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ALKENYLCUPRATE REAGENTS FROM ARENESULFONYLHYDRAZONES

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Abstract: The use of ketone 2,4,6-triisopropylbenzenesulfonylhydrazones to generate alkenylcuprate reagents that add in 1,4-fashion to enones is described.

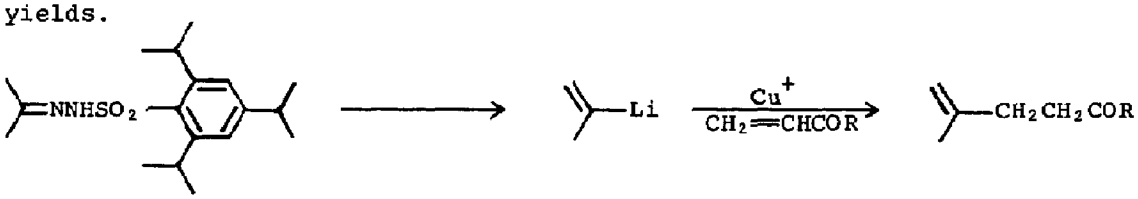
The versatile Umpolung process represented by the transformation I → II appears to have no direct experimental precedent in the literature.[2] We describe here a simple two-step sequence which effects this transformation

I II

for a variety of cyclic and acyclic reactant pairs.

There are relatively few reports in the literature on the use of substituted alkenylcuprate reagents. This is due, in part, to the fact that there are not many ways to generate alkenyllithium reagents. The standard route for their preparation involves metal-halogen exchange on a suitable vinyl halide;[3] however, regiospecific generation of vinyl halides is often difficult.[4,5]

Our method is based on the recent work of Bond[5] reporting the facile preparation of alkenyllithium reagents from 2,4,6-triisopropylbenzenesulfonylhydrazones (trisylhydrazones) in an elegant modification of the Shapiro olefin synthesis.[6] In their work, treatment of such trisylhydrazones with excess n-BuLi in hexane-TMEDA led to the desired alkenyllithium reagents in excellent yields.



It was our purpose to explore the possibility of using the Bond reaction to generate mixed cuprate reagents under reaction conditions which did not require the use of excess base or coordinating solvents such as TMEDA.[7] Attempts to generate the desired alkenylcuprates from toluenesulfonylhydrazones under a variety of base and solvent conditions gave inferior results. We have found that treatment of trisylhydrazones with 2.0 equiv. of tert-BuLi in THF at -78° under N_2 for 30 min followed by warming to 0° gave solutions of the desired vinyllithium reagents. The orange-red solutions generated in this fashion were then transferred under N_2 via a double ended needle to a -78° slurry of phenylthiocopper[8] in THF and stirred for one hr to form the corresponding mixed alkenylcuprates. Addition of a variety of enones to these solutions followed by slow warming over a 2 hr period to ambient temperature gave the desired 1,4-adducts in fair to good yields.[9] The products were characterized by their infrared carbonyl absorption at 1715 ± 5 cm^{-1} for the cyclohexenone and 3-penten-2-one adducts and at 1695 ± 5 cm^{-1} for the chalcone adducts. In the NMR spectra the vinyl protons appear between δ4.75 and 5.6 as singlets, or multiplets depending on the given example. The results are summarized in Table I.

The trisylhydrazones were prepared from the corresponding ketone in excellent yield as reported by Bond.[5] When a 1:1 ratio of trisylhydrazone: enone was employed the desired conjugate adducts 6-8 were obtained in moderate yields. The yields were improved significantly by using a 2:1 ratio of trisylhydrazone:enone as seen in the table.

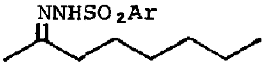
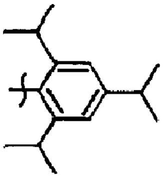
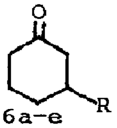
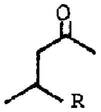
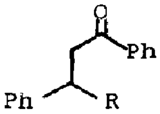
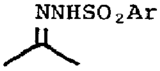
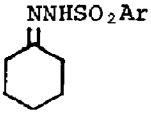
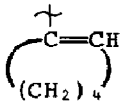
Several attempts to add the cuprates derived from trisylhydrazones 1 and 3 to methylcrotonate or 1-acetylcyclohexene gave less than 10% yields of conjugate adducts.

