

Ferric perchlorate-promoted reaction of [60]fullerene with β -keto esters

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The ferric perchlorate-promoted reaction of [60]fullerene (C_{60}) with ethyl 2-methylacetoacetate generates fullereryl hemiketal as a mixture of *trans* and *cis* isomers, while the reaction with ethyl acetoacetate gives a C_{60} -fused dihydrofuran derivative. A possible reaction mechanism for the formation of these products is proposed.

[60]fullerene, ferric perchlorate, β -keto esters, fullereryl hemiketal, C_{60} -fused dihydrofuran derivative

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Various types of reactions for the functionalization of fullerenes have been developed over the past 20 years [1–3]. However, metal salt-promoted reactions of fullerenes have been somewhat neglected. Recently, we have investigated [60]fullerene (C_{60}) reactions mediated by metal salts such as $Mn(OAc)_3$ [4–16], $Cu(OAc)_2$ [7], $Pb(OAc)_4$ [12], $Pd(OAc)_2$ [17,18], and $Fe(ClO_4)_3$ [19–21] to synthesize certain desired fullerene derivatives. $Fe(ClO_4)_3$ has been employed to promote the reaction of C_{60} with nitriles [19], aldehydes/ketones [20], and substituted malonate esters [21] to prepare C_{60} -fused oxazoles, 1,3-dioxolanes, and lactones. In continuation of our interest in the $Fe(ClO_4)_3$ -mediated reactions of C_{60} [19–21], we report the $Fe(ClO_4)_3$ -promoted reaction of C_{60} with representative β -keto esters such as ethyl 2-methylacetoacetate and ethyl acetoacetate to give fullereryl hemiketal and C_{60} -fused dihydrofuran derivatives.

1 Experimental

1.1 Materials

C_{60} (>99.9 %) was purchased from Henan Puyang Co., Ltd.

Ferric(III) perchlorate was purchased from Alfa Aesar. Ethyl 2-methylacetoacetate, ethyl acetoacetate, acetic anhydride, and *o*-dichlorobenzene were all AR grade reagents. The reaction products were purified by flash chromatography over silica gel (200–300 mesh).

1.2 Instrumentation

The UV-vis spectra were measured in $CHCl_3$ using a Shimadzu UV-2501 PC spectrometer. IR spectra were taken on a Shimadzu FTIR-8600 spectrometer with KBr pellets. 1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AVANVE 300 spectrometer. Mass spectra were recorded on a BIFLEXIII MALDI-TOF mass spectrometer with 4-hydroxy- α -cyanocinnamic acid as the matrix.

1.3 Preparation of fullereryl hemiketal 1

A mixture of C_{60} (36.0 mg, 0.05 mmol), ethyl 2-methylacetoacetate (15 μ L, 0.1 mmol), and acetic anhydride (95 μ L, 1.00 mmol) was dissolved in *o*-dichlorobenzene (6 mL), and then the resulting solution was deoxygenated by means of a

