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TRIALKYLZINCLITHIUM [R_3ZnLi]

A NEW REAGENT FOR CONJUGATE ADDITION TO α,β-UNSATURATED KETONES

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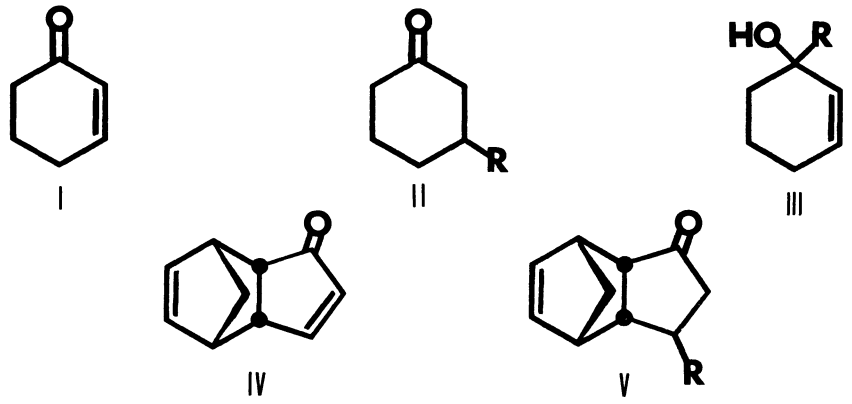
Trialkylzinclithium is readily prepared in THF by mixing zinc chloride (or its TMEDA complex) and alkyllithium in a 1 : 3 mole ratio. Conjugate addition of this new reagent is demonstrated with 2-cyclohexen-1-one (I) and dicyclopentadien-1-one (IV) as α,β-unsaturated ketones.

Although extensive studies have been explored with respect to conjugate addition by cuprate complex[1], very little have been reported by organozinc compounds.[2] We would like to describe trialkylzinclithium[3], R_3ZnLi, as a new reagent to undergo conjugate addition to some α,β-unsaturated carbonyl compounds.

This reagent can readily be prepared in THF by mixing a saturated THF solution of zinc chloride (1.6 to 1.9M)[4] and alkyllithium in a 1:3 ratio (eq. 1). Practically, we found that a precise preparation can be achieved in the presence of triphenylmethane as indicator by adding zinc chloride (Lewis acid) to alkyllithium at 0°C until the red color discharges. The stoichiometry [1:3] of the two components was confirmed by using non-hygroscopic zinc chloride-TMEDA (tetramethylethylenediamine) complex[5] (white needles, mp. 176.0-177.0°C) instead of zinc chloride solution, thus by measuring an accurate weight of the crystals. Tri-n-butylzinclithium:TMEDA infact undergoes conjugate addition in good yield (vide infra). The stoi-

$$3\ RLi + ZnX_2 \longrightarrow R_3ZnLi + 2\ LiX \qquad \text{(eq. 1)}$$

chiometry was further confirmed by observing the reaction mode to 2-cyclohexen-1-one (I) as an α,β-unsaturated ketone with respect to different mole ratios (1:2, 1:3, 1:6) of the two components ($ZnCl_2$, 1.9M in THF and n-BuLi, 1.5M in n-hexane). The reaction was carried out under Ar atmosphere in THF (10-12 ml) at -78°C for 30 min using 0.9 mole equivalent of I (98% pure) to $ZnCl_2$. The G.L.C. analyses of the reaction products clearly indicated that only the reaction condition corresponding to the mole ratio being 1:3 underwent conjugate addition to afford II, the 1,4-adduct. Either the less amount of zinc chloride (1:2) nor the more amount of zinc chloride (1:6) gave no 1,4-adduct at all but gave 1,2-adduct (III) and unchanged starting enone (I), respectively.



