EPOXIDATION OF 5-ALKYLIDENE AND 5-BENZYLIDENE SUBSTITUTED 1,3-DIOXANE-4,6-DIONE DERIVATIVES BY HYDROGEN PEROXIDE WITHOUT CATALYST

Takashi Tsuno and Kunio Sugiyama*
Department of Industrial Chemistry, College of Industrial Technology,
Nihon University, Narashino-shi, Chiba 275, Japan

Abstract —— 5-Alkylidene and 5-benzylidene substituted 1,3-dioxane-4,6-dione derivatives readily reacted with hydrogen peroxide at room temperature without any catalyst to give the corresponding spiro- and polyspirocyclic compounds containing oxirane ring in good yields.

The epoxidation of α,β-unsaturated carbonyl compounds with hydrogen peroxide is one of very important and useful reactions in organic synthesis and has required careful pH control of reaction[1] and/or the presence of catalyst.[2] Catalysts for the epoxidation have been mainly investigated,[2] while there are very few report on α,β-unsaturated carbonyl compounds to be epoxidized with hydrogen peroxide in the absence of catalyst. We noted that 5-alkylidene and 5-benzylidene Meldrum's acids (**1a**, **1b**, **1d**, and **1g**) are very reactive electrophiles and susceptible to attack by some nucleophiles such as sodium methoxide,[3] amines,[4] and aryloxide ions[5] to give the corresponding zwitterionic adducts. Therefore, these Meldrum's acids were expected to be oxidized under milder conditions with hydrogen peroxide alone and such epoxidation of these acids (**1a-g**), 8-alkylidene-6,10-dioxa-7,9-dioxospiro[4.5]decane (**2a-d**), and 3-alkylidene-1,5-dioxa-2,4-dioxospiro[5.5]-undecane (**3a-d**) was tried to afford the corresponding epoxides in good yields.

The starting compounds **1a-d**, **1f**, and **1g** were obtained by the reaction of Meldrum's acid with the corresponding ketones or aldehydes according to a slightly modified procedure of the reported methods.[3a,6] Similarly, **1e**, **2a-d**, and **3a-d** were easily synthesized by the condensation between the corresponding active methylene compounds[7] and ketones or aldehydes.

A typical procedure of the epoxidation is as follows. Isobutylidene Meldrum's acid (**1a**, 1.45 g, 7.3 mmol) was added to a solution of 35 % hydrogen peroxide

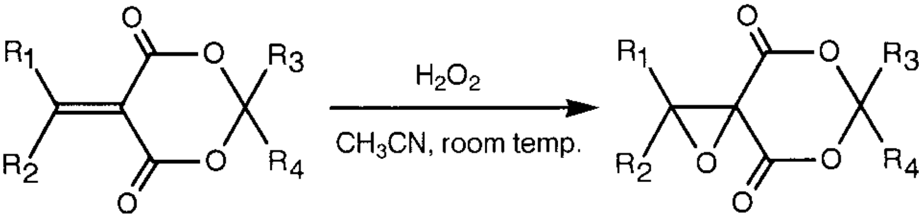

Table 1. Epoxidation of 5-Alkylidene and 5-Benzylidene Substituted 1,3-Dioxane-4,6-dione Derivatives with Hydrogen Peroxide in Acetonitrile[a)]

Entry	Substrate	R_1	R_2	R_3	R_4	Time/min	Epoxide[b)]	Yield/%	mp/°C[c)]
1	**1a**	i-C_3H_7	H	CH_3	CH_3	10	**4a**	76	73-74
2	**1b**	CH_3	CH_3	CH_3	CH_3	30	**4b**	69	124
3	**1c**	-$(CH_2)_4$-		CH_3	CH_3	1200	**4c**	74	116-117
4	**1d**	-$(CH_2)_5$-		CH_3	CH_3	180	**4d**	37	133
5	**1e**	i-C_4H_9	H	CH_3	CH_3	15	**4e**	29	77-78
6	**1f**	c-C_6H_{11}	H	CH_3	CH_3	10	**4f**	67	75-78
7	**1g**	Ph	CH_3	CH_3	CH_3	10	**4g**	54	126-132[d)]
8	**2a**	i-C_3H_7	H	-$(CH_2)_4$-		10	**5a**	74	102
9	**2b**	CH_3	CH_3	-$(CH_2)_4$-		30	**5b**	15	124
10	**2c**	-$(CH_2)_4$-		-$(CH_2)_4$-		60	**5c**	40	145-146
11	**2d**	-$(CH_2)_5$-		-$(CH_2)_4$-		40	**5d**	57	148-152
12	**3a**	i-C_3H_7	H	-$(CH_2)_5$-		10	**6a**	76	96-98
13	**3b**	CH_3	CH_3	-$(CH_2)_5$-		15	**6b**	53	136-137
14	**3c**	-$(CH_2)_4$-		-$(CH_2)_5$-		90	**6c**	49	148-149
15	**3d**	-$(CH_2)_5$-		-$(CH_2)_5$-		40	**6d**	37	158-160

