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Mitsunobu *C*-Alkylation of Meldrum's Acids

Tony K. M. Shing,* Lian-Hai Li, and Kesavaram Narkunan

Department of Chemistry, The Chinese University of Hong Kong, Shatin, Hong Kong

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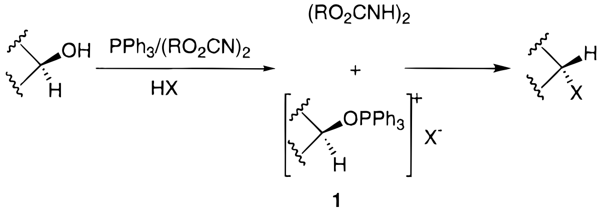
C-Dialkylation of Meldrum's acid (**2a**) and 5-benzyl Meldrum's acid (**2b**) can be achieved through Mitsunobu dehydration using allylic and arylmethyl alcohols as alkylating agents. This is the first time that the Mitsunobu reaction is successfully applied to the *C*-alkylation of a highly enolizable cyclic β-dicarbonyl system. With primary (allylic and arylmethyl) alcohols, the alkylations always take place at the carbon bearing the hydroxy group. For secondary allylic alcohols, a catalytic amount of Pd(0) must be added to enhance the regioselectivity of *C*-alkylation over *O*-alkylation. With $(Ph_3P)_4Pd(0)$ as a catalyst, the reaction occurs specifically at the less hindered carbon, and the configuration of the resultant double bond is always *trans*. Attempts to monoalkylate Meldrum's acids **2a** and **2b** failed.

Introduction

The classic Mitsunobu condensation of an alcohol with an acidic compound in the presence of dialkyl azodicarboxylate and triphenylphosphine has been widely investigated.[1] The reaction involves *in situ* formation of a highly reactive alkoxyphosphonium intermediate[2] that undergoes nucleophilic displacement under mild and nearly neutral conditions with virtually complete inversion of configuration at the electrophilic center. This stereochemical outcome as well as the high compatibility of the reaction conditions with most functional groups render the reaction widely applicable in the synthesis and transformation of natural products.[1,3] Most of the studies concentrate on the formation of carbon−heteroatom bond, and the Mitsunobu protocol has become a powerful method for the introduction of novel functional groups such as those containing C−O, C−S, C−N, and C−X bonds to a molecule (Scheme 1).[1,3,4] However, there are few reports on C−C bond formation based on this protocol in the literature.[5−7]

Meldrum's acid and its 5-substituted derivatives are versatile synthons in organic synthesis.[8] The methods used to synthesize these 5-substituted Meldrum's acids mainly include (i) direct alkylations of Meldrum's acid using alkyl halides in the presence of a base;[8,9] (ii) Michael-type additions of Meldrum's acid to electrophilic olefins[8,12] or to their equivalents;[8,13] (iii) palladium-catalyzed coupling reaction between allyl derivatives (allylic halides and esters) and Meldrum's acid.[8,10,11,14] As part of our ongoing research, we need to develop a mild method to *C*-dialkylate Meldrum's acid directly using alcohols as alkylating agents. For this purpose, the Mitsunobu dehydrative alkylation appears to offer the best promise. Indeed, attempts to employ Mitsunobu condensation to alkylate ambient, active methylenes flanked by two carbonyl groups have been reported.[1,7] Unfortunately, *O*-alkylation was highly competitive and was the preponderant pathway over *C*-alkylation in all cases. In order to develop Mitsunobu alkylation as a powerful C−C bond formation methodology, Falck and his co-workers circumvented this problem by using nonenolizable methylene disulfone as the acidic component and achieved successful dehydrative alkylations with alcohols.[5]

Scheme 1



Results and Discussion

Initially, we attempted to alkylate Meldrum's acid with simple alcohols, 2-propanol and 2-phenylethanol, but only undesired products were obtained. In the former case

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(1) For reviews see: (a) Castro, B. R. *Org. React.* **1983**, *29*, 1. (b) Mitsunobu, O. *Synthesis* **1981**, 1. (c) Hughes, D. L. *Org. React.* **1992**, *41*, 335.

(2) (a) Adam, W.; Narita, N.; Nishizawa, Y. *J. Am. Chem. Soc.* **1984**, *106*, 1843. (b) Hughes, D. L.; Reamer, R. A.; Bergan, J. J.; Grabowski, E. J. *J. Am. Chem. Soc.* **1988**, *110*, 6478. (c) Camp, D.; Jenkins, I. D.; *J. Org. Chem.* **1989**, *54*, 3045. (d) Varasi, M.; Walker, K. A. M.; Maddox, M. L. *J. Org. Chem.* **1987**, *52*, 4235.

(3) For recent applications, see: (a) Kometani, T.; Kondo, H.; Fujimori, Y. *Synthesis* **1988**, 1005. (b) Chida, N.; Ohtsuka, M.; Nakazawa, K.; Ogawa, S. *J. Org. Chem.* **1991**, *56*, 2976. (c) Chida, N.; Ohtsuka, M.; Ogawa, S. *Chem. Lett.* **1988**, 969. (d) Sobi, A.; Sullikowski, G. A. *Tetrahedron Lett.* **1994**, *35*, 3661. (e) Roush, W. R.; Lin, X.-F. *J. Am. Chem. Soc.* **1995**, *117*, 2236. (f) Roush, W. R.; Lin, X.-F. *J. Org. Chem.* **1991**, *56*, 5740; (g) Ramesh, N. G., Balasubramanian, K. K. *Tetrahedron* **1995**, *51*, 255.

