A New Preparation of Ketenes for Intramolecular Cycloadditions

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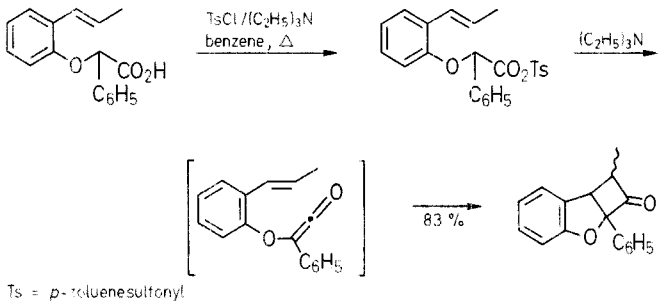
A new preparation of ketenes for intramolecular cycloadditions involves a one-pot synthesis from the appropriate carboxylic acid to the ketene cycloaddition product. A tosylate leaving group rather than the conventional halide ion provides several advantages.

Ketenes which are isolable and stable are far fewer in number than those which can only be trapped by *in situ* reactions. The traditional methods for ketene generation include the dehydrohalogenation of an appropriately substituted acid halide and the zinc dehalogenation of an α-haloacid halide.[1] Both methods normally require the preparation, isolation and purification of an acid halide. During some recent studies on intramolecular cycloaddition reactions of ketenes,[2-5] we discovered a new method for ketene generation which in most instances is a substantial improvement over existing methods.

This preparative method utilizes tosylate as a leaving group rather than the traditional halide. It is not necessary to isolate the tosylate and hence, we have a one-pot synthesis from the carboxylic acid to the ketene cycloaddition product. This method is illustrated below with (*o*-propenylphenoxy)phenylacetic acid (which is readily obtained from *o*-propenylphenol and α-bromophenylacetic acid). The acid is converted to the tosylate and subsequent triethylamine-promoted elimination of *p*-toluenesulfonic acid results in the formation of the corresponding phenoxyketene. Under our reaction conditions, the ketene spontaneously undergoes an intramolecular [2+2]-cycloaddition to afford the corresponding tricyclic ketone. The overall yield of the cycloadduct from the acid is 83%. It is of interest to note that the intermediate tosylate in this elimination reaction is in fact a mixed anhydride.

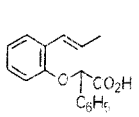
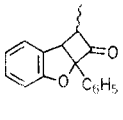
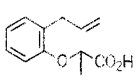
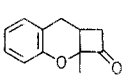
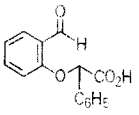
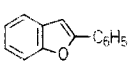
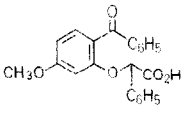
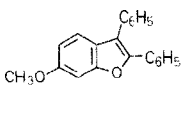


Ts = *p*-toluenesulfonyl

The results obtained by using this new procedure with four different intramolecular systems are contrasted with the conventional acid chloride procedure in the Table. It is apparent that the two procedures afford essentially equivalent yields of cycloadducts. The first two examples in the Table involve *in situ* cycloaddition of the phenoxyketene to a carbon-carbon double bond, and the latter two examples illustrate *in situ* cycloaddition of the phenoxyketene to the carbonyl group of an aldehyde and a ketone, respectively. The carbonyl group cycloadditions afford 2-oxetanones which spontaneously decarboxylate to the corresponding benzofurans. We have demonstrated the intermediacy of phenoxyketenes in these intramolecular ketene carbonyl cycloadditions by trapping the ketene with cyclopentadiene and isolating this cycloaddition product.[6] The structures of the cycloadducts in the Table were determined by IR, ^{1}H- and ^{13}C-NMR spectroscopy; satisfactory elemental analyses were obtained for all the new compounds.

The one-pot preparation of the ketene cycloaddition product from the carboxylic acid *via* the ketene eliminates the acid halide preparation, isolation and purification step, thereby significantly simplifying the snythesis. The reagents used to prepare the acid chlorides (e.g., thionyl chloride and oxalyl chloride) are lachrymators and usually generate hydrogen chloride as a byproduct. The inexpensive *p*-toluenesulfonyl chloride is much easier to handle than these lachrymators and the troublesome hydrogen chloride gas is not generated when an excess of triethylamine is used. We have tried other sulfonyl chlorides and found that benzenesulfonyl chloride and tosyl chloride are equally effective, however, methanesulfonyl chloride is not effective because this reagent reacts with triethylamine.

