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SmI_2-INDUCED REDUCTIVE CROSS-COUPLING OF CARBONYL COMPOUNDS WITH α,β-UNSATURATED ESTERS[1]

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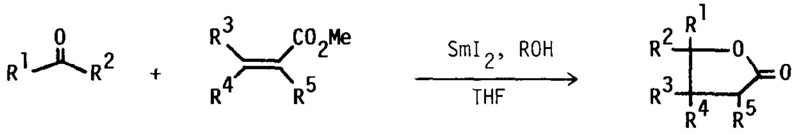
Summary: Reductive cross-coupling of carbonyl compounds with α,β-unsaturated esters by SmI_2 to γ-lactones was *highly accelerated by the addition of hexamethylphosphoric triamide* (HMPA).

Among two-component syntheses of γ-lactone frameworks,[2] the direct cross-coupling of carbonyl compounds with α,β-unsaturated esters through the polarity inversion of either of the two reactants appears to be one of the most straightforward approaches, however, only a few methods have so far been available for this type of coupling; i.e. (1) reductive coupling by electrolytic method[3] and (2) that by zinc metal and chlorotrimethylsilane.[4]

Recently, Fukuzawa et al.[5a] and we[1] independently found that SmI_2[6] is quite effective *for such a coupling reaction (eq 1) and the former group has communicated their results so* far obtained.[5b] Here we wish to describe a highly promoting effect of HMPA on the reaction when used as a co-solvent and some notable remarks with additional examples (Table 1).



(1)

The remarkable enhancement of the coupling rate and yield by added HMPA (ca. 5% in the *solvent) is apparent from Runs 2, 6, 8, 9, and 12. In the cases where disubstituted* γ-lactones were formed, appreciable stereoselectivity[7] was observed in the absence of HMPA, however, it was largely diminished by the addition of HMPA. Precise study on the stereoselection in the reaction is under way. As particular examples, formaldehyde was found to serve as a hydroxymethylating agent though yields were not satisfactory (Runs 4 and 10). A biologically interesting steroidal spirolactone was prepared in one step from 3-O-methylestrone (Run 3) in higher yield than that of previous method (25% in 5 steps).[8] Interestingly, activation of carbonyl function by Cp_2ZrCl_2 was effective here increasing the *yield from 20% (without Cp_2ZrCl_2) to 46%* . A limitation of the present method in the case of β,β-disubstituted acryl esters seems to be apparent (Run 13).

Table 1. SmI_2-induced Reductive Coupling of Carbonyl Compounds with α,β-Unsaturated Esters[a]

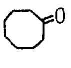
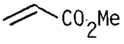
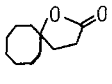
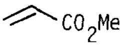
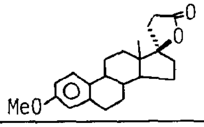
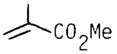
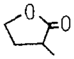
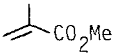
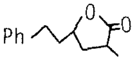
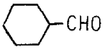
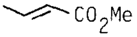
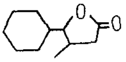
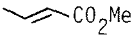
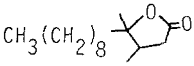
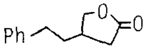
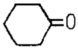
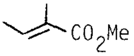
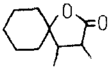
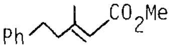
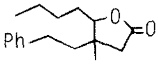
Run	Carbonyl compound	Unsaturated ester	Conditions		Product[b]	%Yield[c] (Ratio)[d]
			Additive	Time		
1			none	4 h		82
2			HMPA	1 min		95
3[e]	3-O-methyl- estrone		Cp_2ZrCl_2	6 h		46

Table 1. (Continued)

4	HCHO[f)]		HMPA	1 min		45[g)]
5			none	6 h		70 (6:1)
6			HMPA	1 min		78 (2.3:1)
7			none	4 h		71 (>20:1)[h)]
8			HMPA	1 min		96 (1:1)
9	2-undecanone		HMPA	1 min		99[i)] (1.4:1)
10	aq. HCHO[j)]		none	3 h		30
11			none	4 h		57 (1.3:1)
12			HMPA	1 min		89 (4.9:1)
13	pentanal		HMPA	1 min		0[k)]

a) The reactions were carried out at 0 °C by using carbonyl compounds (0.1∼1 mmol), α,β-unsaturated esters (0.2∼2 mmol), 2-propanol (0.15∼1.5 mmol), and a SmI$_2$-THF solution (0.1 mol dm^{-3}, 3∼30 ml) under an atmosphere of nitrogen with or without HMPA (1 ml for 1 mmol scale). b) Satisfactory ^{1}H NMR, IR, and analytical data were obtained. c) Isolated yield. d) Isomeric ratio determined by ^{1}H NMR analysis. Configuration was not determined. e) Methyl acrylate (9 eq), Cp$_2$ZrCl$_2$ (1 eq), and SmI$_2$ (9 eq) were used. f) Freshly distilled HCHO (10 eq) was used [see A.B.Smith,III, et al., Org. Syn., **61**, 65 (1983)]. g) GLC yield. h) See ref. 7. i) 2-Undecanone was reported not to react with acrylate by the electroreductive method (ref. 3b). j) 37% solution (5 eq) was used without 2-propanol. k) Pentanol and the reductive homo-coupling product of the α,β-unsaturated ester were detected.

References and Notes

1) Presented at the 52nd National Meeting of the Chemical Society of Japan, Kyoto, Apr 1986. 2) For recent examples of the synthesis of γ-lactones: E.Nakamura, H.Oshino, and I.Kuwajima, J. Am. Chem. Soc., **108**, 3745 (1986); S.Fukuzawa, T.Fujinami, and S.Sakai, J. Chem. Soc., Chem. Commun., **1986**, 475; D.Hoppe, Angew. Chem. Int. Ed. Engl., **23**, 932 (1984). 3) a) T.Shono, H.Ohmizu, S.Kawakami, and H.Sugiyama, Tetrahedron Lett., **21**, 5029 (1980); b) A.Fröling, Recl. Trav. Chim. Pays-Bas, **93**, 47 (1974). 4) E.J.Corey and S.G.Pyne, Tetrahedron Lett., **24**, 2821 (1983). 5) a) S.Fukuzawa, A.Nakanishi, T.Fujinami, and S.Sakai, 52nd National Meeting of the Chemical Society of Japan, Kyoto, Apr 1986; b) Idem., J. Chem. Soc., Chem. Commun., **1986**, 624. 6) P.Girard, J.L.Namy, and H.B.Kagan, J. Am. Chem. Soc., **102**, 2693 (1980). 7) Relative stereochemistries were not determined except for one case (Run 7) where a cis structure was indicated by ^{1}H NMR analogy with quercus lactone (M.Masuda and K.Nishimura, Chem. Lett., **1981**, 1333). On the other hand, Fukuzawa et al. reported that a coupling of benzaldehyde with ethyl crotonate produced a 1:1 mixture of cis- and trans-lactone (ref. 5). 8) E.Ehlinger and P.Magnus, J. Am. Chem. Soc., **102**, 5004 (1980).

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