(4) (a) Manna, S.; Flack, J. R. *Synth. Commun.* **1985**, *15*, 663. (b) Scmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212. (c) Loibner, H.; Zbiral, E. *Helv. Chim. Acta* **1976**, *59*, 2100. (d) Volante, R. P. *Tetrahedron Lett.* **1981**, *22*, 3119. (e) Clive, D. L. J.; Kellner, D. *Tetrahedron Lett.* **1991**, *32*, 7159. (f) Galynker, I.; Still, W. C. *Tetrahedron Lett.* **1982**, *23*, 4461. (g) Chong, J. M.; Park, S. B. *J. Org. Chem.* **1992**, *57*, 2220. (h) Jenny, T. F.; Previsani, N.; Benner, S. A. *Tetrahedron Lett.* **1991**, *32*, 7029. (i) Walker M. A. *J. Org. Chem.* **1995**, *60*, 5352.

(5) Yu, J.; Cho, H.-S.; Falck, J. R. *J. Org. Chem.* **1993**, *58*, 5892.

(6) Macor, J. E.; Wehner, M. *Tetrahedron Lett.* **1991**, *32*, 7195.

(7) (a) Kurihara, T.; Nakajima, Y.; Mitsunobu, O. *Tetrahedron Lett.* **1976**, 2455. (b) Wada, M.; Mitsubonu, O. *Tetrahedron Lett.* **1972**, 1279.

(8) For a review see: Chen B.-C. *Heterocycles* **1991**, *32*, 529.

(9) (a) Chen, C.-C.; Huang, X. *Synthesis* **1982**, 452. (b) Bandgar, B. P.; Jagdale, M. H.; Mane, R. B.; Salunkhe, M. M. *Indian J. Chem.* **1985**, *24B*, 1057. (c) Chen, B. C.; Lue, P. *Org. Prep. Proced. Int.* **1992**, *24*, 185.

(10) (a) Ferroud, D.; Genet, J. P.; Muzart, J. *Tetrahedron Lett.* **1984**, *25*, 4379. (b) Lu, X.; Jiang, X.; Tao, X. *J. Organomet. Chem.* **1988**, *344*, 109.

(11) Prat, M.; Moreno-Manas, M.; Ribas, J. *Tetrahedron* **1988**, *44*, 7205.

(12) (a) Chen, C. C.; Huang, X. *Synthesis* **1984**, 224. (b) Rao Y. K.; Nagarajan, M. *Indian J. Chem.* **1983**, *22B*, 519. (c) Siperko, L. G.; Smith, F. X. *Synth. Commun.* **1979**, *9*, 283. d) Zhong, Q.; Shao, J.; Liu, C. *Youji Huaxue* **1988**, *8*, 466.

(13) Jacobs, R. T.; Wright, A. D.; Smith, F. X. *J. Org. Chem.* **1982**, *47*, 3769.

(14) Oppolzer, W.; Gaudin, J.-M. *Helv. Chim. Acta* **1987**, *70*, 1477.

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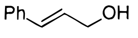
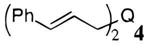
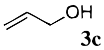
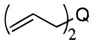
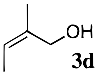
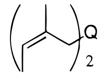
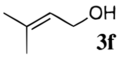
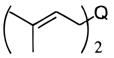
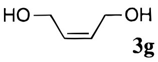
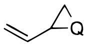
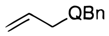
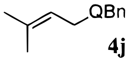
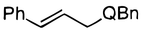
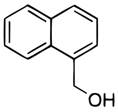
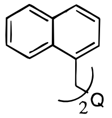
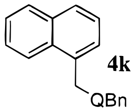
Table 1. Dialkylation of Meldrum's Acid via Mitsunobu Condensation

Entries	Alcohols	Meldrum's Acid	Products[a]	Yields (Method)[c]
1	 **3a**	**2a**	 **4a**	60 (A)
2	 **3c**	**2a**	 **4c**	94 (A)
3	 **3d**	**2a**	 **4d**	59 (A)
4	 **3f**	**2a**	 **4f**	80 (A), 71 (B)
5	 **3g**	**2a**	 **4g**	13 (A), 20 (B)
6	**3c**	**2b**	 **4i**	85 (B)
7	**3f**	**2b**	 **4j**	96 (B)
8	**3a**	**2b**	 **4h**	80 (B)
9	BnOH **3b**	**2a**	Bn_2Q **4b**	40 (A)
10	**3b**	**2b**	**4b**	84 (B)
11	 **3e**	**2a**	 **4e**	73 (A)[b]
12	**3e**	**2b**	 **4k**	75 (B)

[a] QH_2 = Meldrum's acid **2a**; BnQH = 5-benzyl Meldrum's acid **2b**

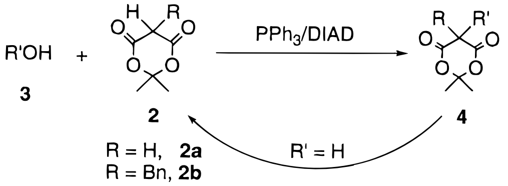
[b] Along with 21% of di(1-naphthalenemethyl)malonate as side product

[c] See Experimental Section

O-alkylation prevailed whereas in the latter case, only transesterification occurred and bis(2-phenylethyl) malonate was harvested as the main product. In fact, the Ph_3P/DIAD system had been reported to catalyze transesterification elsewhere.[15]

Then we investigated the alkylation with reactive primary alcohols such as allyl alcohol and benzyl alcohol. Hence, Meldrum's acid (**2a**) was treated with 2 equiv of allyl alcohol or benzyl alcohol in presence of DIAD and triphenylphosphine in toluene at room temperature. Rewardingly, dialkylated Meldrum's acids were isolated in 60–90% yields. Encouraged by these results, we extended our studies to other reactive primary alcohols as well as using 5-benzyl Meldrum's acid (**2b**) as the nucleophile (Scheme 2). The results are listed in Table 1.

