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Alkylation of Dicarbonyl Compounds with 1-Bromoadamantane in the Presence of Metal Complex Catalysts

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Abstract—Adamantyl-substituted dicarbonyl compounds have been synthesized by reactions of 1-bromoadamantane with ethyl acetoacetate, 1,3-diphenylpropane-1,3-dione, and dimethyl malonate in the presence of iron and manganese complexes.

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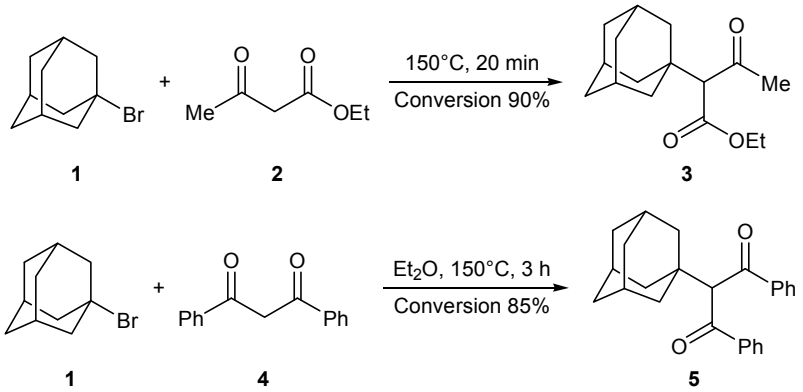
Adamantyl-substituted dicarbonyl compounds are important adamantane derivatives. They attract interest as starting materials for the synthesis of nitrogen heterocycles possessing high biological activity [1]. The most common methods for the synthesis of adamantyl-substituted β-dicarbonyl compounds are based on their reaction with adamantan-1-ol [2–7]. Adamantylation of dicarbonyl compounds is carried out in the presence of Lewis acids such as $Sc(OTf)_3$, $Ga(OTf)_3$, $In(OTf)_3$, or $Cu(OTf)_3$ [2, 3]. Another method is based on the exchange reaction of 1-bromoadamantane with metal acetylacetonates: $Co(acac)_2$, $Cu(acac)_2$, and $Pd(acac)_2$ [4, 5]. 2-Adamantyl-substituted diethyl malonate was prepared by acylation of diethyl malonate with adamantane-1-carbonyl chloride and (adamantan-1-yl)-acetyl chloride [6, 7]. However, these procedures are characterized by low yields, while the exchange reaction requires stoichiometric amount of the metal complex [4, 5].

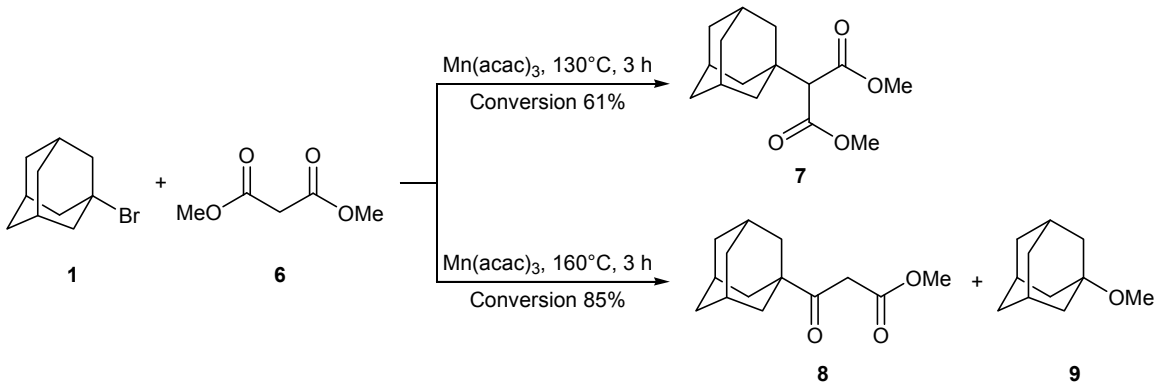
The goal of the present study was to find new efficient metal complex catalysts for the adamantylation of β-dicarbonyl compounds with 1-bromoadamantane.

1-Bromoadamantane (**1**) reacted with ethyl acetoacetate (**2**) in the presence of $Fe(acac)_3$ to give ethyl 2-(adamantan-1-yl)-3-oxobutanoate (**3**) at 150°C (Scheme 1). The reaction was complete in 20 min. Prolonged reaction time affected neither the conversion of **1** nor the yield of **3**. Ethyl acetoacetate (**2**) was taken in excess since it simultaneously acted as reagent and solvent. Taking into account that the initial compounds are solids, analogous reaction of **1** with 1,3-diphenylpropane-1,3-dione (**4**) was carried out in diethyl ether in a sealed ampule (Scheme 2; see table). No reaction was observed in other solvents (hexane,

Scheme 1.



