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ALLYLATION OF MELDRUM'S ACIDS BY ALLYLIC ALCOHOLS USING TETRAKIS[TRIPHENYLPHOSPHINE]-PALLADIUM(0) CATALYSTS

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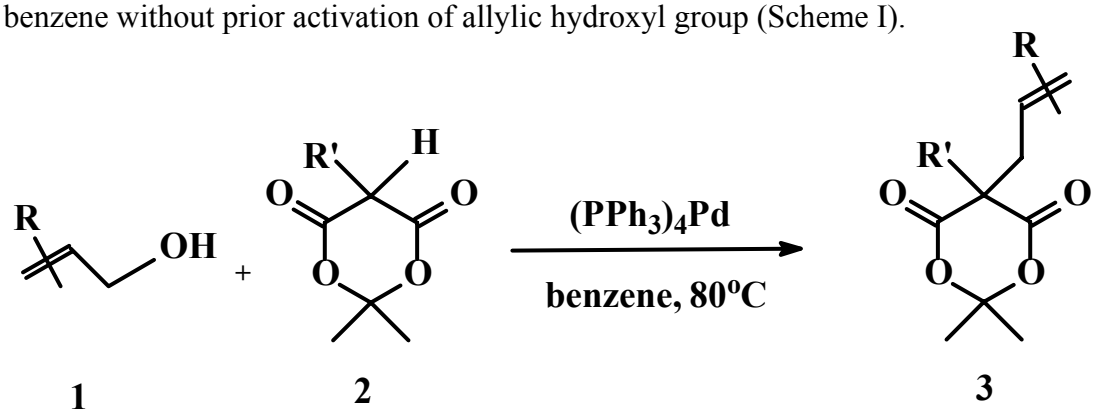
Abstract—Meldrum's acids can be allylated by allylic alcohols using tetrakis[triphenylphosphine]palladium(0) [$(PPh_3)_4Pd$] as a catalyst in benzene at 80℃ without prior activation of allylic hydroxy group.

Meldrum's acid and its 5-substituted derivatives are versatile synthons in organic synthesis.[1] The methods used to synthesize 5-substituted Meldrum's acid mainly include (i) direct alkylations of Meldrum's acid using alkyl halides in the presence of a base.[2] (ii) Michael-type additions of Meldrum's acid to electrophilic olefins[3] or to their equivalents.[4] (iii) palladium catalyzed coupling reaction between allyl derivatives (allylic halides and esters) and Meldrum's acid.[5] (iv) Mitsunobu *C*-allylation of Meldrum's acid.[6]

Palladium-catalyzed allylic substitution with carbon nucleophiles constitutes one of the most important and useful carbon-carbon bond-forming reactions in organic synthesis.[7] In most cases, allyl esters (usually with a stoichiometric amount of a base) or allyl carbonates, which are usually prepared from the corresponding allyl alcohols, have been used as allylating agents. Therefore, if allyl alcohols themselves can be directly used as allylating agents, the steps to prepare the esters or carbonates are no longer needed, and the overall process of the allylation would become highly efficient and atom economical. Although several attempts have been reported in this connection,[8] most of them require rather severe reaction conditions and the design of really effective catalysts for direct conversion of allylic alcohols still remains a major objective catalytic allylation. This is apparently due to the poor leaving ability of the OH group. Accordingly, catalytic conversion of allylic alcohols has been examined in most cases through *in situ* activation of the OH group with the aid of Lewis acids[9] or by converting it into the esters of inorganic acids.[10] We were interested in the reaction of Meldrum's acid with allyl alcohols using tetrakis[triphenylphosphine]palladium(0) [$(PPh_3)_4Pd$] as a catalyst to prepare *C*-allylated products in

refluxing benzene without prior activation of allylic hydroxyl group (Scheme I).



