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TIN(II) CHLORIDE CATALYZED ADDITION OF DIAZO SULFONES, DIAZO PHOSPHINE OXIDES, AND DIAZO PHOSPHONATES TO ALDEHYDES.

Christopher R. Holmquist, Eric J. Roskamp*

Department of Chemistry, Northwestern University,
Evanston, Illinois 60208-3113

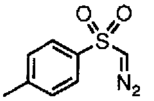
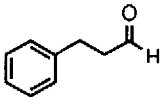
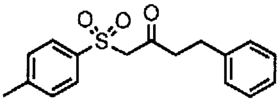
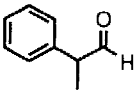
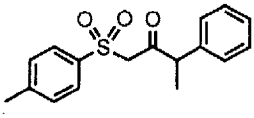
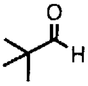
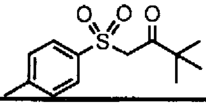
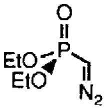
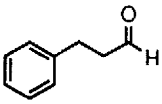
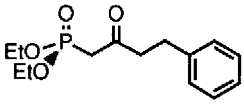
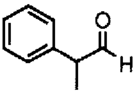
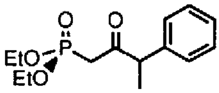
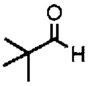
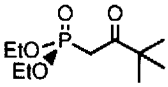
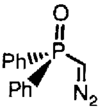
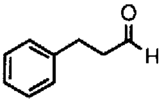
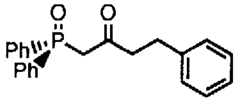
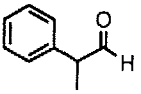
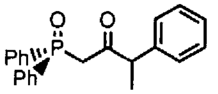
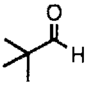
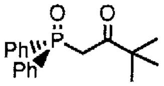
Key Words: Tin(II) chloride, catalyst, β-keto sulfones,
β-keto phosphine oxides, and β-keto phosphonates.

Abstract: Diazo sulfones, diazo phosphine oxides, and diazo phosphonates add to aldehydes in the presence of a catalytic amounts of tin(II) chloride to yield β-keto sulfones, β-keto phosphine oxides, and β-keto phosphonates, respectively. Reactions with primary aldehydes proceed in higher yields, 53-79%, than those of secondary aldehydes, 42-56%. Reactions with tertiary aldehydes, which are more sterically encumbered substrates, give only 5-36% yields.

The chemistry of α-diazo carbonyl compounds has been extensively studied by organic chemists.[1] Several sulfur and phosphorous analogs, such as α-diazosulfones[2a], α-diazophosphonates,[2b] and α-diazophosphine oxides,[2c] have also been prepared and studied.[3] For example, reaction of diazomethyl phosphonates with aldehydes[4] and ketones[5] under basic conditions yields alkynes. If this reaction is run in the presence of amines, enamines are produced.[6]

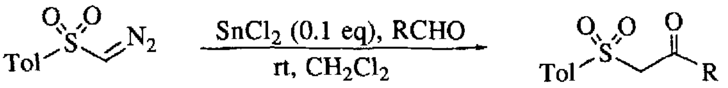
We previously reported that aldehydes are efficiently converted to β-keto esters by reaction with ethyl diazoacetate in the presence of catalytic tin(II) chloride.[7] We now report the extension of this methodology for the preparation of β-keto sulfones, β-keto phosphonates, and β-keto phosphine oxides (eq 1,2). Our new method allows the preparation of these synthetically useful compounds from readily available starting materials under mild, non-basic conditions. β-Keto sulfones, β-keto

Table 1: Tin(II) Catalyzed Insertion of Diazo Compounds.

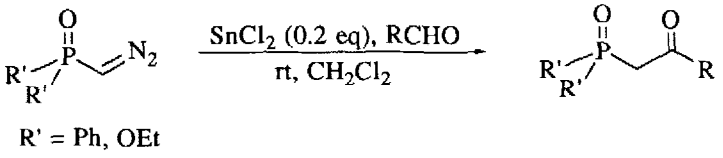
Diazo Compound and Aldehyde	Product:	Yield[a] %	Eq. SnCl$_2$	Time h
 + 		79	0.1	2
+ 		50	0.1	3
+ 		36	0.1	> 4 [b]
 + 		75	0.2	2.5
+ 		56	0.2	3
+ 		< 5 [c]	0.2	> 4 [d]
 + 		53	0.2	8
+ 		42	0.2	8
+ 		< 10 [c]	0.2	> 8 [d]

[a] Isolated yields unless otherwise noted. [b] Reaction run overnight. [c] Yield estimated from the ^{1}H NMR spectrum. [d] Reaction incomplete after 18 hours.

phosphonates, and β-keto phosphine oxides are generally prepared by addition of excess sulfone or phosphonate carbanion to an ester.[8]



(1)



(2)

Tosyl diazomethane, a stable yellow solid, is readily prepared by the method of van Leusen.[2a] When tosyl diazomethane is added to a solution of an aldehyde and a catalytic amount of tin(II) chloride, nitrogen is evolved and the diazo compound is gradually consumed. As shown in Table 1, the yield of the resulting β-keto sulfone is highly dependent on the nature of the aldehyde.

Under similar reaction conditions, diethyl diazomethylphosphonate[2b] and diazomethyl-P,P-diphenyl phosphine oxide[2c] are converted to β-keto phosphonates and β-keto phosphine oxides, as shown in Table 1. Relative to diazosulfones, however, these diazo phosphorus compounds react more slowly. As was observed with both tosyl diazomethane and ethyl diazoacetate, the reaction of diazo phosphorus compounds works best with unencumbered aldehydes.

The following experimental is representative: To a stirred mixture of 0.590 g of hydrocinnamaldehyde (4.40 mmol) and 0.075 g of tin(II) chloride (0.40 mmol) in 5.0 mL of methylene chloride was added a solution of 0.784 g of tosyl diazomethane (4.00 mmol) in 1.0 mL of methylene chloride at room temperature. After a brief induction period, nitrogen evolution was observed. The reaction was followed by TLC until the diazo compound was consumed and nitrogen evolution had ceased. The reaction mixture was filtered and then the volatiles removed in vacuo. The remaining oil was purified[9] by flash column chromatography[10] on silica gel 60 (12:1 petroleum ether/ethyl acetate[11]) to give 0.954 g (79%) of 4-phenyl-1-tosyl-2-butanone.

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9. The only significant side product observed in these reactions is a chloromethyl compound, presumably formed from reaction of the diazo compound with tin(II) chloride or hydrogen chloride.

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