Scheme 2.



chloroform, DMF, DMSO). Prolonged heating resulted in tarring. Such metal complexes as $Rh(PPh_3)_3Cl$, $Pd(PPh_3)_2Cl_2$, $Mo(CO)_6$, and $Cr(CO)_6$ were inactive in this reaction.

An important adamantane derivative is dimethyl 2-(adamantan-1-yl)malonate (**7**). It is used as precursor to adamantane-containing C_{11}–C_{12} esters that are efficient friction modifiers due to their ability to form thin protecting films on a metal surface [8]. The reaction of **1** with dimethyl malonate was catalyzed by $Mn(acac)_3$, and its direction depended on the temperature. Compound **7** was formed in 3 h at 130°C at a **1**:**6**:$Mn(acac)_3$ ratio of 100:100:(1–3). Raising the temperature to 160°C led to the formation of a mixture of methyl 3-(adamantan-1-yl)-3-oxopropanoate (**8**, 48%) and 1-methoxyadamantane (**9**, 34%). Dimethyl malonate was taken in excess to ensure reaction medium.

The structure of the isolated compounds was determined by spectral methods, as well as by comparing with authentic samples and published data [2].

EXPERIMENTAL

The IR spectra were recorded in KBr or mineral oil on a Bruker Vertex 79V spectrometer. The ^1H and ^{13}C NMR spectra were measured from solutions in $CDCl_3$ on a Bruker Avance-400 spectrometer at 400.13 and 100.62 MHz, respectively, relative to tetramethylsilane. The mass spectra were obtained on a Shimadzu GCMS-QP2010Plus instrument (SPB-5 capillary column, 30 m×0.25 mm; carrier gas helium; oven temperature programming from 40 to 300°C at a rate of 8 deg/min; injector temperature 280°C; ion source temperature 200°C; electron impact, 70 eV). The elemental compositions were determined on a Carlo Erba 1106 analyzer.

The progress of reactions, purity of products, and compositions of reaction mixtures were monitored by GLC on a Chrom-5 chromatograph equipped with a 1.2-m×3-mm column packed with 5% of SE-30 on Chromaton N-AW-HMDS; oven temperature programming from 50 to 280°C at a rate of 8 deg/min; carrier

Yields of 2-(adamantan-1-yl)-1,3-diphenylpropane-1,3-dione (**5**) in the reaction of 1,3-diphenylpropane-1,3-dione (**4**) with 1-bromoadamantane in diethyl ether, catalyzed by metal complexes

Catalyst	Molar ratio catalyst:**1**:**4**	Temperature, °C	Reaction time, h	Yield of **5**, %
$Fe(acac)_3$	3:100:100	150	3	79
$Fe(acac)_3$	3:100:100	180	1	64
$Mn(acac)_3$	3:100:100	160	3	75
$Mn(acac)_3$	5:100:100	180	1	72
$Fe(acac)_2$	5:100:100	160	3	73
$Fe(acac)_3 + Et_3N$[a]	3:100:100	100	6	28
$Fe(acac)_3 + Et_3N$	3:100:100	150	3	36
$Fe(acac)_3$[a]	3:100:100	100	6	24

[a] In 1,4-dioxane.

gas helium. All initial compounds were commercial products (from Acros Organics) with a purity of no less than 99%.

General procedure for the alkylation of dicarbonyl compounds with 1-bromoadamantane. The reactions were carried out in a 20-mL glass ampule or a 17-mL stainless-steel high-pressure microreactor (the results of parallel runs almost did not differ). An ampule (microreactor) was charged under argon with 0.3 mmol $Fe(acac)_3$, 10 mmol of 1-bromoadamantane (**1**), and 10–15 mmol of β-dicarbonyl compound. The ampule was sealed (the reactor was hermetically closed) and heated for 0.3–3 h at 150–170°C. When the reaction was complete, the ampule (reactor) was cooled to room temperature and opened, the solvent was distilled off, and the residue was purified by column chromatography on silica gel using hexane–ethyl acetate as eluent. Given below are isolated yields.

