dibenzo-18-crown-6·KOH·MeOH in DMSO. *a.* A suspension of 7.01 g (15 mmol) of the complex dibenzo-18-crown-6·KOH·MeOH containing 11.98% of KOH (according to the potentiometric titration data) in 50 ml of DMSO was cooled to 11–13°C and saturated with acetylene over a period of 7 h under vigorous stirring. Acetone, 16 g (276 mmol), was added over a period of 7 h at that temperature, the mixture was stirred for 2 h under continuous supply of acetylene, neutralized with carbon dioxide, and filtered, and the filtrate was distilled under reduced pressure. A fraction (7.31 g) was collected in a cooled trap (–60 to –70°C); it contained 95% (6.94 g, 120 mmol) of acetone and 2.4% (0.18 g, 2 mmol) of 2-methyl-3-butyn-2-ol. Another fraction boiled in the temperature range from 50 to 90°C (60 mm), 5.02 g; it contained 2% (0.11 g, 2 mmol) of acetone, 24% (1.20 g, 14 mmol) of 2-methyl-3-butyn-2-ol (overall yield 1.38 g, 16 mmol, 6%), and DMSO. Conversion of acetone 56% (Table 2, run no. 7).

b. A suspension of 6.97 g (15 mmol) of dibenzo-18-crown-6·KOH·MeOH (12.06% of KOH, potentiometric titration) in 50 ml of DMSO was vigorously stirred and heated to 130°C over a period of 1 h until a dark brown transparent solution was obtained. The solution was slowly cooled to 20–22°C and saturated with acetylene over a period of 1.5 h, 16 g (276 mmol) of acetone was added over a period of 40 min, and the mixture was stirred for 3 h under continuous supply of acetylene. The mixture was neutralized with carbon dioxide and filtered. The filtrate was distilled to isolate a fraction boiling in the temperature range from 50 to 150°C (724 mm), 23.5 g, which contained 40.3% (9.47 g, 163 mmol) of acetone (conversion 41%), 2.7% (0.63 g, 7.5 mmol) of 2-methyl-3-butyn-2-ol (yield 3%), and DMSO (Table 2, run no. 8).

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