Scheme 2



When primary allylic alcohols (Table 1, entries 1–4, 6–8) were used as alkylating agents, the reaction readily took place at the carbon bearing the hydroxy group, and the configuration of the double bond remained unchanged (entries 1, 3, 8). The dehydrative alkylations also proceeded smoothly with benzyl alcohol and 1-naphthalenemethanol (entries 9–12).

The reaction of Meldrum's acid (**2a**) with *cis*-butene-1,4-diol **3g** (entry 5) is interesting, although in poor yields, and afforded a cyclopropane derivative (**4g**) pre-

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(15) Bitter, S.; Barneis, Z.; Felix, S. *Tetrahedron Lett.* **1975**, 3871.

sumably resulting from tandem intermolecular/intramolecular alkylations. The anticipated dialkylated product was not detected on TLC and by ^{1}H NMR spectroscopy.

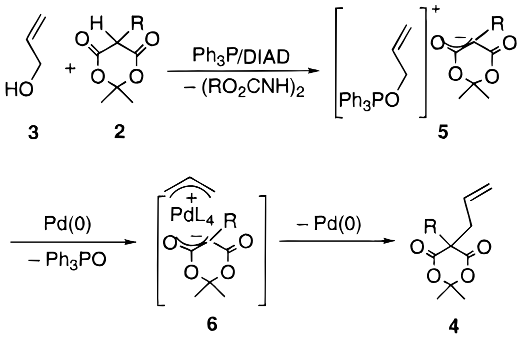
We then studied the alkylations of Meldrum's acid (**2a**) and 5-benzyl Meldrum's acid (**2b**) with allylic secondary alcohols under similar conditions. Unfortunately, either *O*-alkylated or a mixture containing predominantly *O*-alkylated products were obtained. A change of solvent from toluene to THF also met with no success, although the reactions with primary allylic or aryl alcohols worked well in THF (entries 4−8, 10, 12 in Table 1).

The traditional alkylation of stabilized enolate anions have been thoroughly discussed in the literature.[16] The main factors which favor *C*-alkylation are (i) less electropositive metal cations, e.g., lithium can reduce the reactivity of the oxygen through the formation of a tightly associated ion pair to the point where *C*-alkylation is preferred; (ii) polarizable alkylating agents such as alkyl iodides, allylic and benzylic halides; (iii) sterically undemanding alkylating agents; and (iv) any factor that can enhance the effect of the factors mentioned above. We attributed our success with allylic and benzylic alcohols over simple alkyl alcohols to the polarizability of the unsaturated system.

On examination of the reaction intermediate **1** (Scheme 1), we reasoned that two factors should play important roles on the C/O selectivity of the reaction. The first one should be the steric hindrance of the allylic alcohol itself. This mainly contributed to the difference in reactivity of Meldrum's acid toward primary and secondary allylic alcohols. The other factor that may influence the regioselectivity of the reaction is the soft and hard, acidity and basicity (HSAB) of the counterions of the intermediate **1** (Scheme 1). Indeed, the fact that the alkylating agent as well as the counterion of the enolate oxygen may exert a significant influence on the proportion of *C*- and *O*-alkylated products has been correlated by the HSAB appraisal.[17] It is known that the percentage of *O*-alkylated products decreases considerably as the alkylating halide changes from Cl to Br to I.[16,17d,18] There are reports[16−19] on controlling the regioselectivity of the alkylations of active methylene compounds through varying the HSAB of the reaction species. In our reaction, however, the highly reactive alkoxyphosphonium intermediate **1** is a noncoordinated counterion due to its bulkiness and should therefore favor *O*-alkylation.

On the basis of the above analysis, we speculated that we might control the regioselectivity of the reaction by introducing some additives to the reaction mixture. Hence we studied the alkylation of Meldrum's acid with cyclohex-2-en-1-ol by adding lithium iodide or tetrabutylammonium iodide and hoped that such addition would promote *in situ* formation of an allylic iodide which would then promote *C*-alkylation selectivity. However, only the *O*-alkylation product was isolated.

Scheme 3



Then our focus was turned to using Pd(0) as an additive. Gratifyingly, the expected *C*-alkylation product resulted from the reaction of 5-benzyl Meldrum's acid (**2b**) with 2-cyclohex-2-en-1-ol in the presence of (Ph$_3$P)$_4$-Pd(0) as the catalyst in CH$_3$CN at 60 °C for 12 h. Studies on other secondary allylic alcohols were conducted and the results are listed in Table 2.

From the results listed in Table 2, the Pd(0)-catalyzed alkylations of Meldrum's acids **2a** and **2b** proceeded in a regiospecific fashion. In all cases, when nonsymmetric allylic alcohols were employed as alkylation agents the reaction only took place at the less hindered site of the allylic moiety (see entries 2, 5, 11, 12; compare entries 3 and 4; 7 and 9; 8 and 10) and only a *trans* double bond resulted for acyclic alcohols (entries 3−4, 6−13). The yield of the reaction is substrate and temperature dependent. For secondary allylic alcohols, reasonable yields could only be obtained in most cases when the reaction occurred at about 60 °C (entries 1, 2, 6−8, 13 in Table 2). For primary alcohols, the reaction proceeded smoothly at room temperature, but the yield could be improved to some extent at elevated temperature (see entry 10 in Table 2). Attempts to dialkylate Meldrum's acid **2a** with secondary allylic alcohols failed (entries 14, 15).