Ethyl 2-(adamantan-1-yl)-3-oxobutanoate (3). Yield 76%, bp 146–149°C (1 mm). IR spectrum, ν, cm^{-1}: 2978, 2849 (C–H); 1745, 1703 (C=O). ^1H NMR spectrum, δ, ppm: 1.25 t (3H, J = 7 Hz), 1.60–1.79 m (12H, CH_2), 1.96 m (3H, CH), 2.21 s (3H), 3.17 s (1H, CH), 4.12–4.17 m (2H, OCH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.28 (CH_3), 28.64 (CH), 32.21 (CH_3), 36.70 (CH_2), 37.05 (CH_2), 40.13 (C^1), 60.82 (CH), 69.95 (CH_2), 168.75 (C=O), 203.45 (C=O). Mass spectrum, m/z (I_{rel}, %): 264 (3) $[M]^+$, 222 (10.5), 193 (0.6), 176 (1.1), 165 (4), 136 (12), 135 (100), 119 (7.5), 106 (1.6), 105 (4.7), 93 (10), 79 (10), 43 (15). Found, %: C 72.91; H 9.38. $C_{16}H_{24}O_3$. Calculated, %: C 72.69; H 9.15. M 264.36.

2-(Adamantan-1-yl)-1,3-diphenylpropane-1,3-dione (5). Yield 79%, mp 210–211°C. IR spectrum, ν, cm^{-1}: 2911, 2849 (C–H); 1707, 1739 (C=O). ^1H NMR spectrum, δ, ppm: 1.53–1.94 m (12H, CH_2), 2.04 m (3H, CH), 5.41 s (1H, CH), 7.35–7.39 m (4H), 7.47–7.51 m (2H), 7.88–7.90 m (4H). ^{13}C NMR spectrum, δ_C, ppm: 29.13 (CH), 39.86 (CH_2), 40.30 (CH_2), 45.53 (C^1), 63.61 (CH); 128.47, 128.84, 133.19, 138.38 (Ph); 194.20 (C=O). Mass spectrum, m/z (I_{rel}, %): 358 (2.7) $[M]^+$, 340 (21), 253 (19), 252 (10), 135 (5), 105 (100), 93 (4), 92 (6), 91 (7), 79 (6), 77 (33), 67 (2), 41 (2). Found, %: C 83.91; H 7.60. $C_{25}H_{26}O_2$. Calculated, %: C 83.76; H 7.31. M 358.47.

Dimethyl 2-(adamantan-1-yl)malonate (7). Yield 90%, bp 129–130°C (1 mm). ^1H NMR spectrum, δ, ppm: 1.59 (6H, CH_2), 1.90 s (6H, CH_2), 2.06 s (3H, CH), 3.31 s (1H, CH), 3.64 s (6H, OCH_3). ^{13}C NMR spectrum, δ_C, ppm: 28.50 (CH), 36.45 (CH_2), 39.91 (CH_2), 40.24 (CH_2), 41.01 (CH_2), 42.62 (C^1), 49.20 (OCH_3), 52.35 (CH), 167.09 (C=O). Mass spectrum, m/z (I_{rel}, %): 233 (67), 215(9), 191 (50), 173 (3), 149 (4.5), 135 (35), 133 (43), 117 (24), 105 (16), 91 (35), 79 (14), 43 (100). Found, %: C 67.91; H 8.98. $C_{15}H_{22}O_4$. Calculated, %: C 67.64; H 8.33. M 266.33.

Methyl 3-(adamantan-1-yl)-3-oxopropanoate (8). Yield 48%, bp 176–178°C (10 mm). IR spectrum, ν, cm^{-1}: 2910, 2851 (C–H); 1737, 1693 (C=O). ^{13}C NMR spectrum, δ_C, ppm: 30.73 (CH), 39.91 (CH_2), 40.24 (CH_2), 42.62 (CH_2), 49.20 (C^1), 52.35 (CH_3), 167.14 (C=O), 204.52 (C=O). Mass spectrum, m/z (I_{rel}, %): 192 (11), 149 (4.8), 135 (100), 117 (12), 92 (15), 79 (12), 43 (34). Found, %: C 71.71; H 8.98. $C_{14}H_{20}O_3$. Calculated, %: C 71.16; H 8.53. M 236.3.

1-Methoxyadamantane (9). Yield 34%, bp 67–68°C (3 mm). ^{13}C NMR spectrum, δ_C, ppm: 32.62 (CH), 36.41 (CH_2), 40.10 (CH_2), 48.39 (OCH_3), 79.35 (C^1). Mass spectrum, m/z (I_{rel}, %): 166 (14) $[M]^+$, 135 (6), 110 (9), 109 (100), 94 (8), 79 (8), 41 (7). Found, %: C 79.71; H 11.25. $C_{11}H_{18}O$. Calculated, %: C 79.46; H 10.91. M 166.26.

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