The following procedure is illustrative of the general method employed. To a -78° solution of acetophenone trisylhydrazone 3 (2 mmol) in THF (4 mL) was added dropwise a solution of t-BuLi in pentane (4 mmol). After 30 min at -78° the mixture was warmed to 0° where N_2 evolved. The solution was then transferred via a double ended needle to a -78° slurry of PhSCu (2 mmol) in THF (4 mL). After one hr at -78° a solution of cyclohexenone (1 mmol) in THF (0.3 mL) was added dropwise and the mixture was allowed to warm to ambient temperature over a 2 hr period. The reaction was quenched with saturated ammonium chloride solution, filtered, diluted with pentane, and washed with 5% potassium hydroxide solution and brine. Drying followed by solvent removal below room temperature *in vacuo* gave an oily mixture. Preparative

TLC (10% ether, pentane) gave 166 mg (83%) desired 6c. NMR ($CDCl_3$) δ7.30 (m, 5H), 5.12 (AB, 2H), 3.0 (m, 1H), 2.7-1.4 (m, 8H). IR ($CHCl_3$) 1710 cm^{-1}. Anal.: C, H.

TABLE I

CONJUGATE ADDITION OF ALKENYLCUPRATES TO ENONES

Trisylhydrazone	Enone	Product Yield %[a]
 1 Ar = 	2-cyclohexen-1-one A	 6a-e 6a R = $nC_6H_{13}\overset{\vert}{C}{=}CH_2$ (36)[b]
	3-penten-2-one B	 7a,b 7a R = $nC_6H_{13}\overset{\vert}{C}{=}CH_2$ 82[b]
	chalcone C	 8a,b 8a R = $nC_6H_{13}\overset{\vert}{C}{=}CH_2$ (31)[b]
 2	A	6b R = $CH_3CH_2\overset{\vert}{C}{=}CHCH_3$ (43)[c]
	C	8b R = $CH_3CH_2\overset{\vert}{C}{=}CHCH_3$ (40)[c]
 3	A	6c R = $Ph\overset{\vert}{C}{=}CH_2$ 83(70)
	B	7b R = $Ph\overset{\vert}{C}{=}CH_2$ 78
 4	A	6d R = $CH_3\overset{\vert}{C}{=}CH_2$ (51)[d]
 5	A	6e R =  52(30)

[a] Yields reported are for pure compounds isolated by preparative TLC. Yields given in parenthesis indicate a 1:1 ratio of trisylhydrazone:enone was employed; otherwise a 2:1 ratio was employed. [b] No products derived from conjugate addition of 2-octenyllithium were observed. [c] NMR spectra indicate a single undefined olefin geometry was obtained. [d] 0.5 mol equiv. of CuI was used in place of one equiv. of PhSCu.

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References:

1. NIH Postdoctoral Fellow 1980-1981.
2. Addition of an appropriately substituted nucleophile to a carbonyl group followed by elimination and deblocking to effect the same overall transformation has been reported: A. A. Ponaras, Tetrahedron Lett., 3105 (1976).
3. G. Cahiez, D. Bernard and J. F. Normant, Synthesis, 245 (1976); D. Seebach and H. Neumann, Chem. Ber., 111, 2785 (1978).
4. For several recent examples see: R. K. Boeckman Jr. and D. M. Blum, J. Org. Chem., 39, 3307 (1974); J. Hartman and M. Schlosser, Helv. Chim. Acta, 59, 452 (1976); J. F. Normant, C. Chint, G. Cahiez and J. Villieras, Synthesis, 803 (1974).
5. A. R. Chamberlin, J. E. Stemke and F. T. Bond, J. Org. Chem., 43, 147 (1978); A. R. Chamberlin and F. T. Bond, Synthesis, 44 (1979).
6. R. H. Shapiro, Org. React., 23, 405 (1975).
7. House has shown that the presence of donor ligands such as TMEDA are detrimental to the success of cuprate coupling: H. O. House and J. M. Wilkins, J. Org. Chem., 43, 2443 (1978) and references therein.
8. The copper salt employed appears to play a role as attempts to form cuprates from trisylhydrazone 3 and CuI gave only 1,2-addition products upon addition of cyclohexenone. The mixed cuprate has the added advantage that only one mole equiv. of alkenyllithium is required to form a cuprate reagent. G. H. Posner, D.J. Brunelle and L. Sinoway, Synthesis, 662 (1974).
9. All new compounds were fully characterized by NMR, IR and combustion analysis.

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