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$CuBr_2$-Catalyzed Alkenylation of 1-adamantanol with Isopropanol †

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Abstract: The electrophilic adamantylation of olefins is one of the few synthetic approaches to polycyclic framework compounds with the side chains. The reaction of adamantane with lower olefins on aluminosilicate catalysts leads to alkyladamantanes, and in the case of propylene, a noticeable amount of alkenyladamantanes is formed. In a solution of trifluoromethanesulfonic acid, the reaction of adamantane with olefins gives a mixture of mono- and polysubstituted alkyladamantanes in ~10% yield. In order to elaborate convenient preparative methods for the selective introduction of a three-carbon fragment into the adamantane framework, we undertook a study of the reaction of 1-adamantanol with isopropanol in the presence of metal-complex catalysts. We have developed for the first time a $CuBr_2$-catalyzed method for the alkenylation of 1-adamantanol with isopropanol. The reaction proceeds for 4 h at 220 °C giving the corresponding (1*Z*)-prop-1-en-1-yladamantane in high yield.

Keywords: 1-adamantanole; isopropanol; alkenylation; copper catalysis

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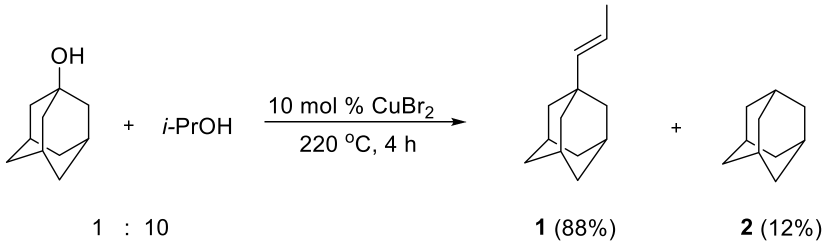
1. Introduction

It is known that adamantane derivatives are a special class of framework compounds-diamond-like hydrocarbons, which are widely used in medicine and technology [1]. Alkenylation of 1-adamantanol with olefins (electrophilic adamantylation of olefins) is one of the few synthetic approaches to polycyclic framework compounds with the side chains. The reaction of adamantane with lower olefins on aluminosilicate catalysts leads to alkyladamantanes, and in the case of propylene, a noticeable amount of alkenyladamantanes is formed. In a solution of trifluoromethanesulfonic acid, the reaction of adamantane with olefins gives a mixture of mono- and polysubstituted alkyladamantanes in ~10% yield [2]. In order to elaborate convenient preparative methods for the selective introduction of a three-carbon fragment into the adamantane framework, we undertook a study of the reaction of 1-adamantanol with isopropanol in the presence of metal-complex catalysts.

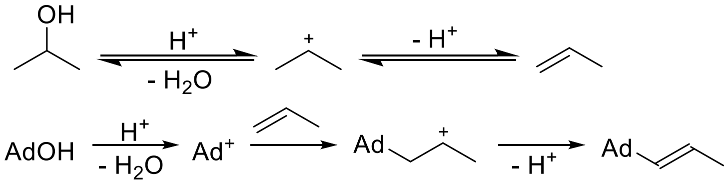
2. Results and Discussion

For first time we have synthesized (1*E*)-prop-1-en-1-yladamantane **1** in 88% yield by the reaction of 1-adamantanol with isopropanol under the action of catalytic amounts of copper (II) bromide (Scheme 1). A by-product of the reaction is adamantane **2**, which is formed in an amount of 12%. The reaction was carried out under the following conditions: $[CuBr_2]$:[1-AdOH]:[*i*-PrOH] = 10:100:1000, 220 °C for 4 h.



Scheme 1. $CuBr_2$-catalyzed reaction of 1-adamantanol with isopropanole.

We assume that isopropanol undergoes dehydration under the reaction conditions to obtain propene, by analogy with the process of isobutylene formation from *tert*-butanol in the presence of $CuBr_2$ supported on HY hierarchical zeolite [3]. Then propene alkenylates 1-adamantanol to give (1*E*)-prop-1-en-1-yladamantane (Scheme 2).