1 **2** **3**

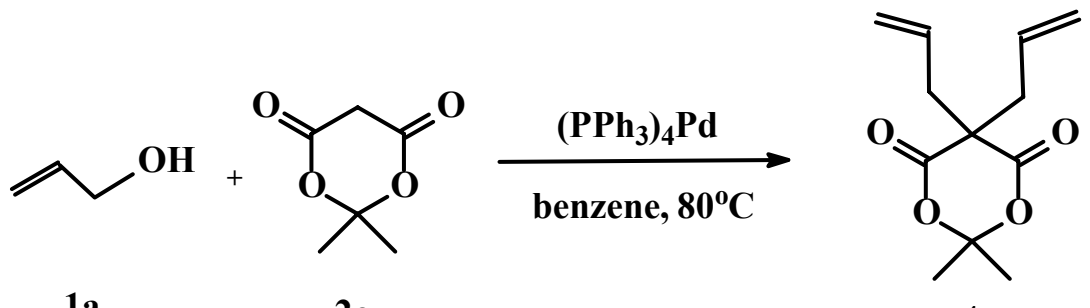
a, R' = Me

b, R' = Bn

Scheme I

The scope of the reaction of various Meldrum's acid with allyl alcohol with $(PPh_3)_4Pd$ in benzene was investigated. We found that the reaction of Meldrum's acid with allyl alcohols with $(PPh_3)_4Pd$ occurred easily in refluxing benzene for 3 h and gave the desired 5-allylated Meldrum's acids (**3**) in good yields. The results are summarized in Table 1.

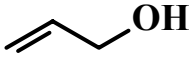
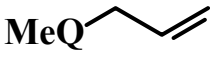
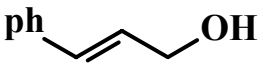
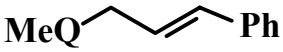
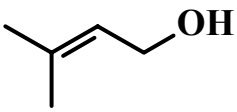
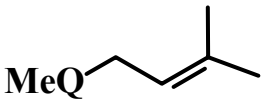
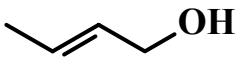
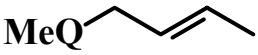
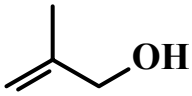
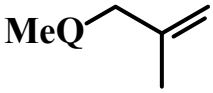
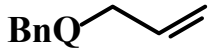
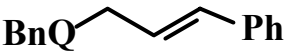
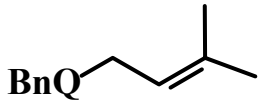
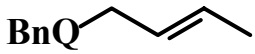
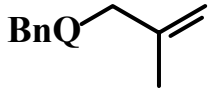
Attempts to synthesize monosubstituted Meldrum's acid selectively using $(PPh_3)_4Pd$ as a catalyst were fruitless. Firstly, the use of 1 equiv. of a primary allylic alcohol (**1a**) with respect to Meldrum's acid (**2c**) was attempted. Surprisingly, in the case only 50% of Meldrum's acid was consumed, and only disubstituted allylated product (**4a**) was produced (Scheme II).[11] Then the reactions of 2.5 equiv. of Meldrum's acid with 1 equiv. of the primary allylic alcohol was investigated. Again, in the case, only disubstituted product (**4a**) was obtained, and no monosubstituted product was detectable. Like most of the other methods[12] used to allylate Meldrum's acids, disubstituted products preponderated. It appears that the monosubstituted Meldrum's acid is more reactive than Meldrum's acid itself in the reaction mixture, and the resultant monosubstituted species will react further with another mole of allylic alcohol in cases where Meldrum's acid is used as the starting material.



1a **2c** **4a**

Scheme II

Table 1. Preparation of 5-allylated Meldrum's acids (**3**).

Entry	Allyl alcohol	Meldrum's acid	Product[a]	Yield (%)
1	 **1a**	**2a**	 **3a**	81
2	 **1b**	**2a**	 **3b**	78
3	 **1c**	**2a**	 **3c**	83
4	 **1d**	**2a**	 **3d**	76
5	 **1e**	**2a**	 **3e**	75
6	**1a**	**2b**	 **3f**	82
7	**1b**	**2b**	 **3g**	80
8	**1c**	**2b**	 **3h**	85
9	**1d**	**2b**	 **3i**	77
10	**1e**	**2b**	 **3j**	84

[a] MeQH = 5-methyl Meldrum's acid (**2a**); BnQH = 5-benzyl Meldrum's acid (**2b**)

In summary, the method described herein provides an approach for the synthesis of 5-allylated Meldrum's acid with good yields by the reaction of various Meldrum's acids with allyl alcohols using $(PPh_3)_4Pd$ as a catalyst in benzene at 80 °C without prior activation of allylic hydroxy group.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded on a Shimadzu IR-27 G spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Unity Plus 400 MHz. Chemical shifts (δ)

were measured in ppm with respect to TMS. MS were obtained on a JEOL JMS D-300 instrument.

Typical procedure for the preparation of 3a

A mixture of allyl alcohol (**1a**) (58.08 mg, 1 mmol), 5-methyl Meldrum's acid (**2a**) (158.15 mg, 1 mmol) and $Pd(PPh_3)_4$ (57.78 mg, 0.05 mmol) in dry benzene (5 mL) was refluxed for 3 h. After cooling, the reaction mixture was quenched with water and extracted with AcOEt. The extract was washed with brine and dried over magnesium sulfate. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane-AcOEt (10:1) to give **3a**.