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nitrogen stream for 10 min. After $\text{Fe}(\text{ClO}_4)_3 \cdot x\text{H}_2\text{O}$ (46.0 mg, 0.10 mmol, dissolved in 1 mL of acetonitrile) was added, the reaction mixture was heated under a nitrogen atmosphere with vigorous stirring in an oil bath preset at 80°C for 20 min. The reaction solution was passed through a silica gel (100–200 mesh) plug to remove any insoluble material. After the solvent was vacuum evaporated, the residue was separated on a silica gel (100–200 mesh) column with carbon disulfide as the eluent to give unreacted C_{60} (24.2 mg, 67%), then with carbon disulfide/toluene as the eluent for *trans*-**1** (6.5 mg, 15%) and then *cis*-**1** (2.6 mg, 6%). *trans*-**1**: ^1H NMR (300 MHz, $\text{CS}_2/\text{CDCl}_3$) δ 5.70 (s, 1H), 4.34 (dq, $J=10.8, 7.1$ Hz, 1H), 4.25 (dq, $J=10.8, 7.1$ Hz, 1H), 2.33 (s, 3H), 2.11 (s, 3H), 1.24 (t, $J=7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $\text{CS}_2/\text{CDCl}_3$ with $\text{Cr}(\text{acac})_3$ as the relaxation reagent, all 1C unless indicated) δ 172.97, 151.80, 151.00, 150.97, 148.22, 147.00, 146.60, 145.68, 145.51 (2C), 145.44, 145.32 (2C), 145.15, 145.11, 145.03, 144.95, 144.82, 144.79, 144.76, 144.70, 144.43, 144.30 (2C), 144.23 (2C), 144.20, 144.17 (2C), 143.83, 143.68, 143.50, 143.42, 141.99, 141.90, 141.84, 141.78, 141.68 (2C), 141.45 (2C), 141.33 (3C), 141.08, 140.99, 140.83 (2C), 140.59, 140.50, 140.23, 138.90, 138.67, 138.13 (2C), 137.75, 137.21, 137.16, 136.37, 107.65, 97.55 ($\text{sp}^3\text{-C}$ of C_{60}), 72.83 ($\text{sp}^3\text{-C}$ of C_{60}), 63.74, 61.63, 22.99, 22.76, 13.33; FT-IR ν/cm^{-1} (KBr) 2924, 1708, 1432, 1378, 1279, 1111, 1042, 1011, 938, 575, 526; UV-vis (CHCl_3) $\lambda_{\text{max}}/\text{nm}$ ($\log \epsilon$) 256 (4.93), 314 (4.45), 427 (3.24), 691 (2.24); MS (-MALDI TOF) m/z 880 (M^+). *cis*-**1**: ^1H NMR (300 MHz, $\text{CS}_2/\text{CDCl}_3$) δ 4.50 (dq, $J=10.9, 7.1$ Hz, 1H), 4.37 (dq, $J=10.9, 7.1$ Hz, 1H), 3.12 (s, 1H), 2.15 (s, 3H), 2.08 (s, 3H), 1.48 (t, $J=7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $\text{CS}_2/\text{DMSO-}d_6$ with $\text{Cr}(\text{acac})_3$ as the relaxation reagent, all 1C unless indicated) δ 169.39, 152.56, 152.16, 151.98, 148.10, 146.10, 145.51, 144.59, 144.40 (2C), 144.35, 144.32, 144.29 (2C), 144.08 (3C), 144.03, 143.93, 143.79, 143.72, 143.52, 143.47, 143.39, 143.21 (3C), 143.19, 143.10, 143.04, 142.86 (2C), 142.56, 141.08, 141.02, 140.79, 140.71 (3C), 140.45, 140.40 (2C), 140.25 (2C), 140.13, 140.08, 140.01, 139.76, 139.69, 139.66, 139.53, 137.71, 137.57 (2C), 137.44, 137.39, 136.82, 136.26, 135.98, 105.67, 95.78 ($\text{sp}^3\text{-C}$ of C_{60}), 73.52 ($\text{sp}^3\text{-C}$ of C_{60}), 65.88, 59.85, 21.10, 17.46, 13.10; FT-IR ν/cm^{-1} (KBr) 2924, 1728, 1448, 1381, 1256, 1158, 1111, 1011, 932, 575, 527; UV-vis (CHCl_3) $\lambda_{\text{max}}/\text{nm}$ ($\log \epsilon$) 255 (5.00), 314 (4.52), 427 (3.30), 693 (2.49); MS (-MALDI TOF) m/z 880 (M^+).

1.4 Preparation of fullerene dihydrofuran **2**

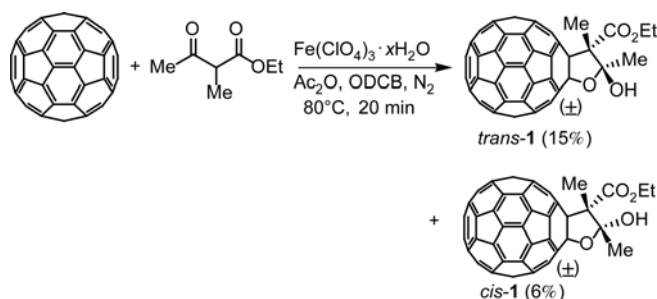
Using the same procedure as for the preparation of fullerene hemiketal **1**, the reaction of C_{60} (36.0 mg, 0.05 mmol) with ethyl acetoacetate (13 μL , 0.1 mmol), $\text{Fe}(\text{ClO}_4)_3 \cdot x\text{H}_2\text{O}$ (46.0 mg, 0.10 mmol), and acetic anhydride (95 μL , 1.00 mmol) at 80°C for 30 min gave the unreacted C_{60} (26.8 mg, 74%)

and C_{60} -fused dihydrofuran derivative **2** [7,22–24] (8.4 mg, 20%).

2 Results and discussion

Our success in the $\text{Fe}(\text{ClO}_4)_3$ -mediated reaction of C_{60} with substituted malonate esters [21] prompted us to extend the substrates to β -keto esters such as ethyl 2-methylacetoacetate and ethyl acetoacetate in the presence of acetic anhydride (Ac_2O).

