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Full Paper

A Convenient Synthesis of Novel Meldrum's Acid C_{60} Fullerene Derivatives

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A series of novel Meldrum's acid C_{60} derivatives were prepared in moderate yields from a convenient one-pot reaction of C_{60}, the Meldrum's acid derivatives, I_2 and 1,8-diazabicyclo-[5,4,0]-undec-7-ene (DBU) in toluene at room temperature under nitrogen atmosphere. All the new compounds were fully characterized by the spectral data and elemental analysis. A carbene intermediate mechanism was proposed for this reaction.

Keywords fullerene C_{60}, Meldrum's acid derivative, carbene, addition, synthesis

Introduction

Functionalization of fullerene is one of the major strategies in exploring the practice use for fullerenes. In the past years, much success has been achieved in the fields of supramolecular chemistry, material science and life science. For example carbazole-linked C_{60} adducts,[1] "Teflon ponytail" fullerene adducts[2] and C_{60}-tetrathiafulvalene[3] have been successfully prepared. They all show the unique physical and chemical properties. Our research group has synthesized a series of C_{60}-pyrrolidine derivatives via one-pot three-component reaction of C_{60}, amino acid and aldehydes which involved 1,3-dipole cycloaddition process.[4,5]

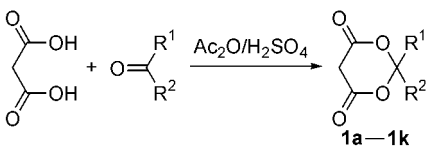
It is well known that malonate esters can add to C_{60} affording corresponding addition products by Bingel-reaction.[6] As the cyclic analog of malonate, Meldrum's acid is a remarkable reagent of versatile reactivity. To the best of our knowledge, the reaction of C_{60} with Meldrum's acid derivatives has not been reported. We now wish to report a simple and efficient synthesis of novel C_{60} Meldrum's acid derivatives under mild reaction conditions.

Results and discussion

A series of Meldrum's acids were first prepared from the reaction of malonate acid with different ketones according to the literature method,[7] all new products **1** were fully characterized (Table 1).

Our synthetic strategy employed common fullerene chemistry, namely, the Hirsch-Bingel reaction, which has been well-studied and utilized for fullerene derivatization. Firstly 0.1 mmol of **1a** was reacted with equal mole C_{60}, I_2 and DBU in dry toluene (30 mL). This reaction took place smoothly at room temperature under N_2 atmosphere. After stirring for 3 h, TLC analysis showed that the starting Meldrum's acid **1a** consumed completely. The reaction mixture was chromatographied using toluene as eluent, and the expected addition product **2a** was obtained in 30% yield which is a black solid [Eq. (1)].

Table 1 Preparation of the Meldrum's acid derivatives **1**



Entry	R^1, R^2	Product	m.p./℃	Yield/%
1	CH_3, CH_3	**1a**[a]	95 (96[b])	80
2	CH_3, CH_2CH_3	**1b**	liquid	48
3	CH_3, $CH_2CH(CH_3)CH_3$	**1c**	42	50
4	CH_3, *n*-C_6H_{13}	**1d**	75	58
5	$(CH_2)_4$	**1e**[a]	64 (65[b])	63
6	$(CH_2)_5$	**1f**[a]	93 (94[b])	60
7	CH_3, Ph	**1g**	liquid	25
8	CH_3, 4-CH_3-C_6H_4	**1h**	48	28
9	CH_3, 4-NO_2-C_6H_4	**1i**	65	23
10	$C_6H_5CH_2$, $C_6H_5CH_2$	**1j**	liquid	20
11	CH_3, 4-F-C_6H_4	**1k**	liquid	13

[a] Known product, all the solid products were recrystallized from ethanol (98%). [b] Literature reported m.p.

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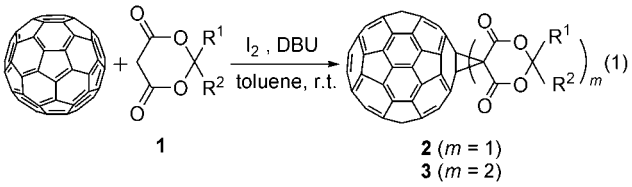


The C_{60} Meldrum's acid derivative **2a** gave the satisfied elemental analysis and showed basic peak at 863 (M^++1) in ESI-MS. The ^{1}H NMR spectrum of **2a** exhibited two methyl groups at δ 2.15. Infrared spectrum also showed the strong carbonyl absorption at 1758 cm^{-1}, and another strong band at 526 cm^{-1} due to C_{60} feature absorption was also observed.