On the basis of our experimental results, we propose that the Pd(0)-mediated Mitsunobu condensation of Meldrum's acid with allylic alcohols should proceed through the pathway shown in Scheme 3. Addition of a catalytic amount of Pd(0) could reverse the *C* verses *O* selectivity of the alkylation and also reverse the reaction site to the less sterically hindered position (like a S$_N$2′ reaction) along the secondary allylic alcohol moiety which contains an alkenic methylene. As shown in the intermediate **6**, the Pd(0) plays its role in controlling the C/O selectivity by making both the acidity of allylic moiety and the basicity of the carbanion softer while the steric factor controls the regioselectivity along the allyl moiety.

Attempts to synthesize monosubstituted Meldrum's acids selectively through the Mitsunobu dehydrative alkylations including the one mediated by Pd(0) mentioned above were fruitless. Firstly, the use of 1 equiv of a primary allylic alcohol with respect to Meldrum's acid was attempted. Surprisingly, in all cases only 50% of Meldrum's acid was consumed, and only disubstituted alkylated products were produced. Then the reactions of 5 mol equiv of Meldrum's acid with 1 equiv of the primary allylic alcohol were investigated. Again, in all

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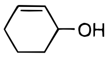
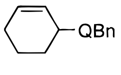
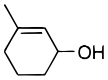
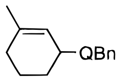
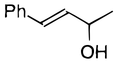
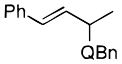
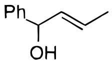
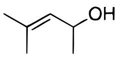
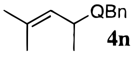
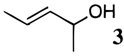
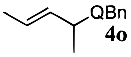
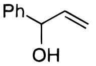
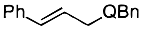
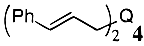
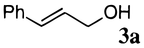
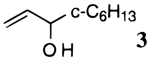
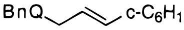
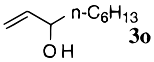
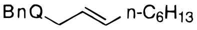
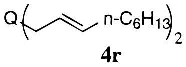
(16) (a) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Menlo Park, CA, 1972; Chapter 9, p 492. (b) Stowell, J. C. *Carbanions in Organic Synthesis;* Wiley: New York, 1979; Chapter 6, p 191. (c) Carruthers, W. *Some Modern Methods of Organic Synthesis*, 3rd ed.; Cambridge University Press: New York, 1986; Chapter 1. (d) Caine, D. In *Comprehensive Organic Synthesis;* Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, p 54.

(17) (a) Pearson, R. G.; Songstand, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827. (b) Pearson, R. G. *J. Chem. Educ.* **1968**, *45*, 643. (c) Ho, T. L. *Tetrahedron* **1985**, *41*, 1. (d) Le Noble, W. J.; Puerta, J. E. *Tetrahedron Lett.* **1966**, *10*, 1087.

(18) (a) Zook, H. D.; Miller, J. A. *J. Org. Chem.* **1971**, *36*, 1112. (b) Heiszwolf, G. J.; Kloosterziel, H. *Recl. Trav. Chim. Pays-Bas*, **1970**, *89*, 1153.

(19) (a) Schick, H.; Schwarz, H.; Finger, A.; Schwarz, S. *Tetrahedron* **1982**, *38*, 1279. (b) Rajamannar, T.; Palani, N.; Balasubramanian, K. K. *Synth. Commun.* **1993**, *23*, 1279. (c) Fujiwara, M.; Hitomi, K.; Baba, A.; Matsuda, H. *Chem. Lett.* **1994**, 875. (d) Schultz, G.; Motyka, L. A.; Plummer, M. *J. Am. Chem. Soc.* **1986**, *108*, 1056. (e) Pickersgill, I. F.; Marchington, A. P.; Rayner, C. M. *J. Chem. Soc., Chem. Commun.* **1994**, 2597. (f) Bedekar, A. V.; Watanabe, T.; Tanaka, K.; Fuji, K. *Synthesis* **1995**, 1069.

Table 2. Alkylation of Meldrum's Acid via Mitsunobu Condensation Mediated by Pd(0)[a]

Entries	Alcohols	Meldrum's Acid	Products[b]	Yields (T °C)[c]
1	 **3h**	**2b**	 **4s**	73 (60) no reaction (rt)
2	 **3i**	**2b**	 **4l**	53 (60) no reaction (rt)
3	 **3k**	**2b**	 **4m**	84 (60)
4	 **3j**	**2b**	**4m**	85 (60)
5	 **3l**	**2b**	 **4n**	65 (60)
6	 **3m**	**2b**	 **4o**	81 (60), 11 (rt)
7	 **3n**	**2b**	 **4h**	90 (60), 17 (rt)
8	**3n**	**2a**	 **4a**	80 (60) no reaction (rt)
9	 **3a**	**2b**	**4h**	95 (60)
10	**3a**	**2a**	**4a**	90 (60), 72 (rt)
11	 **3p**	**2b**	 **4q**	73 (60)
12	 **3o**	**2b**	 **4p**	84 (60)
13	**3o**	**2a**	 **4r**	71 (60) no reaction (rt)
14	**3h**	**2a**	complex mixture	35 (60) no reaction (rt)
15	**3m**	**2a**	complex mixture	40 (60)

[a] Tetrakis(triphenylphosphine)palladium(0) was used as the catalyst
[b] QH_2 = Meldrum's acid **2a**; BnQH = 5-benzyl Meldrum's acid **2b**
[c] Reaction temperature

the cases, only disubstituted products were obtained, and no monosubstituted products were detectable. Like most of the other methods[20] used to alkylate 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.

