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Practical β-masked formylation and acetylation of electron-deficient olefins utilizing tetra(*n*-butyl)ammonium peroxydisulfate

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ABSTRACT

Various electron-deficient olefins reacted readily with 1,3-dioxolane or 2-methyl-1,3-dioxlane in the presence of TBAP to afford the corresponding 1,3-dioxolanylated or 2-methyl-1,3-dioxolanylated products in a complete regioselective manner in good to excellent yields.

Carbon–carbon bond formation via radical addition to alkenes is one of the most important synthetic methodologies in the construction of organic molecules. In such radical addition reactions, it is the key point that the adduct radicals should be trapped by a donor subsequent to the C–C bond formation in order to prevent radical polymerization. Organotin and organomercury hydride have been utilized for such a task.[1]

Regioselective β-masked formylation of electron-deficient olefins is a very important and useful reaction. In the addition of 2-lithio-1,3-dithiane to α,β-unsaturated carbonyl compounds, the ratio of 1,2- and 1,4-addition was remarkably dependent upon the reaction system with the predominant formation of 1,2-addition products.[2] 1,3-Dioxolanylation at electron-deficient olefins is synthetically equivalent to formylation since 1,3-dioxolane unit can be readily converted to the aldehyde group selectively under various reaction conditions.[3] A few groups reported that 1,3-dioxolanyl radical generated by photo-irradiation added to electron-deficient olefins to give the insufficient results of 1,3-dioxolanylated products.[4] Therefore, highly regioselective 1,3-dioxolanylation at the β-position of electron-deficient olefins has been desired.

Previously we have described the synthesis of tetra(*n*-butyl)ammonium peroxydisulfate (TBAP), a new type of peroxydisulfate soluble in organic solvents, by introducing tetra(*n*-butyl)ammonium moiety as a cation.[5d] By utilizing TBAP as the key reagent in organic solvent, we have developed useful organic reactions, for example, iodination of electron-deficient olefins,[5a] epoxidation of α,β-unsaturated ketones,[5b] tetrahydropyranylation of alcohols,[5c] and tetrahydrofuranylation.[5d]

In continuation of our research on utilizing TBAP for useful organic reactions, we have recently found that electron-deficient olefins (**1**) react readily with 1,3-dioxolane in the presence of TBAP (**2**) at 25 °C to afford 1,3-dioxolanylated products (**3**) in a complete regioselective manner in good to excellent yields (Table 1).[6]

Practical and efficient 1,3-dioxolanylation of α,β-unsaturated carboxylates (runs 1–4), cycloalkenones (runs 5–7), and sulfone (run 8) can be successfully carried out in 1,3-dioxolane used as a solvent and the reagent in the presence of TBAP (2 equiv) at 25 °C under Ar. After the complete 1,3-dioxolanylation reaction, tetra(*n*-butyl)ammonium sulfonic acid, a byproduct derived from TBAP, was isolated and identified.

In connection with this novel reaction, we have also examined the addition of 2-methyl-1,3-dioxolan-2-yl radical to electron-deficient olefins since the 2-methyl-1,3-dioxolanylation reaction[4a,7] is equivalent to acetylation at the β-position of electron-deficient olefins (Table 2).[8]

For the 2-methyl-1,3-dioxolanylation reaction, 1,2-dichloroethane was used as a solvent together with a excess amount of 2-methyl-1,3-dioxolane in the presence of TBAP (2.0 equiv). Higher reaction temperature (70 °C) compared with 25 °C of the 1,3-dioxolanylation reaction was required to complete the reaction most probably due to the steric hindrance of 2-methyl group of 2-methyl-1,3-dioxolane. This reaction is particularly noteworthy since the 1,4-dioxo compounds[9] are known to be valuable

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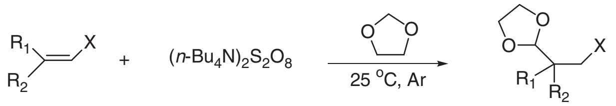
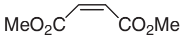
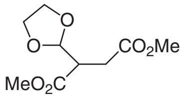
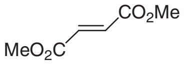
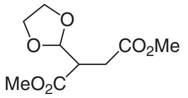
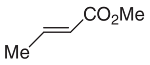
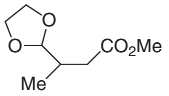
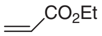
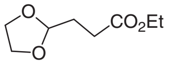
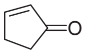
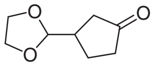
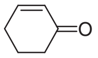
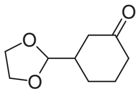
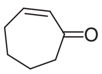
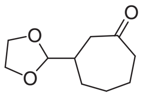
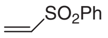
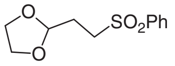
Table 1
β-(1,3-Dioxolanylation) of electron-deficient olefins

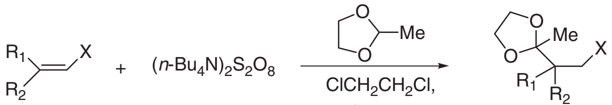


1 2 3

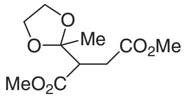
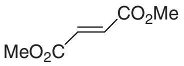
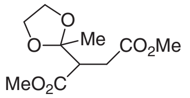
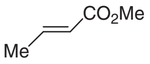
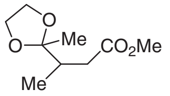
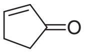
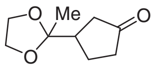
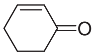
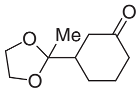
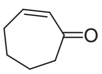
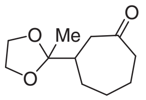
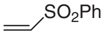
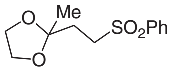
Run	Olefin (**1**)	Rxn time (h)	Product (**3**)	Yield[a] (%)
1		1.5		98
2		1.5		98
3		15		98
4		20		71
5		18		97
6		54		73
7		44		90
8		3		99

[a] Isolated yield after flash column chromatography.