In order to improve the yield of **2a**, different ratios of starting materials were tried (Table 2).

Table 2 Effect of the substrates' molar ratios of **1a**, DBU, I_2 and C_{60} on the reaction[a]

Entry	Molar ratio of **1a** : DBU : I_2 : C_{60}	Yield[b] of **2a**/%	Yield[b] of (**3a**+**3a'**)/%
1	1 : 1 : 1 : 1	30	0
2	2 : 2 : 2 : 1	35	10
3	3 : 3 : 3 : 1	41	18
4	4 : 4 : 4 : 1	30	25
5	5 : 5 : 5 : 1	25	29

[a] The reaction was carried at room temperature in the nitrogen atmosphere. [b] Isolated yields.

As showed in Table 2, increasing the amounts of **1a**, DBU and I_2 favored the reaction. When the molar ratio of **1a**, DBU, I_2, C_{60} is 3 : 3 : 3 : 1, the highest yield of **2a** was 41%, while the yield of double addition product **3a**+**3a'** also increased (Table 2, Entry 3). Further increasing the proportion, the reaction proceeded vigorously and the yield of multi-addition product **3a**+**3a'** increased to 29%, while that of **2a** decreased (Table 2, Entry 4, 5). The bisadducts **3a**, **3a'** is a mixture of two regioisomeric which can easily be separated by chromatography using toluene as eluent. Two isomers were determined from ^{1}H NMR, IR, ESI-MS and elemental analysis seperately. Two isomers both showed basic peak at 1005 in ESI-MS and similar data of elemental analysis. Only ^{1}H NMR data of **3a**, **3a'** are different because of regioisomerization.[8]

It was found that the reaction temperature also effected the yield of **2a**, and room temperature is most suitable for this reaction. Under higher temperature, the yield of mono-addition product **2a** decreased sharply because of the appearance of a great deal of multi-addition products (Table 3).

As showed in Table 4, the optimal reaction time is 3 h. It was also noticed that when the reaction was carried out in air, no expected addition products **2** was isolated. Under the optimal reaction conditions, a series of C_{60} Meldrum's acid derivatives were prepared, all results are summarized in Table 5.

Table 3 Effects of temperature on the reaction of **1a**, DBU, I_2 and C_{60}[a]

Entry	Temperature/℃	Yield[b]/%
1	0	8
2	20	39
3	30	41
4	40	30
5	50	25
6	60	15

[a] The reaction was carried out under nitrogen atmosphere, the molar ratio of **1a**, DBU, I_2 and C_{60} was 3 : 3 : 3 : 1. [b] Isolated yields.

Table 4 Effects of time on the reaction of **1a**, DBU, I_2 and C_{60}[a]

Entry	Time/min	Yield[b]/%
1	30	8
2	60	20
3	90	30
4	120	35
5	150	38
6	180	41
7	210	41
8	240	41

[a] The reaction was carried out under nitrogen atmosphere, the molar ratio of **1a**, DBU, I_2 and C_{60} was 3 : 3 : 3 : 1. [b] Isolated yields.

Table 5 Preparation of Meldrum's acid C_{60} derivatives **2**[a]

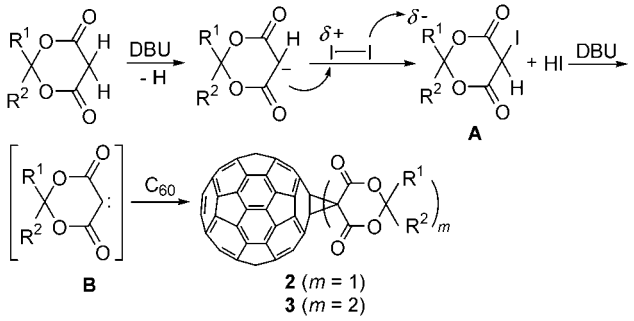
Entry	Reactant	Product	Yield[b]/%
1	**1a**	**2a**	41
2	**1b**	**2b**	41
3	**1c**	**2c**	40
4	**1d**	**2d**	39
5	**1e**	**2e**	41
6	**1f**	**2f**	39
7	**1g**	**2g**	35
8	**1h**	**2h**	38
9	**1i**	**2i**	33
10	**1j**	**2j**	30
11	**1k**	**2k**	28

[a] Reaction was carried out at room temperature under nitrogen atmosphere, the molar ratio of **1**, DBU, I_2 and C_{60} was 3 : 3 : 3 : 1. [b] Isolated yields.