The reaction of C_{60} with ethyl 2-methylacetoacetate was found to exclusively give hemiketal **1** as a mixture of the *trans* and *cis* isomers rather than a C_{60} -fused lactone (Scheme 1). The *trans* and *cis* isomers of hemiketal **1** differed significantly in polarity and could be easily separated by column chromatography over silica gel giving 15% and 6% yields (45% and 18% based on consumed C_{60}), respectively.



Scheme 1 $\text{Fe}(\text{ClO}_4)_3$ -mediated reaction of C_{60} with 2-methylacetoacetate in the presence of Ac_2O .

The identities of both *trans*-**1** and *cis*-**1** isomers were confirmed by MS, ^1H NMR, ^{13}C NMR, FT-IR, and UV-vis spectra. In the ^1H NMR spectra of both *trans*-**1** and *cis*-**1** isomers, the two methylene protons in the ethoxy group were nonequivalent and split as two double quartets due to the adjacent chiral center, which was analogous to those of C_{60} -fused lactones [21]. The assignments of *trans*-**1** and *cis*-**1** isomers were confirmed by nuclear Overhauser enhancement spectroscopy (NOESY) spectra (Figure 1), where a cross peak between the methyl protons (δ 1.48) of the ethoxy group and hydroxyl proton (δ 3.12) could only be found in the *cis*-**1** isomer. ^{13}C NMR spectra of *trans*-**1** and *cis*-**1** isomers showed similar spectral patterns. The two sp^3 -carbons of the C_{60} cage were located at δ 72.83–73.52 and δ 95.78–97.55, and the observation of at least 46 lines in the δ 135–153 range for the 58 sp^2 -carbons of the C_{60} skeleton including some overlapped ones was consistent with the C_1 symmetry of their molecular structures. The chemical shift for the hemiketal carbon in the *trans* isomer (δ 107.65) was shifted downfield about 2 relative to that in the *cis* isomer (δ 105.67). A similar phenomenon has been previously observed [25,26].

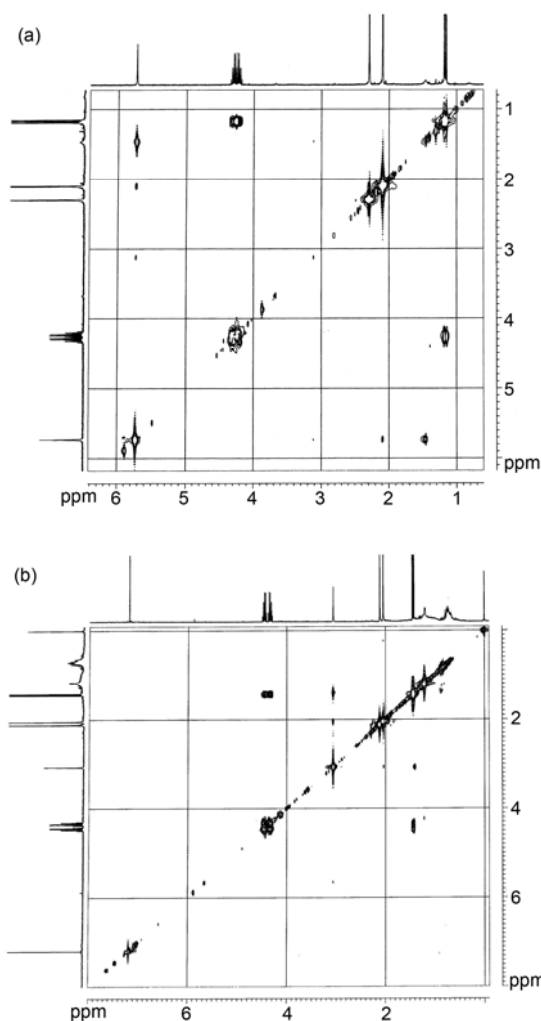


Figure 1 (a) NOESY spectra of the *trans* isomer of hemiketal **1**. (b) NOESY spectra of the *cis* isomer of hemiketal **1**.

Theoretical calculations were further exploited to support our assignments of *trans-1* and *cis-1* isomers. The relative energy of the *trans-1* and *cis-1* isomers calculated at the B3LYP/6-31G* level showed that the *trans-1* isomer was 0.65 kcal/mol more stable than the *cis-1* isomer (Figure 2), consistent with the higher product yield of the *trans-1* isomer.

Fullerenyl hemiketals and kemiacetals are scarce in the literature [27]. Here we provide a new protocol to access fullerenyl hemiketals via a simple one-pot procedure. In addition, the hydroxy group of hemiketals **1** has the potential for further functionalization such as esterification and etherification to obtain various fullerene derivatives.