Experimental Section

Melting points are reported in degrees Celsius and are uncorrected. Infrared (IR) spectra were recorded on a FT-IR spectrometer as thin films on NaCl disks for liquid. Nuclear magnetic resonance (NMR) spectra were measured in solutions of $CDCl_3$ at 250 MHz (^1H) or at 62.9 MHz (^{13}C) . Spin−spin coupling constants (J) were measured directly from the spectra. Carbon and hydrogen elemental analyses were car-

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[20] (a) McNab, H. *Chem. Soc. Rev.* **1979**, *7*, 345. (b) Fieser, L. F.; Fieser, M. In *Reagents for Organic Synthesis;* John Wiley: New York, 1967; Vol. 1, p 526.

ried out at the MEDAC Ltd, Department of Chemistry, Brunel University, Uxbridge, England. All reactions were monitored by analytical thin-layer chromatography (TLC) on aluminum precoated with silica gel $60F_{254}$ (E. Merck), and compounds were visualized with a spray of 5% w/v dodecamolybdophosphoric acid in ethanol and subsequent heating. All columns were packed wet using E. Merck silica gel 60 (230−400 mesh) as the stationary phase and eluted using flash chromatographic technique. Toluene was distilled over sodium and stored in the presence of activated 4 Å molecular sieves. THF was distilled from sodium benzophenone ketyl under a nitrogen atmosphere. Acetonitrile was distilled over calcium hydride and stored over activated 4 Å molecular sieves. Most alcohols **3a**−**c** and **3e**−**h** were available from commercial resources as A. R. reagents and were used directly without further purification. Others were synthesized through $NaBH_4$/$CeCl_3$ or DIBAL reduction or Grignard reaction of the corresponding ketones or aldehydes. The resultant alcohols displayed satisfactory ^1H NMR spectra. Meldrum's acid[21] and 5-benzyl Meldrum's acid[22] were synthesized according to the literature procedures.

General Procedures for Alkylation of Meldrum's Acid through Mitsunobu Condensation. Method A: Toluene as Solvent. To a stirred solution of an alcohol (2.5 mmol), Ph_3P (2.5 mmol), and Meldrum's acid (1 mmol) in toluene (50 mL) at 0 °C was added dropwise DIAD (3 mmol) under N_2. The reaction mixture was allowed to stir at rt for 1 h and concentrated under reduced pressure to yield a crude product which was dissolved in ether. Hexane was then added to precipitate the Ph_3PO formed. The resultant mixture was filtered and the filtrate was concentrated. The residue was fractionated on a silica gel column to give the product.

Method B: THF as solvent. To a stirred solution of Ph_3P (2 mmol) in THF (8 mL) at − 78 °C under N_2 was added dropwise DIAD (2 mmol) at −78 °C over 10 min. To the stirring reaction mixture at −78 °C was added alcohol (3 mmol) dropwise and allowed to stir for a further 5 min. To the resultant mixture at −78 °C was added a solution of 1 mmol of Meldrum's acid (**2a**) {2 mmol for 5-benzyl Meldrum's acid (**2b**)} in THF (2 mL) dropwise and allowed to stir for another 5 min. The reaction mixture was then stirred at rt for 4 h and was concentrated under reduced pressure. The residue was fractionated on a silica gel column to afford the product.

5,5-Dicinnamyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4a). A white solid was isolated in 60% yield from cinnamyl alcohol (**3a**) and Meldrum's acid via method A: mp 134 °C (hexane−$CHCl_3$) (lit.[11] mp 131 °C); IR (KBr), 3011, 2922, 1772, 1739, 1261, 950, 744 cm^{-1}; ^1H NMR δ 1.56 (s, 6H), 2.96 (d, J = 7.7 Hz, 4H), 6.09 (dt, J = 15.7, 7.8 Hz, 2H), 6.55 (d, J = 15.8 Hz, 2H), 7.20−7.35 (m, 10H); ^{13}C NMR δ 29.8, 42.1, 56.4, 105.9, 122.0, 126.4, 128.0, 128.7, 136.1, 136.4, 168.7. Anal. Calcd for $C_{24}H_{24}O_4$: C, 76.57; H, 6.42. Found: C, 76.57; H, 6.40.

5,5-Dibenzyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4b). A white solid was isolated in 40% yield from benzyl alcohol (**3b**) and Meldrum's acid via method A and in 84% yield from benzyl alcohol (**3b**) and 5-benzyl Meldrum's acid via Method B: mp 232−233 °C (hexane−$CHCl_3$) (lit.[9a] mp 232−233 °C); IR (KBr), 1765, 1732, 1455 cm^{-1}; ^1H NMR δ 0.64 (s, 6H), 3.46 (s, 4H), 7.18−7.30 (m, 10H); ^{13}C NMR δ 28.7, 45.1, 60.2, 105.9, 127.9, 128.9, 130.3, 135.1, 168.2. Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.05; H, 6.21. Found: C, 73.88; H, 6.17.

5,5-Diallyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4c).[10] An oil was obtained in 94% yield from allylic alcohol (**3c**) and Meldrum's acid (**2a**) via method A: IR (neat), 3082, 3004, 1776, 1743, 1268, 939 cm^{-1}; ^1H NMR δ 1.67 (s, 6H), 2.73 (d, J = 7.5 Hz, 4H), 5.10−5.26 (m, 4H), 5.60−5.80 (m, 2H); ^{13}C NMR δ 29.9, 42.8, 55.6, 105.8, 121.3, 131.0, 168.4.

5,5-Bis((*Z*)-2-methylbut-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4d). A white solid was isolated in 59% yield from (*Z*)-2-methylbut-2-en-1-ol (**3d**) and Meldrum's acid (**2a**) via method A: mp 89 °C (hexane); IR (KBr), 2994, 2939, 2860, 1769, 1734, 1357, 1272, 951 cm^{-1}; ^1H NMR δ 1.40−1.66 (m, 18H), 2.71 (s, 4H), 5.37−5.44 (m, 2H); ^{13}C NMR δ 13.6, 17.1, 29.6, 49.2, 56.5, 105.5, 126.5, 130.1, 169.0. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.71 H, 8.64.