A possible reaction pathway for the formation of **2** and **3** was proposed as follows (Scheme 1).

Under basic reaction condition, **1** reacted with I_2 to give the α-iodine-subsituted product **A** which was eliminated HI by DBU to form the carbene intermediate **B**. Then it added to C_{60} to form the mono-addition product **2** or double addition product **3** depending on the concentration of carbene intermediate **B** in the reaction system.[9]

Scheme 1 Proposed reaction pathway for the formation of **2** and **3**



Experimental

All reagents and solvents were purified before use. C_{60} (99.9%) was purchased from Wuhan University. Other reagents were purchased from Sigma Chemical Co. (St. Louis, MO, USA). ^{1}H NMR and ^{19}F NMR spectra were recorded in $CDCl_3$ using Bruker AM-300 instruments with Me_4Si and CF_3COOH ($\delta_{CFCl_3} = \delta_{CF_3COOH} - 77$) as the internal standard respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Lower resolution mass spectra were obtained on an Applied Biosystems Mariner time-of-flight mass spectrometer using electrospray ionization technique (ESI). Elemental analysis was performed in this institute.

General procedure for synthesis of Meldrum's acids 1

A mixture of malonic acid (1.04 g, 0.01 mol), concentrated sulfuric acid (2—3 d) and acetic acid (1.02 g, 0.01 mol) was stirred at 60 ℃ for 15 min. After it was cooled to room temperature, the ketone (0.58 g, 0.01 mol) was added dropwise to the mixture within 30—60 min. Upon completion of addition, the resulting reaction mixture was stirred for 1 h. We can get the solids or liquid products by column chromatography using petroleum ether/acetic ester/chloroform=2/2/1 (*V*/*V*/*V*) as the eluent to get the reaction products **1a** (1.15 g, 80%).

2,2-Dimethyl-1,3-dioxane-4,6-dione (**1a**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.62 (s, 2H), 1.80 (s, 6H); IR (KBr) *v*: 2930, 1754, 1265 cm^{-1}; MS *m/z* (EI$^-$): 143 (M^+-1).

2-Ethyl-2-methyl-1,3-dioxane-4,6-dione (**1b**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.65 (s, 2H), 2.01 (q, *J*=7 Hz, 2H), 1.75 (s, 3H), 1.18 (t, *J*=7 Hz, 3H); IR (KBr) *v*: 2986, 2947, 1468, 1301, 1755 cm^{-1}; MS *m/z* (EI$^-$): 157 (M^+-1).

2-(2-Methylpropyl)-2-methyl-1,3-dioxane-4,6-dione (**1c**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.60 (s, 2H), 1.91—1.98 (m, *J*=7 Hz, 1H), 1.86 (d, *J*=7 Hz, 2H), 1.75 (s, 3H), 1.01 (d, *J*=7 Hz, 6H); IR (KBr) *v*: 2961, 2929, 2875, 1755, 1470 cm^{-1}; MS *m/z* (EI$^-$): 185 (M^+-1).

2-Hexyl-2-methyl-1,3-dioxane-4,6-dione (**1d**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.62 (s, 2H), 1.94 (t, *J*=7 Hz, 2H), 1.73 (s, 3H), 1.44—1.56 (m, *J*=7 Hz, 2H), 1.25—1.38 (m, 6H), 0.89 (t, *J*=7 Hz, 3H); IR (KBr) *v*: 2930, 2851, 1746, 1224 cm^{-1}; MS *m/z* (EI$^-$): 213 (M^+-1).

2-Butylene-1,3-dioxane-4,6-dione (**1e**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.62 (s, 2H), 2.21 (t, *J*=7 Hz, 4H), 1.86 (t, *J*=7 Hz, 4H); IR (KBr) *v*: 2912, 2880, 1435, 1781 cm^{-1}; MS *m/z* (EI$^-$): 169 (M^+-1).

2-Pentylene-1,3-dioxane-4,6-dione (**1f**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.62 (s, 2H), 2.04 (t, *J*=7 Hz, 4H), 1.68—1.80 (m, *J*=7 Hz, 4H), 1.55 (t, *J*=7 Hz, 2H); IR (KBr) *v*: 2963, 2866, 1754, 1454, 1372 cm^{-1}; MS *m/z* (EI$^-$): 183 (M^+-1).