5-Allyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (3a)

Oily compound. IR (neat) ν : 2987, 2943, 1775, 1743, 1456, 1240, 696 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 1.46 (s, 3H), 1.55 (s, 3H), 1.57 (s, 3H), 2.56 (td, *J* = 0.8, 7.6 Hz, 2H), 4.99-5.03 (m, 2H), 5.43-5.54 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 23.7, 28.4, 29.2, 43.8, 49.5, 104.6, 120.5, 130.6, 169.3. EI-MS: 199 (M^++1, 28), 198 (M^+, 3), 141 (46), 123 (45), 95 (54), 67 (100). HRMS (EI) Calcd for $C_{10}H_{14}O_4$: 198.0892. Found: 198.0891.

5-Cinnamyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (3b)

mp 58-60 °C (AcOEt/hexane). IR (KBr) ν : 3027, 2965, 1777, 1741, 1677, 1456, 1205, 744, 689 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 1.62 (s, 3H), 1.68 (s, 3H), 1.71 (s, 3H), 2.90 (d, *J* = 7.6 Hz, 2H), 5.99-6.08 (m, 1H), 6.51 (d, *J* = 15.6 Hz, 1H), 7.20-7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 24.2, 28.7, 29.5, 43.2, 50.3, 105.1, 121.8, 126.3, 127.8, 128.5, 135.7, 136.3, 169.9. EI-MS: 274 (M^+, 19), 215 (100), 144 (59), 129 (90), 117 (61), 91 (54). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 70.23; H, 6.52.

5-(3-Methylbut-2-enyl)-2,2,5-trimethyl-1,3-dioxane-4,6-dione (3c)

Oily compound. IR (neat) ν : 2983, 2936, 1775, 1743, 1673, 1454, 1270, 761 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 1.57 (s, 6H), 1.63 (s, 3H), 1.65 (d, *J* = 4.0 Hz, 6H), 2.68 (d, *J* = 7.6 Hz, 2H), 4.93-4.98 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 17.7, 24.0, 25.7, 28.6, 29.6, 38.9, 49.7, 104.8, 116.9, 137.8, 170.2. EI-MS: 226 (M^+, 83), 153 (55), 141 (49), 125 (48), 113 (100), 95 (36), 81 (29). HRMS (EI) Calcd for $C_{12}H_{18}O_4$: 226.1205. Found: 226.1203.

5-(But-2-enyl)-2,2,5-trimethyl-1,3-dioxane-4,6-dione (3d)

Oily compound. IR (neat) ν : 2993, 2941, 1771, 1743, 1671, 1454, 1269, 685 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 1.49 (s, 3H), 1.51-1.53 (m,3H), 1.59 (s, 3H), 1.61 (s, 3H), 2.54 (d, *J* = 7.6 Hz, 2H), 5.13-5.22 (m, 1H), 5.45-5.53 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 17.6, 23.7, 28.5, 29.4, 43.0, 50.1, 104.7, 123.4, 131.6, 169.7. EI-MS: 212 (M^+, 36), 155 (25), 137 (26), 95 (51), 67 (100). HRMS (EI) Calcd for

$C_{11}H_{16}O_4$: 212.1048. Found: 212.1047.

5-(2-Methylallyl)-2,2,5-trimethyl-1,3-dioxane-4,6-dione (3e)

Oily compound. IR (neat) ν : 2986, 2943, 1775, 1744, 1456, 1245, 674 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 1.52 (s. 3H), 1.58 (s, 3H), 1.60 (s, 3H), 1.62 (s, 3H), 2.64 (s, 2H), 4.66 (t, *J* = 0.8 Hz, 1H), 4.77 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 25.1, 28.4, 29.6, 47.7, 49.3, 104.9, 116.3, 139.6, 169.7. EI-MS: 212 (M^+, 37), 155 (100), 109 (52), 95 (46), 67 (49). HRMS (EI) Calcd for $C_{11}H_{16}O_4$: 212.1048. Found: 212.1045.

5-Allyl-5-benzyl-2,2-dimethyl-1,3-dioxane-4,6-dione (3f)

mp 81-82 °C (hexane) (lit.,[6] 82 °C). IR (KBr) ν : 1770, 1735 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 0.68 (s, 3H), 1.53 (s, 3H), 2.88 (d, *J* = 7.6 Hz, 2H), 3.33 (s, 2H), 5.19-5.28 (m, 2H), 5.66-5.72 (m, 1H), 7.18-7.19 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 28.7, 29.7, 43.8, 44.3, 57.9, 105.9, 121.4, 127.8, 128.8, 130.2, 130.6, 135.1, 168.4. EI-MS: 274 (M^+, 0.16), 143 (76), 129 (73), 115 (60), 91 (100), 65 (58). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 70.18; H, 6.56.

