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Colloid and Nanosized Catalysts in Organic Synthesis: V.[1] Reactions of Alkyl Halides and Alcohols with β-Diketones in the Presence of Metal Nanoparticles

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Abstract—Reaction of copper, nickel, and iron nanoparticles with β-diketones directly yields corresponding metal β-diketonates. Reaction of alkyl halides, β-diketones, and nanodispersed metals leads to a mixture of monoketone and the alkylated β-diketone. When alcohol is used as the alkylating agent instead of alkyl halide, corresponding ester is formed.

Keywords: catalysis, nanoparticle, alkylation, β-diketone, alcohol, alkyl halide, ester

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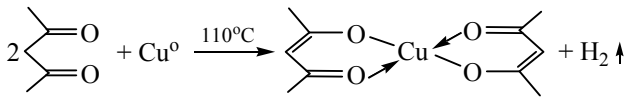
β-Diketones are widely used as core reagents for preparation of drugs, dyes, and certain heterocyclic compounds. The reported methods of β-diketones alkylation include reaction of metal diketonates with alkyl halides [2] and direct alkylation of β-diketones with strained propellane hydrocarbons [3, 4]. The both approaches suffer from serious drawbacks: the first method implies additional stage of the β-diketonate preparation, whereas limited choice of alkylating agents is available for the second method. In view of the above, development of β-diketones modification methods is of primary importance.

Previously we demonstrated that reaction of 1-bromoadamantane with 2,4-pentanedione in the presence of equimolar amount of copper nanoparticles yielded 3-(adamant-1-yl)pentate-2,4-dione. We suggested that the reaction proceeded through formation of copper 2,4-pentadionate intermediate. In order to support this suggestion, in this work we attempted the reaction of nanodispersed copper with 2,4-pentanedione. Violent reaction with gas evolution occurred upon heating of the components (the β-diketone being in excess) above 100ºC.



To the best of our knowledge, direct interaction of metal nanoparticles with 2,4-pentanedione was not previously reported. However, our experiment revealed that reaction of nanodispersed copper with 2,4-pentanedione resulted in formation of almost stoichiometric amount of copper pentadionate. We found that the described reaction occurred in the cases of other transition metal nanoparticles, in particular, nickel, cobalt, and iron. In the presence of nickel, the reaction proceeded readily without heating.

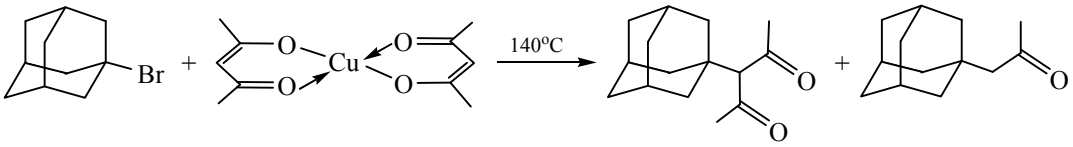
From the point of view of selectivity and simplicity, the reported method is advantageous over the traditional methods of metals acetylacetonates synthesis in the presence of bases and solvents upon prolonged heating [5, 6]. In the case of the reported reaction with metal nanoparticles, the reaction was complete in 5 (Ni) to 30 (Cu) min. The yields were close to quantitative, and no additional reagents were needed.

Pure copper(II) 2,4-pentadionate was isolated and introduced into the reaction with 1-bromoadamantane (Scheme 1).

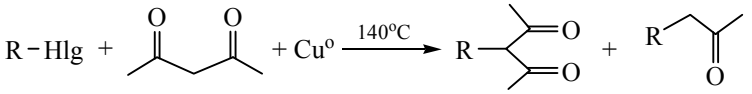
The reaction was complete within 12 h, and 3-adamant-1-ylpentan-2,4-dione was formed with 64% yield. Chromatography–mass spectrometry of the product confirmed formation of 1-adamantylacetone as side product. Properties of the isolated products coincided with the reference data [7, 8]. Structure of 3-

[1] For communication IV, see [1].

Scheme 1.



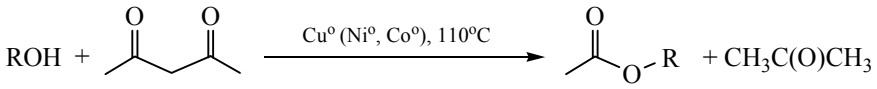
Scheme 2.



Ia–Ic **IIa–IIc**

R = 1-adamantyl , Hlg = Br (**a**); R = benzyl, Hlg = Cl (**b**); R = 1-octyl, Hlg = I (**c**).

Scheme 3.



IVa–IVd **Va–Vd**

R = 1-hexyl (**a**), 1-octyl (**b**), cyclohexyl (**c**), benzyl (**d**).

adamant-1-ylpentan-2,4-dione was further confirmed by ^{1}H NMR spectroscopy.