2-Methyl-2-phenyl-1,3-dioxane-4,6-dione (**1g**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.24—7.34 (m, 5H), 3.44 (d, *J*=20 Hz, 1H), 2.98 (d, *J*=20 Hz, 1H), 1.98 (s, 3H); IR (KBr) *v*: 2919, 2850, 1727, 1601, 1123, 1078 cm^{-1}; MS *m/z* (EI$^-$): 205 (M^+-1).

2-Methyl-2-(4-methylphenyl)-1,3-dioxane-4,6-dione (**1h**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.20—7.40 (m, 4H), 3.44 (d, *J*=20 Hz, 1H), 2.98 (d, *J*=20 Hz, 1H), 2.37 (s, 3H), 1.95 (s, 3H); IR (KBr) *v*: 3033, 2920, 1623, 1348, 1159 cm^{-1}; MS *m/z* (EI$^-$): 219 (M^+-1).

2-Methyl-2-(4-nitrophenyl)-1,3-dioxane-4,6-dione (**1i**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.70—8.30 (m, 4H), 3.52 (d, *J*=20 Hz, 1H), 3.00 (d, *J*=20 Hz, 1H), 2.08 (s, 3H); IR (KBr) *v*: 3081, 2899, 1768, 1523, 1357, 1294 cm^{-1}; MS *m/z* (EI$^-$): 250 (M^+-1).

2,2-Dibenzyl-1,3-dioxane-4,6-dione (**1j**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.20—7.40 (m, 10H), 3.32 (s, 4H), 2.18 (s, 2H); IR (KBr) *v*: 3030, 2921, 1759, 1280 cm^{-1}; MS *m/z* (EI$^-$): 295 (M^+-1).

2-(4-Fluorophenyl)-2-methyl-1,3-dioxane-4,6-dione (**1k**): ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 7.17—7.43 (m, 4H), 3.48 (d, *J*=20 Hz, 1H), 2.98 (d, *J*=20 Hz, 1H), 1.95 (s, 3H); ^{19}F NMR ($CDCl_3$, 300 MHz) δ: −104.5 (s, 1F); IR (KBr) *v*: 2912, 2851, 1656, 1261, 1120, 1099, 1017 cm^{-1}; MS *m/z* (EI$^-$): 223 (M^+-1).

General procedure for synthesis of C_{60} Meldrum's acid derivatives 2

To a stirred solution of C_{60} (72.0 mg, 0.1 mmol), **1a** (43.2 mg, 0.3 mmol), and I_2 (76.1 mg, 0.3 mmol) in dry toluene (30 mL) was added dropwise a solution of DBU (45.6 mg, 0.3 mmol) in dry toluene (10 mL) under nitrogen at room temperature. Upon completion of addition, the resulting reaction mixture was continuously stirred for 3 h. Then the reaction mixture was chromatographied using toluene as eluant to gave black solids **2a** (35 mg, 41%) and black solids **3a**+**3a**' (18 mg, 18%). The bisadducts **3a**, **3a**' also can be easily separated by chromatography using toluene as eluent.

2a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.18 (s, 6H); IR (KBr) *v*: 2920, 1758, 1273, 576, 526 cm^{-1}; MS *m/z* (ESI$^-$): 863 (M+1). Anal. calcd for $C_{66}H_6O_4$ (862): C 91.88, H 0.70; found C 91.56, H 1.02.

2b: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.39 (q, *J*=7 Hz, 2H), 2.19 (s, 3H), 1.28 (t, *J*=7 Hz, 3H); IR (KBr) *v*: 2922, 2850, 1756, 1285, 577, 526 cm^{-1}; MS *m/z*

(ESI$^-$): 877 (M^++1). Anal. calcd for $C_{67}H_8O_4$ (876): C 91.78, H 0.91; found C 91.45, H 1.24.

2c: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.35 (m, J=7 Hz, 1H), 2.33—2.36 (d, J=7 Hz, 2H), 2.14 (s, 3H), 1.11 (d, J=7 Hz, 6H); IR (KBr) v: 2961, 2929, 2875, 1755, 1470, 577, 524 cm^{-1}; MS *m/z* (ESI$^-$): 905 (M^++1). Anal. calcd for $C_{69}H_{12}O_4$ (904): C 91.59, H 1.33; found C 91.27, H 1.61.

