Utility of Phosphonium-Substituted Ester Enolates as Synthetic Intermediates. A Novel Trialkylphosphine-Catalyzed [3,3] Rearrangement of Allylic Acrylates

Takeshi Hanamoto, Yoshiyasu Baba, and Junji Inanaga*

Institute for Molecular Science, Myodaiji, Okazaki 444, Japan

Received November 3, 1992

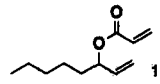
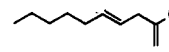
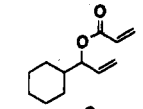
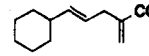
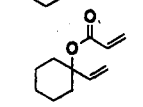
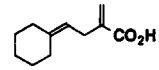
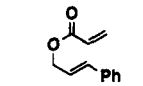
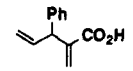
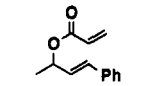
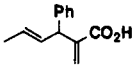
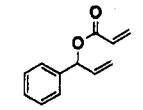
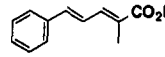
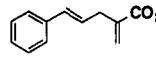
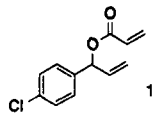
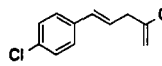
Summary: A novel Ireland-type [3,3] rearrangement which utilizes a catalytic amount of a trialkylphosphine with allylic acrylates has been developed as a synthetic entry into α-methylene-γ,δ-unsaturated carboxylic acids.

Since the significant breakthrough by Ireland, the ester enolate Claisen rearrangement has been a synthetically useful process for the construction of carbon–carbon bonds especially in a stereospecific manner.[1,2] For the generation of ester enolates, the following methods have so far been employed: (i) deprotonation of esters by strong bases, (ii) conjugate addition of alkylmetal reagents to α,β-unsaturated esters, and (iii) reduction of α-halo esters or α,β-unsaturated esters by chemical or electrolytic methods.[2-4] In all cases, however, stoichiometric quantities of reagents are required. We report here a novel trialkylphosphine-catalyzed Ireland-type [3,3] rearrangement of allylic acrylates in which the corresponding ester enoate intermediate is catalytically generated by the conjugate addition of trialkylphosphine under neutral conditions.

In connection with our recent interest in phosphonium-substituted ester enolates as potentially useful synthetic intermediates,[5-7] we planned to use them as new precursors for the Ireland rearrangement: Nucleophilic attack of trialkylphosphine to the β-carbon of an allylic acrylate (1) followed by silylation of the resulting phosphonium-substituted enolate would produce the corresponding ketene silyl acetal **A**, which then undergoes a [3,3] sigmatropic rearrangement to give the new intermediate **B**. The deprotonation of **B** by a base should afford the trialkylsilyl α-methylene-γ,δ-unsaturated carboxylate (2) with liberation of the trialkylphosphine to be recycled as a catalyst (Scheme I).

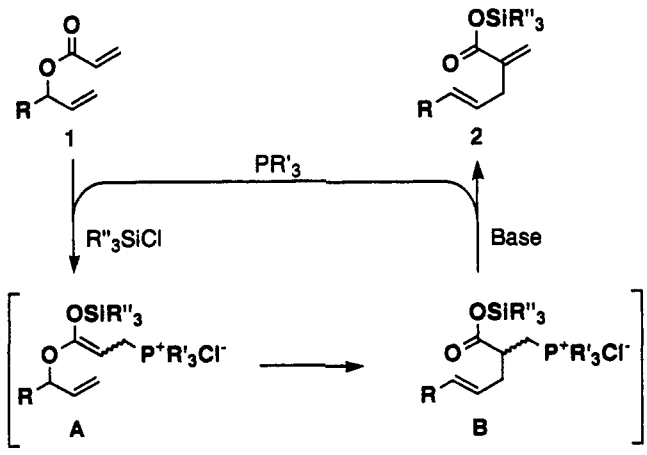
According to the above working hypothesis, allylic acrylates **1a–c** were treated with tricyclohexylphosphine (PCy_3, 0.1 equiv), TESCl (3.0 equiv), and DBU (2.5 equiv)

Table I. Trialkylphosphine-Catalyzed [3,3] Rearrangement of Allylic Acrylates

substrate	condn[a]	product[b]	ratio[c]	% yield[d]
 1a	A	 2a	>99:1	84
 1b	A	 2b	>99:1	79
 1c	A	 2c	>99:1	87
 1d	A[e]	 2d	82:18[f]	67
 1e	A	 2e	92:8[f]	66
 1f	A	 2f'	87:13[f]	83
1f	B	 2f	91:9	68
 1g	B	 2g	94:6	77

[a] Condition A: PCy_3 (0.1 equiv), TESCl (3.0 equiv), DBU (2.5 equiv), CH_3CN, 50 °C, 24 h. Condition B: PCy_3 (0.05 equiv), TMSCl (5.5 equiv), DBU (0.9 equiv), diisopropylethylamine (1.5 equiv), CH_3CN, 80 °C, 24 h. [b] A major isomer is shown. The minor one is the corresponding regioisomer concerning the 2-olefinic double bond, α-endo or α-exo. [c] Determined by ^1H NMR (270 MHz) analysis. [d] Combined isolated yield. [e] The reaction was conducted at 80 °C. [f] The ratio is based on the weight of the separated isomers.

Scheme I



(1) (a) Ireland, R. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 5897. (b) Ireland, R. E.; Mueller, R. H.; Willard, A. F. *J. Am. Chem. Soc.* **1976**, *98*, 2868. (c) Ireland, R. E.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 1155. (d) Ireland, R. E.; Wipf, P.; Armstrong, J. D., III *J. Org. Chem.* **1991**, *56*, 650 and references cited therein.