Table. Intramolecular [2+2]-Cycloaddition Reactions of Phenoxyketenes Generated by the Tosylate and the Acid Chloride Procedures

Entry	Acid	Cycloadduct	Yield (%)		m.p. (°C)	Lit. m.p. (°C)
			Chloride Method[9]	Tosylate Method		
1			85	83	95–96	95–96[5]
2			43	50	65–66	65–66[5]
3			75	78	120–121	121–122[8]
4			82	84	120–121	–[9]

The utilization of the tosylate procedure for the preparation of diphenylketene from diphenylacetic acid is not effective because the initially formed diphenylketene competes for the diphenylacetic acid. We have demonstrated[7] that diphenylketene is formed by this procedure as evidenced by the ketene band in the infrared spectrum of the reaction solution at 2100 cm^{-1}.

It is clear that intramolecular ketene cycloaddition reactions will prove to be a powerful synthetic tool for the organic chemist and this tosylate method provides an improved and simplified one-pot synthesis of the cycloadduct from the carboxylic acid.

6-Methyl-2-oxa-1-phenyl-3,4-benzobicyclo[3.2.0]heptan-7-one; Typical Procedure:

A solution of (*o*-propenylphenoxy)phenylacetic acid (1.2 g, 4.5 mmol) in benzene (50 ml) is added over 5 h through a syringe to a refluxing solution of triethylamine (2.3 g, 22.5 mmol) and *p*-toluenesulfonyl chloride (1.7 g, 9 mmol) in benzene (50 ml). After the addition is complete, the mixture is gently refluxed for 6 h. Upon cooling, the mixture is washed with water (3 × 50 ml) and then concentrated *in vacuo* to about 30 ml. This concentrate is stirred with 3% aqueous sodium hydroxide solution (250 ml) for 10 h to remove excess tosyl chloride. The benzene layer is dried with magnesium sulfate, filtered, and the benzene evaporated under reduced pressure. The residue is purified by column chromatography on silica gel (3% ethyl acetate in hexane) to give the cycloaddition product as a white solid; yield: 0.9 g (83%); m.p. 95–96°C (Lit.[5] m.p. 95–96°C). The IR spectrum, and the ^{1}H- and ^{13}C-NMR spectra of the cycloadduct are identical with the reported data.[5]

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(1) Ward, R.D., The Preparation of Ketenes, in: *The Chemistry of Ketenes, Allenes and Related Compounds*, Patai, S. (ed.), Interscience Publications, New York, 1980, pp. 223–277.
(2) Snider, B.B., Hui, R.A.H.F., Kulkarni, Y.S. *J. Am. Chem. Soc.* **1985**, *107*, 2194.
(3) Marko, I., Rosmans, B., Hesbain-Frisque, A., Ghosez, L. *J. Am. Chem. Soc.* **1985**, *107*, 2192.
(4) Kulkarni, Y.S., Snider, B.B. *J. Org. Chem.* **1985**, *50*, 2809.
(5) Brady, W.T., Giang, Y.F. *J. Org. Chem.* **1985**, *50*, 5177.
(6) The [2+2]-cyclopentadiene adduct of the phenoxyketene (entry 3 in the Table) has been isolated and characterized by the presence of the cyclobutanone carbonyl group at 1778 cm^{-1} in the IR-, and by analysis of the ^{1}H- and ^{13}C-NMR spectra.
(7) Our experience suggests that this tosylate procedure works best for intramolecular ketene cycloaddition reactions, because the ketene functionality immediately undergoes cycloaddition due to the proximity of the unsaturated linkage thus eliminating competing reactions for the ketene.
(8) Stetler, H., Siehnhold, E. *Chem. Ber.* **1955**, *88*, 271.
Angeloni, A.S., Delmoro, F, Tramontini, M. *Ann. Chim. (Rome)* **1963**, *53*, 1751.
(9) This benzofuran is a new compound, white solid, m.p. 120–121°C. The preparation of this compound *via* the acid chloride method has been described:
Brady, W.T., Giang, Y.F. *J. Org. Chem.* **1986**, *51*, 2145.