2d: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.38 (t, J=7 Hz, 2H), 2.15 (s, 3H), 1.64—1.76 (m, J=7 Hz, 2H), 1.38—1.28 (m, 6H), 0.89 (t, J=7 Hz, 3H); IR (KBr) v: 2920, 2849, 1756, 1276, 577, 526 cm^{-1}; MS *m/z* (ESI$^-$): 933 (M^++1). Anal. calcd for $C_{71}H_{16}O_4$ (932): C 91.42, H 1.72; found C 91.05, H 2.03.

2e: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.70 (t, J=7 Hz, 4H), 2.05 (t, J=7 Hz, 4H); IR (KBr) v: 2920, 2849, 1755, 1275, 578, 526 cm^{-1}; MS *m/z* (ESI$^-$): 889 (M^++1). Anal. calcd for $C_{68}H_8O_4$ (888): C 91.89, H 0.90; found C 91.63, H 1.22.

2f: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.43 (t, J=7 Hz, 4H), 1.84—1.96 (m, J=7 Hz, 4H), 1.63 (t, J=7 Hz, 2H); IR (KBr) v: 2922, 2850, 1755, 1285, 576, 526 cm^{-1}; MS *m/z* (ESI$^-$): 903 (M^++1). Anal. calcd for $C_{69}H_{10}O_4$ (902): C 91.80, H 1.11; found C 91.59, H 1.47.

2g: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.10—7.80 (m, 5H), 2.18 (s, 3H); IR (KBr) v: 3006, 2921, 1763, 1634, 1232, 525 cm^{-1}; MS *m/z* (ESI$^-$): 925 (M^++1). Anal. calcd for $C_{71}H_8O_4$ (924): C 92.21, H 0.87; found C 91.85, H 1.23.

2h: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.15—7.55 (m, 4H), 2.37 (s, 3H), 2.18 (s, 3H); IR (KBr) v: 3007, 2921, 1764, 1635, 1234, 526 cm^{-1}; MS *m/z* (ESI$^-$): 939 (M+1). Anal. calcd for $C_{72}H_{10}O_4$ (938): C 92.11, H 1.07; found C 91.77, H 1.41.

2i: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.93—8.23 (m, 4H), 2.18 (s, 3H); IR (KBr) v: 2920, 2850, 1763, 1635, 1526, 1232, 1013, 526 cm^{-1}; MS *m/z* (ESI$^-$): 970 (M^++1). Anal. calcd for $C_{71}H_7O_6N$ (969): C 87.93, H 0.72; found C 87.74, H 1.05.

2j: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.18—7.55 (m, 10H), 3.55 (s, 4H); IR (KBr) v: 3030, 2921, 1758, 1271, 526 cm^{-1}; MS *m/z* (ESI$^-$): 1015 (M^++1). Anal. calcd for $C_{78}H_{14}O_4$ (1014): C 92.31, H 1.38; found C 92.03, H 1.58.

2k: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.02—7.70 (m, 4H), 2.18 (s, 3H); ^{19}F NMR ($CDCl_3$, 300 MHz) δ: −104.5 (s, 1F); IR (KBr) v: 2919, 2850, 1762, 1234, 1014, 836, 527 cm^{-1}; MS *m/z* (ESI$^-$): 943 (M^++1). Anal. calcd for $C_{71}H_7O_4F$ (942): C 90.45, H 0.74; found C 90.14, H 1.06.

3a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.13, 2.10, 2.04 (3s, 12H); IR (KBr) v: 2919, 2850, 1754, 1274, 526 cm^{-1}; MS *m/z* (ESI$^-$): 1005 (M^++1). Anal. calcd for $C_{72}H_{12}O_8$ (1004): C 86.06, H 1.20; found C 85.74, H 1.50.

3a': ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.22 (s, 6H), 2.08 (s, 6H); IR (KBr) v: 2921, 1755, 1263, 526 cm^{-1}; MS *m/z* (ESI$^-$): 1005 (M^++1). Anal. calcd for $C_{72}H_{12}O_8$ (1004): C 86.06, H 1.20; found C 85.76, H 1.55.

Conclusion

In summary, a series of novel Meldrum's acid C_{60} derivatives were prepared from a convenient one-pot reaction of Meldrum's acid derivatives, C_{60}, I_2 and DBU at room temperature via [1+2] cycloaddition of the corresponding carbene intermediates with C_{60}. In the case of more **1**, DBU and I_2, the Bingel reaction will give multiple addition products. The physical and chemical properties of the new compounds **2** and **3** are under further investigation.

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