a) All reactions were carried out at room temperature under an argon atmosphere. b) All epoxides gave satisfactory ir, ^1H, and ^{13}C nmr spectra, and elementary analyses. c) Melting points are uncorrected. d) Decomposed.

(3 ml) in acetonitrile[8] (17 ml) with stirring at room temperature. The reaction was monitored by the disappearance of **1a** with tlc (Silica gel, Merck, 60 F_{254}, hexane:acetone=8:2, v/v). After 10 min, to the reaction mixture was added 10 % sodium hydrogensulfite solution (20 ml) and extracted with dichloromethane (20 ml × 2). The organic layer was dried over anhydrous magnesium sulfate, and concentrated to give crude crystals. Recrystallization from ether/hexane gave the epoxide, 2-isopropyl-6,6-dimethyl-1,5,7-trioxa-4,8-dioxospiro[2.5]octane (**4a**, 1.19 g, 76 %) mp 73-74 °C; ir ($CHCl_3$) 1740 and 1760 cm^{-1}; ^1H nmr ($CDCl_3$) δ=1.01(3H,

d, J=7.1 Hz), 1.20(3H, d, J=7.1 Hz), 1.82(3H, s), 1.85(3H, s), 1.99(1H, d septet, J=9.3 and 7.1 Hz), and 3.43(1H, d, J=9.3 Hz); ^{13}C nmr ($CDCl_3$) δ=18.3(q), 19.9(q), 26.4(d), 27.6(q), 28.3(q), 55.4(s), 73.5(d), 105.9(s), 161.7(s), and 163.7(s); Anal. Found: C, 56.07 %; H, 6.71 %. Calcd for $C_{10}H_{14}O_5$: C, 56.07 %; H, 6.59 %. Similarly, the epoxidation of **1b-g**, **2a-d**, and **3a-d** was carried out and yields were shown as Table 1.

The epoxidation with hydrogen peroxide in acetonitrile is possible to proceed via peroxycarboximidic acid,[9] then, we have investigated the solvent effect on the epoxidation of **1a** and **1g** by the use of several other solvents in order to clarify this question (Table 2). When methanol or t-butyl alcohol as solvent was employed, both of **1a** and **1g** allowed rapidly to react with hydrogen peroxide. However, the epoxidation of two-phase system using benzene as solvent proceeded quite slowly, although these conditions have eventually completed oxidation. Therefore, it is suggested that the epoxidation of **1a-g**, **2a-d**, and **3a-d** occurred directly with hydrogen peroxide.

Table 2. Solvent Effect on Epoxidation of **1a** and **1g** with Hydrogen Peroxide[a)]

1	Solvent	Time	Yield/%
a	MeOH	10 min	62
	t-BuOH	10 min	88
	Benzene[b)]	22 h	85
g	MeOH	10 min	62
	t-BuOH	10 min	75
	Benzene[b)]	24 h	78

a) All reactions were carried out in the presence of **1a** or **1g** (7 mmol) and 35 % hydrogen peroxide (3 ml) in solvent (17 ml). b) Two-phase system.

The epoxidation of usual olefins with hydrogen peroxide alone affords products of incomplete oxidation or no products. The epoxidation of α,β-unsaturated esters has been performed by using peracids[9,10] or alkaline hydrogen peroxide.[1a] Diethyl ethylidenemalonate, a compound analogous to 5-alkylidene substituted 1,3-dioxane-4,6-diones, has been epoxidized only with alkaline hydrogen peroxide.[1a] However, the epoxidation of **1a-g**, **2a-d**, and **3a-d** with hydrogen peroxide alone took place completely and more reactively than that of ordinary olefins.

Thus, it is particularly interesting to note that the epoxidation of **1a-g**, **2a-d**, and **3a-d** with hydrogen peroxide proceeds at room temperature, without the use of bufferring system and catalyst.

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