To our knowledge, we were the first to conduct the one-pot reaction between alkyl halide, 2,4-pentanedione, and nanodispersed copper, without the prior formation of copper 2,4-pentanedionate. The one-pot synthesis significantly simplified alkylation of β-diketones, but it was necessary to investigate the possibility of the Wurtz reaction between the alkyl halide and metal under the reaction conditions. 1-Bromoadamantane, benzyl chloride, and 1-iodoctane were used as alkylating agents. The reaction was carried out at the 3-fold molar excess of 2,4-pentanedione for 8–12 h at 110–140ºC (Scheme 2).

The reaction resulted in formation of 3-alkyl(aralkyl)-2,4-pentanediones **Ia–Ic** mixtures with the corresponding 1-alkyl(aralkyl)propan-2-ones **IIa–IIc**. The product ratio varied from 1 : 9 to 1 : 1, the total yield reaching 80 mol %. No significant amounts of the Wurtz reaction products were isolated.

1-Adamantylpropan-2-one (**IIa**), 4-phenylbutan-2-one (**IIb**), and undecan-2-one (**IIc**) were apparently formed due to decomposition of the target diketones under the reaction conditions. Optimization of the reaction conditions and elucidation of the side products formation mechanism are outside the scope of this paper and will be reported separately.

Further, we carried out the reactions of 2,4-pentanedione with 1-bromoadamantane or benzyl chloride in the presence of nickel nanoparticles. 3-(Adamant-1-yl)-pentan-2,4-dione (**IIa**) and 2-benzylpentan-2,4-dione (**IIb**), respectively, were obtained, and their structures were confirmed by ^{1}H NMR and mass spectrometry. It was found that in the case of nickel nanoparticles the diketone was the major product (up to 77 wt %), but total yield of the reaction products was somewhat lower than in the presence of copper nanoparticles.

Previously it was shown that metal nanoparticles catalyzed alkylation of ketones with alcohols [9, 10]. As alcohols are generally better available than the corresponding alkyl halides, we attempted alkylation of 2,4-pentanedione with alcohols.

Reaction of alcohols with 2,4-pentanedione in the presence of transition metal nanoparticles was carried out at 110ºC; the volatile product distilled off in the course of the reaction was identified as acetone. The only reaction products were acetates **Va–Vg**, instead of the expected dicarbonyl compounds (Scheme 3).

The above-described reaction is not convenient to prepare the corresponding esters, but it is peculiar from

the fundamental point of view. According to the referenced procedures, such reactions of β-diketones proceed at 150-250ºC or for up to 100 h at 60ºC in the presence of large excess of alkali or hydrogen chloride (the catalyst to diketone molar ratio of ≥ 1 : 1) [11, 12]. In this work we utilized Ni, Co, and Cu nanoparticles without any other catalyst, and the reaction time was of 8 h at 110ºC. The esters **Va**–**Vd** were formed with yield up to 98%. Nickel and cobalt nanoparticles were more active catalysts of the reaction than copper ones.

We suggest that due to the high reactivity, the metal nanoparticles could directly react with alcohols to give the alcoholates: $2ROH + M^0 = (RO)_2M + H_2$. Further reaction stages were similar to the mechanism of alcoholysis in the presence of alkali [11]. Evidently, such transformations resulted in formation of acetone and the corresponding esters.

To conclude, in this work we have reported for the first time that alkyl halides react with β-diketones in the presence of nanodispersed metals to give the alkylation products. The reaction of alcohols with β-diketones in the presence of metal nanoparticles yields corresponding esters.

EXPERIMENTAL

^{1}H NMR spectra were recorded using the Varian Mercury 300 spectrometer (300 MHz, CCl_4 solution, HMDS or TMS as the internal reference). Chromatography–mass spectral analysis was carried out with the Varian Saturn 2100T/GC3900 device.

Copper(II) acetylacetonate. 3.4 g (0.053 mol) of copper nanoparticles and 25 mL (0.244 mol) of 2,4-pentanedione were heated at 110ºC for 1 h. Then the reaction mixture was filtered, excess of 2,4-pentanedione was distilled off, and the solid product was dried to give 13.7 g (0.052 mol, 99%) of copper acetylacetonate. mp 284–286ºC, decomp. (286ºC, decomp. [13]).