Scheme 2. Plausible mechanism of the reactions of alkenylation of 1-adamantanol with isopropanole.

The structure of the resulting compound **1** was established by ^1H, ^{13}C NMR spectroscopy, as well as by comparison with known samples and literature data [4].

The reaction apparently occurs under thermodynamic control, since, according to the results of B3LYP/6-31G(d) calculations, (1*E*)-prop-1-en-1-yladamantane is 5.0 kcal/mol more stable than (1*Z*)-prop-1-en-1-yladamantane (Table 1).

Table 1. Gibbs free energies at 298 K [B3LYP/6-31G(d)] for isomers of prop-1-en-1-yladamantane.

Substrate	**ΔG° (substrate), au**	**ΔΔG° (substrate), au**
(1*E*)-prop-1-en-1-yladamantane	−507.165318	−0.007970
(1*Z*)-prop-1-en-1-yladamantane	−507.157348	0

A by-product of the reaction is adamantane **2**, the content of which reaches 12%. Presumably, its formation can be explained by intermolecular hydride transfer to the 1-adamantyl cation from the tertiary CH group of the isopropanol molecule, which is then converted into acetone.

3. Conclusions

Thus, we have developed for the first time a $CuBr_2$-catalyzed method for the alkenylation of 1-adamantanol with isopropanol. The reaction proceeds for 4 h at 220 °C giving the corresponding (1*E*)-prop-1-en-1-yladamantane in high yield.

4. Experimental Part

1-Adamantanol, isopropanol, $CuBr_2$ (Acros) were commercial reagents. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-II 400 Ascend instrument (400 MHz for ^1H and 100 MHz for ^{13}C in $CDCl_3$). Mass spectra were run on a Shimadzu GCMS-QP2010Plus mass spectrometer (SPB-5 capillary column, 30m × 0.25 mm, helium as the carrier gas, temperature programming from 40 to 300 °C at 8 °C/min, evaporation temperature of 280 °C, ion source temperature of 200 °C, and ionization energy of 70 eV). The course of the reaction and the purity of the products were monitored by gas liquid chromatography on a Shimadzu GC-9A, GC-2014 instrument [2m×3mm column, SE-30 silicone (5%) on Chromaton N-AW-HMDS as the stationary phase, temperature programming from 50 to 270 °C at 8 °C/min, helium as the carrier gas (47 mL/min)]. All quantum-chemical calculations were performed using B3LYP/6-31G(d) basis set as implemented in Gaussian 09 software [5].

The synthesis of (1E)-prop-1-en-1-yladamantane (***1***) [4]. The reactions were carried out in a glass ampoule (V=10 mL) placed in a stainless steel microautoclave (V=17 mL) with constant stirring and controlled heating. The ampoule was loaded with 0.1 mmol (22 mg) of $CuBr_2$, 1 mmol (152 mg) of 1-adamantanol, and 10 mmol (600 mg) of isopropanol. The sealed ampoule was placed in an autoclave, which was hermetically sealed and heated at 220 °C for 4 h. After the reaction, the autoclave was cooled to room temperature. The ampoule was opened and the reaction mixture was filtered through a paper filter. Then the reaction mixture was neutralized, the organic layer was extracted with methylene chloride and filtered. Methylene chloride was distilled off. The products were isolated by column chromatography (silica gel, eluent–petroleum ether). Yield 88%. ^{1}H NMR ($CDCl_3$) δ 5.24–5.38 (m, 2 H, CH=CH), 1.40–2.20 (m, 14 H, 4 CH, 5 CH_2, adamantyl), 1.67 (d, *J* = 4.8 Hz, 3 H, Me). ^{13}C NMR ($CDCl_3$) δ 143.33, 119.36, 42.66, 37.12, 28.72, 18.34. MS, *m*/*z* (I_{rel}, %): 176 $[M]^+$ (72), 120 (24), 119 (83), 91 (100), 79 (37).

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Conflicts of Interest: The authors declare no conflict of interest.

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