Table 2
β-(2-Methyl-1,3-dioxolanylation) of electron-deficient olefins



1 2 5

Run	Olefin (**1**)	Time (min)	Product (**5**)	Yield[a] (%)
1		20		96
2		30		70
3		150		99
4		30		60
5		90		66
6		90		80
7		30		48

[a] Isolated yield after flash column chromatography.

precursors for the synthesis of cyclopentanoids and furanoids,[10] heteroaromatics,[11] and also bioactive natural products such as *cis*-jasmone, rethrolones, and prostaglandin B_2.[12]

In summary, we have shown that various types of electron-deficient olefins reacted readily with 1,3-dioxolane or 2-methyl-1,3-dioxlane in the presence of TBAP to provide the corresponding 1,3-dioxolanylated or 2-methyl-1,3-dioxolanylated products, formylation or acetylation equivalents, in a complete regioselective way in good to excellent yields. These novel 1,4-addition reactions are practically useful for the synthesis of formyl and acetyl functional groups which could play a commanding role in the construction of complex molecular architecture. Further studies to determine the scope and the reaction mechanism are actively going on, and the results will be reported in due course.

Acknowledgments

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3. Ji, H.-B. *Eur. J. Org. Chem.* **2003**, 3659. Other important references cited therein.
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6. *Typical experimental procedure:* Dimethyl maleate (72.1 mg, 0.50 mmol) and TBAP (677.0 mg, 1.0 mmol) were added to dry 1,3-dioxolane (5 mL), and the reaction mixture was stirred at 25 °C for 1.5 h under Ar. The reaction mixture was concentrated to give a viscous oil which was diluted with H_2O (5 mL), then extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were dried over anhyd $MgSO_4$, filtered and concentrated to give an oily residue which was flash chromatographed (SiO_2, Et_2O/hexane = 1:3) to afford pure dimethyl 2-(1,3-dioxolan-2-yl)butanedioate (106.9 mg, 98%). IR (NaCl, neat) 1737, 1187, 1023, 946 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.63 (dd, 1H, –CHC*H*H–, $J_1 = 17.1$ Hz, $J_2 = 4.9$ Hz), 2.80 (dd, 1H, –CHCH*H*–, $J_1 = 17.1$ Hz, $J_2 = 9.3$ Hz), 3.25 (br q, 1H, –C*H*CH_2–), 3.68 (s, 3H, –OCH_3), 3.75 (s, 3H, –OCH_3), 3.85–4.01 (m, 4H, –CH_2CH_2–), 5.19 (d, 1H, –CHC*H*–, $J = 4.4$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.90, 45.54, 51.74, 52.16, 65.24, 102.60, 102.62, 171.28, 172.25, MS (EI) *m*/*z* (rel. intensity %) 99 (11), 73 (100), 59 (27), 55 (38), 45 (48).
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8. *Typical experimental procedure:* A mixture of methyl crotonate (50.1 mg, 0.50 mmol), TBAP (677.0 mg, 1.0 mmol) and 2-methyl-1,3-dioxolane (881.1 mg, 10.0 mmol) in anhyd dichloroethane (2 mL) was heated at 70 °C for 2.5 h under Ar. The reaction mixture was concentrated to give a viscous oil which was diluted with saturated aqueous $NaHCO_3$ (1 mL) and distilled H_2O (10 mL). The product was extracted with Et_2O (10 mL × 3), and the combined organic layers were dried over anhyd $MgSO_4$, filtered and concentrated. The oily residue was purified by flash chromatography on SiO_2 (Et_2O/hexane = 1:3) to afford methyl 3-(2-methyl-1,3-dioxolan-2-yl)butanoate (93.0 mg, 99 %). IR (NaCl, neat) 1733, 1195, 1160, 1051, 951 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 102 (d, 3H, CH_3CH–, $J = 6.8$ Hz), 1.27 (s, 3H, CH_3C–), 2.09 (dd, 1H, –CHC*H*H–, $J_1 = 15.1$ Hz, $J_2 = 8.3$ Hz), 2.27–2.37 (m, 1H, –C*H*CH_2–), 2.57 (dd, 1H, –CHCH*H*–, $J_1 = 15.1$ Hz, $J_2 = 5.4$ Hz), 3.67 (s, 3H, –CO_2CH_3), 3.87–4.01 (m, 4H, –CH_2CH_2–);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.49, 20.56, 36.76, 38.48, 51.49, 64.64, 64.72, 111.28, 173.74; MS (EI) m/z (rel. intensity %) 87 (100), 59 (4), 43 (45).

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