3-(Adamantan-1-yl)pentan-2,4-dione (Ia). *a.* A mixture of 3.7 g (0.058 mol) of copper nanoparticles, 24 g (0.24 mol) of 2,4-pentanedione, and 10 g (0.046 mol) of 1-bromoadamantane was heated for 6 h at 100–140ºC. Then the reaction mixture was cooled down, treated with 10 wt % aqueous sulfuric acid, stirred, and filtered. The filtrate was extracted with diethyl ether and washed with water. The ether and excess of 2,4-pentanedione were distilled off from the organic fraction, and the product was isolated by vacuum distillation to give 7 g (0.03 mol, 65%) of 3-(adamantan-1-yl)pentan-2,4-dione **Ia**, bp 222–224ºC (20 mmHg), mp 89–91ºC (mp 90ºC [7]). ^{1}H NMR spectrum, δ, ppm: 1.55–1.64 m (12H, $6CH_2$), 1.92 s (3H, 3CH), 2.07 s (6H, $2CH_2CO$), 3.3 s [1H, $CH(CO)_2$]. Mass spectrum (electron ionization, 70 eV), *m/e* (I_{rel}, %): 234 $[M]^+$ (6), 192 $[M - CH_3 - CO]^+$ (9), 149 $[AdCH_2]^+$ (6), 135 $[Ad]^+$ (100).

b. A mixture of 10 g (0.038 mol) of copper(II) acetylacetonate, 15 g (0.07 mol) of 1-bromoadamantane, and 10 g (0.1 mol) of 2,4-pentanedione was heated at 130–140ºC for 10 h. The reaction product was isolated as described in procedure *a* to give 8.2 g (0.035 mol, 45%) of 3-(adamantan-1-yl)pentan-2,4-dione **Ia.** The product parameters were identical to those of the compound obtained via procedure *a*.

6.3 g (0.033 mol, 47%) of adamantan-1-yl-propan-2-one **IIa** was isolated in the course of the reaction mixture distillation. bp 150–53ºC (20 mmHg), n_D^{20} 1.5016 {bp 102–104ºC (2 mmHg), n_D^{20} 1.5011 [14]}. Mass spectrum (electron ionization, 70 eV), *m/e* (I_{rel}, %): 192 $[M]^+$ (8), 149 $[AdCH_2]^+$ (5), 135 $[Ad]^+$ (100).

c. A mixture of 3 g (0.051 mol) of nickel nanoparticles and 20 g (0.20 mol) of 2,4-pentanedione was heated for 1 h at 110ºC. Then 21.5 g (0.1 mol) of 1-bromoadamantane was added, and the resulting mixture was heated for 12 h at 130–140ºC. The reaction product was isolated as described in procedure *a* to give 15.4 g (0.066 mol, 66%) of 3-(adamantan-1-yl)pentan-2,4-dione **Ia**. The product parameters were identical to those of the compound obtained via procedure *a*.

3-Benzylpentan-2,4-dione (Ib). *a.* A mixture of 3.5 g (0.055 mol) of copper nanoparticles and 17 g (0.17 mol) of 2,4-pentanedione was heated for 1 h at 110ºC. Then 7 g (0.055 mol) of benzyl chloride was added, and the resulting mixture was heated for 8 h at 130-140ºC. The reaction product was isolated as described in preparation of **Ia** to give 5.75 g (0.03 mol, 55%) of 2-benzylpentan-2,4-dione **Ib**, bp 175–178ºC (25 mmHg) {bp 150–154ºC (15 mmHg) [15]}. ^{1}H NMR spectrum, δ, ppm: 2.02 s (6H, $2CH_3CO$), 2.78 d (2H, CH_2), 3.57 s (0.2H, CH of the keto form), 7.06–7.50 m (5H, C_6H_5), 9.76 br.s (0.8H, OH of the enol form).

8.1 g (0.055 mol, 43%) of 4-phenylbutan-2-one **IIb** was isolated in the course of the reaction mixture distillation. bp 234–236ºC (bp 235ºC [16]). ^{1}H NMR

spectrum, δ, ppm: 1.90 s (2H, CH_3), 2.53 t (2H, CH_2, *J* 14.4 Hz), 2.70 t (2H, CH_2, *J* 14.2 Hz), 6.92–7.08 m (5H, C_6H_5).

b. A mixture of 3 g (0.051 mol) of nickel nanoparticles and 10 mL (0.098 mol) of 2,4-pentanedione was heated for 1 h at 110ºC. Then 11.5 mL (0.1 mol) of benzyl chloride was added, and the resulting mixture was heated for 8 h at 130–150ºC. The reaction product was isolated as described in procedure *a* to give 3-benzylpentan-2,4-dione **Ib;** yield 36%, bp 175–178ºC (10 mmHg).