5,5-Bis(naphthalenylmethyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4e). A white solid was harvested in 73% yield from 1-naphthalenemethanol (**3e**) and Meldrum's acid (**2a**) via method A: mp 155 °C (hexane−diethyl ether); IR (KBr), 3051, 2992, 2941, 1768, 1735, 1348, 1274, 1199, 778 cm^{-1}; ^1H NMR δ 0.44 (s, 6H), 4.16 (s, 4H), 7.35−7.81 (m, 12H), 8.33 (d, J = 8.5 Hz, 2H); ^{13}C NMR δ 28.6, 40.9, 58.9, 105.6, 124.6, 125.2, 126.0, 126.4, 128.5, 128.6, 129.2, 131.4, 132.0, 134.0, 168.6. Anal. Calcd for $C_{28}H_{24}O_4$: C, 79.22; H, 5.70. Found: C, 79.93; H, 5.74.

5,5-Bis(3-methylbut-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4f). A syrup was obtained in 80% yield from 3-methylbut-2-en-1-ol (**3f**) and Meldrum's acid (**2a**) via method A and in 71% yield via method B: IR (neat), 2970, 2919, 1770, 1745, 1379, 1337, 1264, 1097, 955 cm^{-1}; ^1H NMR δ 1.55−1.75 (m, 18H), 2.74 (d, J = 8.0 Hz, 4H), 5.00−5.07 (m, 2H); ^{13}C NMR δ 17.8, 25.7, 29.6, 37.7, 55.3, 105.4, 117.4, 137.7, 169.2. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.29; H, 8.55.

2,2-Dimethyl-2′-vinylspiro[1,3-dioxane-5,1′-cyclopropane]-4,6-dione (4g). A syrup was isolated in 13% yield from *cis*-but-2-en-1,4-diol (**3g**) and Meldrum's acid (**2a**) via method A and in 20% yield via method B: IR (neat), 2993, 2926, 1765, 1737, 1324, 1196, 967 cm^{-1}; ^1H NMR δ 1.73 (s, 3H), 1.78 (s, 3H), 2.23 (dd, J = 4.5, 8.6 Hz, 1H), 2.37 (dd, J = 4.4, 9.1 Hz, 1H), 2.78 (q, J = 9.0 Hz, 1H), 5.32−5.50 (m, 2H), 5.68−5.85 (m, 1H); ^{13}C NMR δ 24.8, 27.8, 29.8, 31.7, 43.0, 105.2, 121.8, 131.5, 167.5. Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.17; H, 6.24.

5-Benzyl-5-cinnamyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4h). A white solid was harvested in 80% yield from cinnamyl alcohol (**3a**) and 5-benzyl Meldrum's acid (**2b**) via method A: mp 149 °C (hexane); IR (KBr), 3034, 2995, 2937, 1772, 1739, 1264, 707 cm^{-1}; ^1H NMR δ 0.68 (s, 3H), 1.40 (s, 3H), 3.04 (d, J = 8.1 Hz, 2H), 3.38 (s, 2H), 6.00−6.13 (m, 1H), 6.55 (d, J = 15.9 Hz, 1H), 7.19−7.34 (m, 10H); ^{13}C NMR δ 28.8, 29.7, 43.4, 44.0, 58.4, 106.0, 121.6, 126.4, 127.9, 128.0, 128.7, 128.9, 130.4, 135.2, 136.1, 136.4, 168.6. Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.36; H, 6.31.

5-Allyl-5-benzyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4i). A white solid was obtained in 85% yield from allylic alcohol (**3c**) and 5-benzyl Meldrum's acid (**2b**) via method B: mp 82 °C (hexane); IR (KBr), 3062, 2996, 2940, 1773, 1734, 1275, 1207, 1085, 933, 717 cm^{-1}; ^1H NMR δ 0.68 (s, 3H), 1.53 (s, 3H), 2.88 (d, J = 7.6 Hz, 2H), 3.33 (s, 2H), 5.18−5.30 (m, 2H), 5.61−5.79 (m, 1H), 7.17−7.28 (m, 5H); ^{13}C NMR δ 28.8, 29.8, 44.0, 44.3, 58.1, 105.9, 121.4, 127.9, 128.9, 130.4, 130.7, 168.4. Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 70.26; H, 6.64.

5-Benzyl-5-(3-methylbut-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4j). A white solid was harvested from 3-methylbut-2-ene-1-ol (**3f**) and 5-benzyl Meldrum's acid (**2b**) via method B in 96% yield: mp 86 °C (hexane); IR (KBr), 3001, 2940, 2940, 1771, 1738, 1453, 1260, 706 cm^{-1}; ^1H NMR δ 0.70 (s, 3H), 1.51 (s, 3H), 1.68 (s, 3H), 1.70 (s, 3H), 2.88 (d, J = 7.9 Hz, 2H), 3.33 (s, 2H), 5.01−5.09 (m, 1H), 7.16−7.28 (m, 5H); ^{13}C NMR δ 18.0, 25.9, 28.9, 29.5, 39.2, 43.9, 57.9, 105.8, 117.0, 127.8, 128.9, 130.4, 135.5, 168.9. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.65 H, 7.55.