As a primary step to know synthetic versatility of the triorganozinc reagents, were prepared several reagents having sterically or electronically different components as shown in Table 1. In this case, non-volatile enone IV was used for accurate estimation on reaction yields. In any cases in Table 1, no 1,2-adduct was obtained. As for Entry 1 to 3, little significant effect of the counter halide anion was observed with respect to the mode of addition although their yields were somewhat different. The steric effect of R in the complex was examined using primary, secondary and tertiary butyllithium (Entry 4 to 8). Sterical bulkiness affected not to the mode of addition but to the reaction velocity, since the more bulky reagents gave less amount of 1,4-adducts for a limited reaction period. Phenyl and acetylenic complexes

Table 1

Reaction Condition and Yields of 1,4-Adduct in R_3ZnLi-2LiX Addition to IV[a)]

Entry	R_3ZnLi-2LiX		Reaction Temp. (°C)	Reaction Period (min)	Product (V) R	Isolated Yield[b)] of 1,4-adduct (%)
	R	X				
1	Me	Cl	0	30	Me	92
2	Me	Br	0	30	Me	76
3	Me	I	0	30	Me	68
4	n-Bu	Cl	-78	60	n-Bu	73
5	n-Bu	Cl	-78 to 0	120	n-Bu	92
6	n-Bu/TMEDA	Cl	0	30	n-Bu	86
7	sec-Bu	Cl	-78	60	sec-Bu	66[c)]
8	tert-Bu	Cl	-78	60	tert-Bu	58[c)]
9	Ph	Cl	-78	180	Ph	15[c)]
10	1-butynyl	Cl	-78	180	1-butynyl	0[c)]

a) The reactions were carried out under Ar atmosphere in THF (13 ml) with ca. 1 mmol of the ketone (IV), and the zinc reagents were used slightly excess to the ketone. The reaction mixture was worked up by damping it into NH_4Cl-aq. soln. and then the products were taken up by ether. They were analyzed by NMR, IR, Mass, TLC and then chromatographed (SiO_2: Et_2O-hexane mixture). b) The yields were not maximized.
c) Starting material was also recovered.

(Entry 9 and 10) afforded poor or no addition product probably due to stabilized covalent carbon zinc bonds.

Although no unequivocal mechanistic interpretation exists at present for the triorganozinc reaction, it is likely that the primary interaction of carbonyl group (in unsaturated ketones) with zinc consists of formation of a complex $R_3\bar{Z}n\text{-}\bar{O}\text{=}\overset{|}{C}\text{-CH=CH-} \longleftrightarrow R_3\bar{Z}n\text{-O-}\overset{|}{C}\text{=CH-}\overset{+}{C}\text{H-}$ in which R group obtains additional anionic activation to undergo transfer to the sterically accessible β-carbon atom. It should, thus, be noted that for synthetic purposes this reaction might be relevant to addition to unhindered unsaturated ketones.

REFERENCES AND NOTES

1. G. H. Posner, "Organic Reactions", Vol. 19, Chapter 1, John Wiley & Sons (1972) New York.
2. Diphenylzinc was reported to add in a 1,4 manner to benzalacetophenone (90-91%): H. Gilman and R. H. Kirby, J. Am. Chem. Soc., 63, 2046 (1941).
3. Formation of the "ate" complex has been suggested spectroscopically with diethylzinc and 1,1-diphenyl-n-hexyllithium in 1:1 stoichiometry: R. Waack and M. A. Doran, J. Am. Chem. Soc., 85, 2861 (1963), see also G. Wittig, F. J. Meyer and G. Lange, Ann., 571, 167 (1951).
4. This was measured by taking an aliquot of the solution and evaporated to dryness until the residual weight became constant. House et al. claimed that the saturated concentration is 0.35M at 23°C and 2°C: H. O. House, D. S. Crumrine, A. Y. Teranishi and H. D. Ohmstead, J. Am. Chem. Soc., 95, 3310 (1973).
5. The complex was prepared by mixing 19 ml of a saturated $ZnCl_2$-THF soln. and 5 ml of TMEDA and allowing to stand for several hours at r.t. The crude crystals separated were collected and recrystallized from THF. Elemental analysis [calculated as $C_6H_{16}N_2ZnCl_2$: C, 28.54; H, 6.39; N, 11.09 and found C, 28.78; H, 6.37; N, 11.15] indicates this as 1:1 $ZnCl_2$-TMEDA complex, sparingly soluble to water.

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