

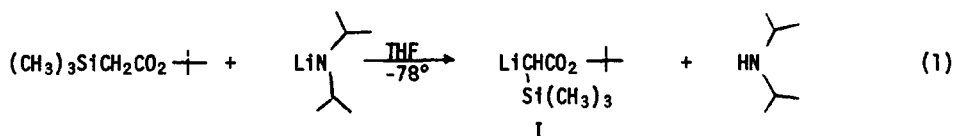
REACTION OF LITHIO TERT-BUTYL TRIMETHYLSILYLACETATE WITH
ALDEHYDES AND KETONES. A SYNTHESIS OF α,β -UNSATURATED ESTERS.

Stephen L. Hartzell, Donald F. Sullivan and Michael W. Rathke*

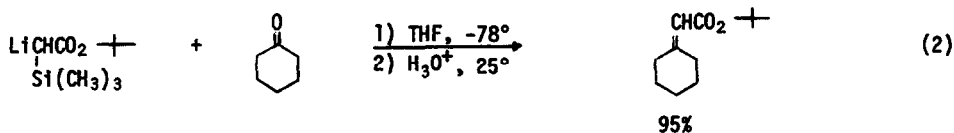
Department of Chemistry, Michigan State University, East Lansing, Michigan 48824

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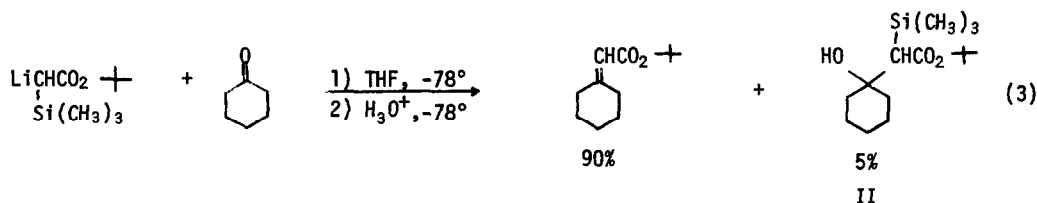
Addition of tert-butyl trimethylsilylacetate¹ to tetrahydrofuran (THF) solutions of lithium diisopropylamide at -78° produces the lithium ester enolate, I, (eq 1) as a white precipitate. Attempts to isolate I have been unsuccessful; however, suspensions of I in THF are stable



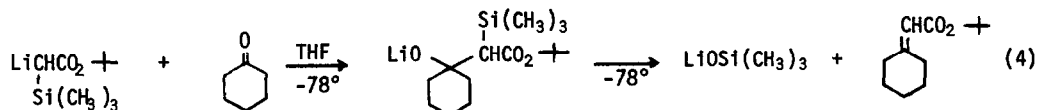
indefinitely at dry ice temperatures. Addition of one equivalent of cyclohexanone to a suspension of I causes immediate dissolution of the solid. Warming to room temperature followed by quenching with dilute aqueous acid gives tert-butyl cyclohexylideneacetate in 95% yield (eq 2).



Quenching the reaction mixture at -78° shortly after mixing gives similar results except that small amounts of the β -hydroxyester, II, are also obtained (eq 3).



Compound II was isolated by preparative glpc and is stable to the room temperature quenching procedure. Consequently, tert-butyl cyclohexylideneacetate must be formed prior to the quenching step, most likely by the sequence shown in eq 4.²



Application of this procedure to a variety of aldehydes and ketones gave excellent yields of the corresponding α,β -unsaturated esters as shown in Table I. Conjugated aldehydes react with the reagent in a 1,2 fashion and thus provide a synthesis of esters with extended conjugation, as shown by the entries for crotonaldehyde and cinnamaldehyde.

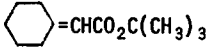
The Wittig³ reaction or its phosphonate modification⁴ appears to be the most useful alternative method for converting aldehydes or ketones into α,β -unsaturated esters. Although a direct comparison of yields is probably not reasonable, the following observations are made. The lithium ester enolate, I, appears to be much more reactive than the various phosphorus ylides. Reactions of I with the aldehydes or ketones of Table I are complete shortly after mixing at -78° , while reactions of phosphorus ylides with similar aldehydes or ketones are normally completed either at room temperature or at the reflux temperature of solvents such as benzene or ethanol.³

Reaction of cyclohexanone with the phosphonate ylide of ethyl acetate is reported to give 6% of the nonconjugated ester.⁵ The present procedure gives less than 0.4% of the corresponding non-conjugated isomer.

Finally the present procedure has the advantage of a simple work-up without the complications presented by phosphorus compounds.

The following procedure for the conversion of cyclohexanone into tert-butyl cyclohexylideneacetate is representative. A 100 ml. round-bottomed flask equipped with magnetic stirring, septum inlet and mercury bubbler is flushed with nitrogen and immersed in an

Table I. Reaction of Carbonyl Compounds with Lithio Tert-butyl Trimethylsilylacetate

Carbonyl Compound	Product ^a	Yield, % ^b	Bp/mmHg	n_D^{22}
Acetaldehyde	$\text{CH}_3\text{CH}=\text{CHCO}_2\text{C}(\text{CH}_3)_3$	98 (93)	150/760	1.4249
Isobutyraldehyde	$(\text{CH}_3)_2\text{CHCH}=\text{CHCO}_2\text{C}(\text{CH}_3)_3$	94 (66)	98/41	1.4327
Benzaldehyde	$\text{C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{C}(\text{CH}_3)_3$	97 (75)	103-105/0.5	1.5300
Crotonaldehyde	$\text{CH}_3\text{CH}=\text{CH}-\text{CH}=\text{CHCO}_2\text{C}(\text{CH}_3)_3$	92 (78)	85-90/8	1.4784
Cinnamaldehyde	$\text{C}_6\text{H}_5\text{CH}=\text{CH}-\text{CH}=\text{CHCO}_2\text{C}(\text{CH}_3)_3$	95 (58)	171-178/7	1.5858
Acetone	$(\text{CH}_3)_2\text{C}=\text{CHCO}_2\text{C}(\text{CH}_3)_3$	96 (53)	164/760	1.4391
Cyclohexanone		95 (90)	121-123/16	1.4738

^a All products gave satisfactory elemental analyses and exhibited spectral properties in accordance with assigned structures.

^b Glpc yields, isolated yields in parentheses.

ice-water bath. The flask is charged with a hexane solution of n-butyllithium (12.5 ml, 25mmol) and 3.6 ml (25mmol) of diisopropylamine is injected over a 2 minute period. Following complete addition, the hexane is removed under reduced pressure and the residue of lithium diisopropylamide is dissolved in 25 ml of THF. The flask is immersed in a dry ice-acetone bath and tert-butyl trimethylsilylacetate¹ (5.5 ml, 25mmol) is added dropwise over a 2 minute period. After an additional 10 minutes of stirring, 2.6 ml of cyclohexanone (25mmol) is injected. The solution is then allowed to reach room temperature and quenched by the addition of 25 ml of 3N hydrochloric acid. Extraction with pentane and vacuum distillation of the organic phase gives 4.5g (90% yield) of tert-butyl cyclohexylideneacetate, b.p. 121-3°/16mm.

Acknowledgment

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