5-Benzyl-5-(naphthalenylmethyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4k). A white solid was obtained from 1-naphthalenemethanol (**3e**) and 5-benzyl Meldrum's acid (**2b**) via method B in 75% yield: mp 108 °C; IR (KBr), 3035, 2940, 1787, 1730, 1450, 1271, 953, 703 cm^{-1}; ^1H NMR δ 0.44 (s, 3H), 0.59 (s, 3H), 3.61 (s, 2H), 4.00 (s, 2H), 7.20−7.80 (m, 11H), 8.22 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 28.2, 28.9, 30.0, 41.1, 44.9, 59.6, 105.8, 124.4, 125.3, 126.1, 126.5, 127.8, 128.5, 128.7, 128.8, 129.2, 130.6, 131.3, 131.9, 134.0, 135.1, 168.5. Anal. Calcd for $C_{24}H_{22}O_4$: C, 76.98; H, 5.92. Found: C, 76.70; H, 5.88.

General Procedures for Alkylation of Meldrum's Acid through Mitsunobu Condensation Mediated by Pd(0). To a solution of Ph_3P (0.2 mmol) and 14 mg of $(Ph_3P)_4Pd(0)$ in

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(21) Davidson, D.; Bernhard, S. A. *J. Am. Chem. Soc.* **1948**, *70*, 3426.

(22) Wright, A. D.; Haslego, M. L.; Smith, F. X. *Tetrahedron Lett.* **1979**, 2325 and references cited therein.

CH_3CN (3 mL) at 0 °C under N_2 was added DIAD (0.2 mmol) and the mixture allowed to stir at 0 °C for 5 min. Allylic alcohol (0.3 mmol) was then added at 0 °C, and the resultant mixture was stirred for a further 10 min. A solution of 0.2 mmol of 5-benzyl Meldrum's acid (**2b**) {0.1 mmol for Meldrum's acid (**2a**)} in CH_3CN (1 mL) was added dropwise. The reaction mixture was allowed to stir at 60 °C for 12 h, diluted with diethyl ether, and filtered through a layer of silica gel. Removal of solvents from the filtrate under reduced pressure followed by fractionaion of the residue using flash chromatography afforded the required products.

5-Benzyl-5-(cyclohex-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4s). A white solid was isolated in 73% yield from 5-benzyl Meldrum's acid (**2b**) and cyclohex-2-en-1-ol (**3h**): mp 126.5−127 °C (hexane); IR (KBr), 2930, 1767, 1728, 1458, 1395, 1345, 1275, 1020, 951, 704 cm^{-1}; ^1H NMR δ 0.63 (s, 3H), 1.55−1.75 (m, 5H), 1.72−2.15 (m, 4H), 3.10 (br s, 1H), 3.39 and 3.55 (AB q, J_{AB} = 12.8 Hz, 2H), 5.84−6.10 (m, 2H), 7.20−7.43 (m, 5H); ^{13}C NMR δ 21.9, 24.7, 25.3, 28.8, 29.4, 39.2, 46.7, 61.2, 105.6, 124.6, 127.6, 128.8, 130.9, 135.8, 167.7, 168.1. Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.34; H, 7.06.

5-Benzyl-5-(3-methylcyclohex-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4l). A white solid was harvested in 53% yield from 5-benzyl Meldrum's acid (**2b**) and 3-methylcyclohex-2-en-1-ol (**3i**); mp 102.5−103 °C (hexane); IR (KBr), 2965, 2924, 1770, 1735, 1496, 1458, 1394, 1344, 1273, 1025, 951, 704 cm^{-1}; $_1H$ NMR δ 0.67 (s, 3H), 1.55−2.13 (m, 13H), 3.11 (br s, 1H), 3.45 and 3.54 (AB q, J_{AB} = 12.8 Hz, 2H), 5.51 (br s, 1H), 7.20−7.50 (m, 5H); ^{13}C NMR δ 22.2, 24.2, 24.7,28.7, 29.5, 39.1, 47.4, 61.4, 105.5, 118.9, 127.5, 128.7, 131.0, 136.1, 138.6, 168.1. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 73.12; H, 7.41.

5-Benzyl-5-(1-methylcinnamyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4m). A syrup was isloated in 84% yield from 5-benzyl Meldrum's acid (**2b**) and 1-methylcinnamyl alcohol (**3k**), and 85% from 5-benzyl Meldrum's acid (**2b**) and (*E*)-1-phenylbut-2-en-1-ol (**3j**): IR (neat), 3031, 2938, 1769, 1737, 1494, 1455, 1392, 1346, 1277, 1206, 1098, 1046, 951, 754, 704 cm^{-1}; ^1H NMR δ 0.67 (s, 3H), 1.36 (d, J = 6.9 Hz, 3H), 1.57 (s, 3H), 3.26 (dq, J = 9.7, 6.9 Hz, 1H), 3.41 (s, 2H), 6.29 (dd, J = 15.8, 9.7 Hz, 1H), 6.62 (d, J = 15.8 Hz, 1H), 7.20−7.60 (m, 10H); ^{13}C NMR δ 16.9, 28.9, 29.3, 41.3, 48.2, 61.4, 105.8, 126.5, 127.5, 127.8, 128.6, 128.8, 130.8, 133.2, 135.9, 136.7, 167.8, 168.5. Anal. Calcd for $C_{23}H_{24}O_4$: C, 75.80; H, 6.64. Found: C, 75.88; H, 6.41.

5-Benzyl-5-(1,3-dimethylbut-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4n). A white solid was obtained in 65% yield from 5-benzyl Meldrum's acid (**2b**) and 4-methylpent-3-en-2-ol (**3l**): mp 89.5−90 °C (hexane); IR (KBr), 3003, 2952, 1766, 1735, 1493, 1455, 1392, 1278, 1059, 954, 704 cm^{-1}; ^1H NMR δ 0.67 (s, 3H), 1.46 (d, J = 7.3 Hz, 3H), 1.53 (s, 3H), 1.64 (s, rotamer, 4H), 1.67 (s, rotamer, 2H), 3.10−3.15 (m, 1H), 3.25 and 3.53 (AB q, J_{AB} = 12.7 Hz, 2H), 5.53 (q, J = 6.3 Hz, 1H), 7.20−7.50 (m, 5H); ^{13}C NMR δ 13.4, 13.5, 14.5, 28.6, 29.5, 40.9, 52.7, 61.2, 105.4, 125.1, 127.5, 128.7, 130.9, 134.8, 136.0, 167.8, 168.7. Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 71.92; H, 7.71.