3-*n*-Octylpentan-2,4-dione (Ic). A mixture of 7 g (0.109 mol) of copper nanoparticles and 40 g (0.4 mol) of 2,4-pentanedione was heated for 1 h at 110ºC. Then 47.6 g (0.198 mol) of 1-iodooctane was added, and the resulting mixture was heated for 8 h at 120–130ºC. The reaction product was isolated as described in preparation of **Ia** to give 28.6 g (0.135 mol, 68%) of 3-*n*-octylpentan-2,4-dione **Ic,** bp 145–146ºC (10 mmHg) {145–148ºC (11 mmHg) [17]}. Mass spectrum (electron ionization, 70 eV), *m/e* (I_{rel}, %): 197 [$M - CH_3$]$^+$ (1), 183 [$M - C_2H_5$]$^+$ (2), 169 [$M - C_3H_7$]$^+$ (2), 155 [$M - C_4H_9$]$^+$ (2), 127 [$M - C_6H_{13}$]$^+$ (1), 113 [$M - C_7H_{15}$]$^+$ (2), 71 [$CH_3COCH_2CH_2$]$^+$ (100), 57 [CH_3COCH_2]$^+$ (70), 43 [CH_3CO]$^+$ (26).

4.8 g (0.029 mol, 15%) of *n*-undecan-2-one **IIc** was isolated in the course of the reaction mixture distillation. bp 221–223ºC (bp 226ºC [18]). ^{1}H NMR spectrum, δ, ppm: 0.83 t (3H, CH_3, *J* 11.4 Hz), 1.11-1.51 m (14H, $7CH_2$), 1.96 s (3H, $COCH_3$), 2.28 t (2H, CH_2CO, *J* 14 Hz).

***n*-Hexyl acetate (Va)**. A mixture of 3 g (0.051 mol) of nickel nanoparticles and 11.7 g (0.117 mol) of 2,4-pentanedione was heated for 1 h at 110ºC. Then 13.5 mL (0.108 mol) of 1-hexanol was added, and the resulting mixture was heated for 4 h at 130–140ºC, the evolving acetone being distilled off. The reaction mixture was filtered, and *n*-hexyl acetate was isolated by distillation. Yield 11.8 g (0.082 mol, 76%), bp 170–172ºC (169.2ºC [18]). ^{1}H NMR spectrum, δ, ppm: 0.84 t (3H, CH_3, *J* 13.2 Hz), 1.26 m (6H, $3CH_2$), 1.41–1.51 m (2H, CH_2), 1.92 s (3H, CH_3COO), 3.93 t (2H, CH_2O, *J* 13.5 Hz).

***n*-Octyl acetate (Vb)** was prepared similarly from 3 g (0.051 mol) of nickel nanoparticles, 12 g (0.12 mol) of 2,4-pentanedione, and 13 g (0.1 mol) of 1-octanol. Yield 12.7 g (0.074 mol, 74%), bp 210–212ºC (bp 210ºC [19]). ^{1}H NMR spectrum, δ, ppm: 0.83 t (3H, CH_3, *J* 12 Hz), 1.24 m (10H, $5CH_2$), 1.53 m (2H, CH_2), 1.89 s (3H, CH_3COO), 3.91 t (2H, CH_2O, *J* 13.5 Hz).

Cyclohexyl acetate (Vc). *a.* Prepared similarly from 6.4 g (0.1 mol) of copper nanoparticles, 14.6 g (0.146 mol) of 2,4-pentanedione and 9.6 g (0.096 mol) of cyclohexanol. Yield 9.8 g (0.068 mol, 71%), bp 175–177ºC (173ºC [19]). ^{1}H NMR spectrum, δ, ppm: 1.17–1.31 m (6H, $3CH_2$), 1.71 m (4H, $2CH_2$), 1.89 s (3H, CH_3COO), 4.58 c (1H, CH–O).

b. Prepared similarly from 3 g (0.051 mol) of nickel nanoparticles, 12 g (0.12 mol) of 2,4-pentanedione, and 10.8 g (0.1 mol) of cyclohexanone. Yield 10.5 g (0.073 mol, 73%), bp 175–177ºC.

Benzyl acetate (Vd). *a.* Prepared similarly from 3 g (0.051 mol) of cobalt nanoparticles, 12 g (0.12 mol) of 2,4-pentanedione, and 10.8 g (0.1 mol) of benzyl alcohol. Yield 14.7 g (0.098 mol, 98%), bp 210–212ºC (213.5ºC [18]). ^{1}H NMR spectrum, δ, ppm: 1.85 s (3H, CH_3COO), 4.91 s (2H, CH_2O), 7.09–7.17 m (5H, C_6H_5).

b. Prepared similarly from 3 g (0.051 mol) of nickel nanoparticles, 12 g (0.12 mol) of 2,4-pentanedione, and 10.8 g (0.1 mol) of benzyl alcohol. Yield 14.5 g (0.097 mol, 97%), bp 209–213ºC.

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