(2) An excellent review for the thermal, aliphatic Claisen rearrangement: Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423.

(3) Aoki, Y.; Kuwajima, I. *Tetrahedron Lett.* **1990**, *31*, 7457.

(4) (a) Troll, T.; Wiedemann, J. *Tetrahedron Lett.* **1992**, *33*, 3847. (b) Baldwin, J. E.; Walker, J. A. *J. Chem. Soc., Chem. Commun.* **1973**, 117.

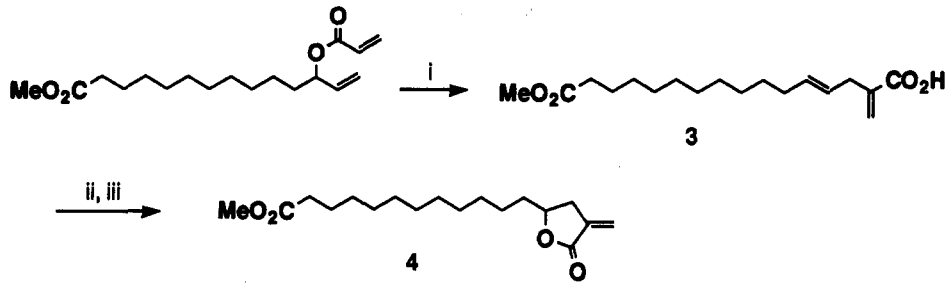
(5) We have found an efficient trialkylphosphine-catalyzed addition reaction of alcohols to α,β-unsaturated alkynoic acid esters: Baba, Y.; Inanaga, J. Presented at the 59th Semiannual Meeting of the Chemical Society of Japan, Yokohama, April 1990.

(6) For the dimerization of acrylates in the presence of a phosphine catalyst, see: (a) Myman, F. *Brit. Pat.* 1100350, 1965; *Chem. Abstr.* **1968**, *69*, 10093w. (b) Kitazume, S. *Japan Kokai*, *77*, 105, 115, 1977; *Chem. Abstr.* **1978**, *88*, 89131f. (c) Nemec, J. W.; Wuchter, R. B. *US Pat.* 4145559, 1979; *Chem. Abstr.* **1979**, *91*, 4960q. (d) Amri, H.; Rambaud, M.; Villieras, J. *Tetrahedron Lett.* **1989**, *30*, 7381.

(7) For phosphoniosilylation of enones and related reactions, see: (a) Kozikowski, A. P.; Jung, S. H. *J. Org. Chem.* **1986**, *51*, 3400. (b) Kim, S.; Lee, P. H. *Tetrahedron Lett.* **1988**, *29*, 5413. (c) Takanami, T.; Suda, K.; Ohmori, H. *Tetrahedron Lett.* **1990**, *31*, 677 and references cited therein.

0022-3263/93/1958-0299$04.00/0

Scheme II[a]



[a] Key: (i) condition A, 80%; (ii) I_2, CH_3CN, 0 °C, 1 h, 92%; (iii) $^nBu_3SnH$, PhH, 55 °C, 15 h, 63%.

in acetonitrile at 50 °C for 24 h (condition A).[8] As expected, the reactions proceeded cleanly to exclusively afford the desired α-methylene-γ,δ-unsaturated carboxylic acids **2a–c** in good yields (Table I).[9] The addition of TESCl was found to be indispensable for the rearrangement,[10] and DBU turned out to be the best base for the deprotonation of the rearranged phosphonium salt **B**. In the reactions of **1d** and **1e**, partial isomerization of the double bonds of the primary α-methylene compounds occurred to give the fully conjugated carboxylic acids under the conditions, and the isomerized acid became the major product in the case of an allylic benzylic acrylate **1f**. However, such isomerization was considerably suppressed using a limited amount of DBU and diisopropylethylamine (condition B).

As shown in Scheme II, the conditions for the rearrangement are so mild as to permit the coexistence of another ester function in the molecule. The synthetic utility of this process was further demonstrated by converting a rearranged product **3** to the corresponding α-methylene-γ-butyrolactone **4**[11] (Scheme II).

While mechanistic details of the rearrangement remain to be explored, the whole process (including the preparation of allylic acrylates) provides a synthetically unique route to α-methylene-γ-butyrolactones from aldehydes and ketones.[11]

Supplementary Material Available: Spectral and analytical data for all reaction products (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(8) The following procedure is representative. To a solution of **1a** (24.3 mg, 0.13 mmol) in dry acetonitrile (2.6 mL) were added DBU (49.8 μL, 0.33 mmol), TESCl (67.2 μL, 0.40 mmol), and PCy_3 (25% w/w in toluene purchased from Kanto Chemical Co, 16.8 μL, 10 mol %) at room temperature under argon. The reaction mixture was then heated to 50 °C for 24 h. Usual extractive workup followed by purification by preparative TLC (silica gel, ether/hexane = 1/1) afforded (*E*)-2-methylene-4-decenoic acid (**2a**, 20.5 mg, 84%).

(9) A limitation of the present method was, however, recognized in the reactions of (*E*)-2-octen-4-yl acrylate and 2-cyclohexen-1-yl acrylate, in which the rearrangement did not take place under the stated conditions.

(10) In the absence of TESCl, no rearrangement was observed while dimerization of acrylates occurred to produce α-methyleneglutaric acid derivatives.

(11) For reviews of the synthesis and biological activities of α-methylene-γ-butyrolactones, see: (a) Hoffman, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94. (b) Grieco, P. A. *Synthesis* **1975**, 67. (c) Gammill, R. B.; Wilson, C. A.; Bryson, T. A. *Synth. Commun.* **1975**, *5*, 245.