5-Benzyl-5-((*E*)-1-methylbut-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4o). A syrup was isolated in 81% yield from 5-benzyl Meldrum's acid (**2b**) and (*E*)-pent-3-en-2-ol (**3m**): IR (neat), 2972, 2939, 1770, 1740, 1496, 1456, 1393, 1352, 1277, 1207, 1011, 952, 704 cm^{-1}; ^1H NMR δ 0.67 (s, 3H), 1.26 (d, J = 7.0 Hz, 3H), 1.62 (s, 3H), 1.81 (d, J = 6.3 Hz, 3H), 3.04 (dq, J = 9.3, 7.0 Hz, 1H), 3.36 (s, 2H), 5.47 (dd, J = 15.2, 9.3 Hz, 1H), 5.71 (dq, J = 15.2 Hz, 6.3 Hz, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR δ 16.8, 17.8, 28.9, 29.3, 41.0, 47.8, 61.4, 105.6, 127.5, 128.8, 129.1, 130.4,130.8, 136.1, 167.9. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.22; H, 7.34

5-Benzyl-5-((*E*)-non-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4p). A syrup was isolated in 84% yield from 5-benzyl Meldrum's acid (**2b**) and non-1-en-3-ol (**3o**): IR (neat), 2956, 2927, 1772, 1743, 1458, 1392, 1356, 1266, 1205, 953, 703 cm^{-1}; ^1H NMR δ 0.77 (s, 3H), 0.96 (t, J = 6.8 Hz, 3H), 1.25−1.45 (m, 8H), 1.60 (s, 3H), 2.07 (q, J = 6.7 Hz, 2H), 2.91 (d, J = 7.6 Hz, 2H), 3.40 (s, 2H), 5.38 (dt, J = 15.2, 7.6 Hz, 1H), 5.75 (dt, J = 15.2, 6.7 Hz, 1H), 7.2−7.5 (m, 5H); ^{13}C NMR δ 14.0, 22.5, 28.8, 29.0, 29.6, 31.7, 32.5, 43.6, 43.8, 58.5, 105.7, 121.9, 127.7, 128.8, 130.3, 135.5, 137.9, 168.6. Anal. Calcd for $C_{22}H_{30}O_4$: C,73.71; H, 8.43. Found: C,73.81; H, 8.61.

5-Benzyl-5-((*E*)-3-cyclohexylprop-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4q). A white solid was harvested in 73% yield from 5-benzyl Meldrum's acid (**2b**) and 1-cyclohexylprop-2-en-1-ol (**3p**): mp 79.5−80 °C (hexane); IR (KBr), 2929, 2851, 1774, 1741, 1494, 1448, 1394, 1359, 1263, 1201, 1073, 952, 706 cm^{-1}; ^1H NMR δ 0.75 (s, 3H), 1.08−1.45 (m, 5H), 1.61 (s, 3H), 1.65−1.90 (m, 5H),1.92−2.05 (m, 1H), 2.90 (d, J = 7.5 Hz, 2H), 3.40 (s, 2H), 5.33 (dt, J = 15.4, 7.5 Hz, 1H), 5.71 (dd, J = 15.4, 6.5 Hz, 1H), 7.2−7.4 (m, 5H); ^{13}C NMR δ 25.9, 26.1, 28.8, 29.6, 32.6, 40.5, 43.7, 43.8, 58.5, 105.7, 119.24, 127.7, 128.8, 130.3, 135.5, 143.5, 168.6. Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13 H, 7.92. Found: C, 74.30; H, 7.85.

5,5-Di((*E*)-non-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4r). A syrup was isolated in 71% yield from 5-benzyl Meldrum's acid (**2b**) and non-1-en-3-ol (**3o**): IR (neat), 2956, 2926, 1777, 1746, 1458, 1436, 1392, 1264, 973 cm^{-1}; ^1H NMR δ 0.87 (t, J = 6.9 Hz, 6H),1.15−1.45 (m, 16H), 1.65 (s, 6H), 1,96 (q, J = 6.8 Hz, 4H), 2.66 (d, J = 7.6 Hz , 4H), 5.28 (dt, J = 15.2, 7.6 Hz, 2H), 5.61 (dt, J = 15.2, 6.7 Hz , 2H); ^{13}C NMR δ 14.0, 22.5, 28.8, 29.0, 29.9, 31.7, 32.5, 42.0, 105.5, 122.4, 137.6, 168.8. Anal. Calcd for $C_{24}H_{40}O_4$: C, 73.42; H, 10.27. Found: C, 73.15; H, 10.11.

5,5-Dicinnamyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4a). A white solid was obtained in 90% yield from cinnamyl alcohol (**3a**) and Meldrum's acid (**2a**) and in 80% yield from 1-phenylprop-2-en-1-ol (**3n**) and Meldrum's acid (**2a**).

5-Benzyl-5-cinnamyl-2,2-dimethyl-1,3-dioxane-4,6-dione (4h). A white solid was harvested in 95% yield from cinnamyl alcohol (**3a**) and 5-benzyl Meldrum's acid (**2b**) and in 90% yield from 1-phenylprop-2-en-1-ol (**3n**) and 5-benzyl Meldrum's acid (**2b**).

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