In comparison, the reaction of C_{60} with ethyl acetoacetate afforded neither a C_{60} -fused lactone nor a hemiketal derivative, instead yielding mainly the known C_{60} -fused dihydrofuran derivative **2** [7,22–24] in 20% yield (77% based on consumed C_{60}) (Scheme 2).

Although the exact pathway is not known for the formation of hemiketal **1** and C_{60} -fused dihydrofuran derivative **2**, a possible reaction mechanism is shown in Scheme 3.

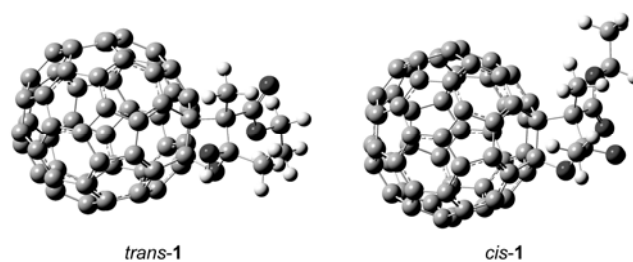
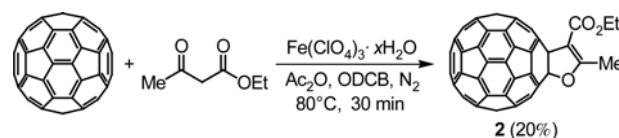
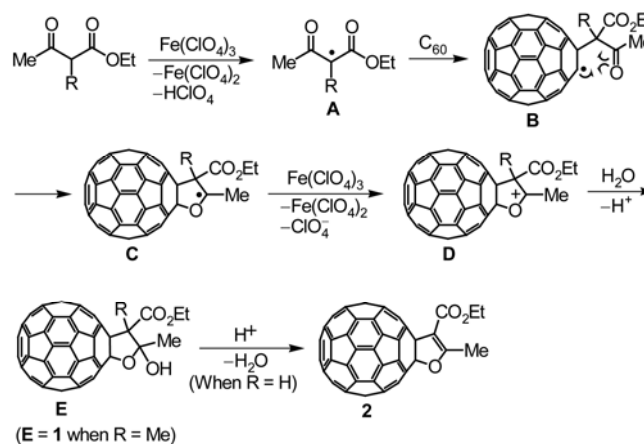


Figure 2 Optimized geometries of the *trans* and *cis* isomers of hemiketal **1**.



Scheme 2 $Fe(ClO_4)_3$ -mediated reaction of C_{60} with ethyl acetoacetate in the presence of Ac_2O .



Scheme 3 Proposed reaction mechanism for the formation of products **1** and **2**.

Ethyl 2-methylacetoacetate, or ethyl acetoacetate reacts with $Fe(ClO_4)_3$ to generate radical **A** along with the formation of $Fe(ClO_4)_2$ and $HClO_4$ [28,29]. Addition of radical **A** to C_{60} produces fullerene radical **B**, which undergoes intramolecular cyclization to give radical **C**. Oxidation of radical **C** by another molecule of $Fe(ClO_4)_3$ results in cation **D** accompanied by counteranion ClO_4^- and $Fe(ClO_4)_2$. However, an alternative pathway leading to **D** via the oxidation of **B** followed by cyclization cannot be excluded. The addition of H_2O , originated from the water of hydration in $Fe(ClO_4)_3 \cdot xH_2O$ or concomitant water in the system, to cation **D** with the loss of H^+ results in **E**, which is actually hemiketal **1** when $R=Me$. In the case of $R=H$, elimination of H_2O from intermediate **E** catalyzed by H^+ gives the C_{60} -fused dihydrofuran derivative **2**. Other alternative reaction mechanisms may exist. For example, when ethyl acetoacetate is employed as the substrate, a reaction pathway via enolate salt

formation followed by homolytical addition to C₆₀ and subsequent cyclization may also operate [7]. In addition, direct loss of H⁺ from intermediate **D** can also produce a C₆₀-fused dihydrofuran derivative **2** when R = H.

3 Conclusion

The Fe(ClO₄)₃-mediated reaction of C₆₀ with β-keto esters such as ethyl 2-methylacetoacetate and ethyl acetoacetate under similar reaction conditions resulted in fullereryl hemiketal **1** and C₆₀-fused dihydrofuran derivative **2**, respectively. A plausible reaction mechanism involving the same type of intermediates in the first several steps is proposed to explain the formation of both products **1** and **2**.

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