5-Benzyl-5-cinnamyl-2,2-dimethyl-1,3-dioxane-4,6-dione (3g)

mp 148-150 °C (hexane) (lit.,[6] 149 °C). IR (KBr) ν : 1769, 1735 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 0.69 (s, 3H), 1.40 (s, 3H), 3.04 (d, *J* = 7.6 Hz, 2H), 3.38 (s, 2H), 6.03-6.11 (m, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 7.20-7.32 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 28.7, 29.6, 43.4, 43.9, 58.3, 106.0, 121.4, 126.3, 127.8, 127.9, 128.6, 128.9, 130.2, 135.1, 136.0, 136.2, 168.5. EI-MS: 350 (M^+, 0.06), 145 (24), 129 (70), 117 (86), 115 (93), 91 (100), 77 (45), 65 (33). Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.57; H, 6.18.

5-Benzyl-5-(3-methylbut-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (3h)

mp 86-88 °C (hexane) (lit.,[6] 86 °C). IR (KBr) ν : 1771, 1737 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 0.71 (s, 3H), 1.51 (s, 3H), 1.66 (s, 3H), 1.70 (s, 3H), 2.88 (d, *J* = 8.0 Hz, 2H), 3.34 (s, 2H), 5.03-5.07 (m, 1H), 7.18-7.27 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 17.9, 25.9, 28.8, 29.4, 39.1, 43.8, 57.8, 105.8, 116.9, 127.7, 128.8, 130.2, 135.4, 168.9. EI-MS: 302 (M^+, 0.04), 185 (29), 145 (32), 129 (36), 115 (45), 91 (100), 77 (59), 69 (91), 65 (41). Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.42; H, 7.56.

5-Benzyl-5-(but-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (3i)

mp 52-54 °C ($CHCl_3$/hexane). IR (KBr) ν : 1769, 1739 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 0.68 (s, 3H), 1.48 (s, 3H), 1.64 (s, 3H), 2.78 (d, *J* = 7.6 Hz, 2H), 3.28 (s, 2H), 5.26-5.35 (m, 1H), 5.60-5.87 (m, 1H), 7.15-7.30 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 17.9, 28.7, 29.5, 43.2, 43.6, 58.4, 105.8, 123.3, 127.7, 128.7, 130.1, 132.2, 135.3, 168.5. EI-MS: 288 (M^+, 4), 231 (100), 213 (41), 202 (18), 186 (32), 129 (18), 91

(17). Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.68; H, 6.78.

5-Benzyl-5-(2-methylallyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (3j)

mp 150-152 °C ($CHCl_3$/hexane). IR (KBr) ν : 1770, 1732 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 0.66 (s, 3H), 1.52 (s, 3H), 1.75 (s, 3H), 2.89 (s, 2H), 3.33 (s, 2H), 4.89 (d, *J* = 0.8 Hz, 1H), 4.95 (m, 1H), 7.18-7.28 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 23.5, 28.9, 29.4, 44.7, 47.7, 57.9, 105.9, 117.6, 127.8, 128.8, 130.3, 135.0, 139.3, 168.4. EI-MS: 288 (M^+, 8), 231 (59), 213 (47), 202 (49), 171 (41), 157 (100), 91 (74). Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.67; H, 6.75.

5,5-Diallyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4a)

As described for **3a**, reaction of allyl alcohol (**1a**) (58.08 mg, 1 mmol) with Meldrum's acid (360.3 mg, 2.5 mmol) and $Pd(PPh_3)_4$ (57.78 mg, 0.05 mmol) in dry benzene (5 mL) at 80 °C afforded **4a** (85%) as an oil. IR (neat) ν : 3082, 2999, 2930, 1771, 1744, 1641, 1441, 1267, 729 cm^{-1}. ^1H NMR ($CDCl_3$) δ : 1.69 (s, 6H), 2.75 (d, *J* = 7.4 Hz, 4H), 5.18-5.27 (m, 4H), 5.60-5.81 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ : 29.8, 42.7, 55.4, 105.7, 121.2, 130.8, 168.3. EI-MS: 225 (M^++1, 4), 224 (M^+, 0.2), 209 (0.8), 166 (15), 149 (48), 138 (31), 121 (70), 93 (76), 79 (100), 77 (19). HRMS (EI) Calcd for $C_{12}H_{16}O_4$: 224.1048 Found: 224.1046.

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