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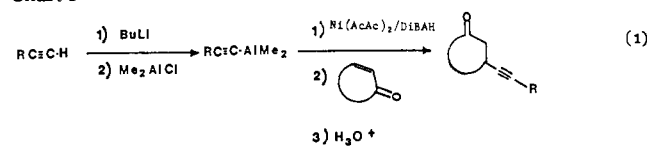
Nickel-Catalyzed Conjugate Addition of Organoaluminum Acetylides to α,β -Enones

Sir:

Conjugate addition of organometallic compounds to α,β -unsaturated ketones is a widely employed reaction in organic synthesis. Organocuprates are commonly employed for 1,4 addition of alkyl and alkenyl groups to α,β -unsaturated ketones;¹ however, cuprates cannot be used in *alkynylation* reactions owing presumably to the strength of the alkynyl-copper(I) ligand bond.² Several sequences have been reported, however, which do achieve conjugate addition of alkynyl units, but each suffers severe limitations. Both acetylenic alanes³ and boranes⁴ conjugately add to α,β -enones but only to those capable of achieving an *S-cis* conformation. Of the methods reported which can be applied to fixed *S-trans* enones (such as 2-cyclohexenone), one^{4a} requires a convenient hydroxyl functional group for direction of *intramolecular* attack by an alane; the other⁵ is indirect and involves addition of di(*tri-n*-butylstannyl)ethylene by cuprate addition and subsequent oxidative elimination of a stannyl group to give, overall, conjugate addition of acetylide to the enone. Extension to alkyl acetylides by this latter method has not been reported. We recently noted⁶ that a catalyst prepared from Ni(acac)₂ and diisobutylaluminum hydride (1:1) would catalyze the conjugate addition of (alkenyl)zirconium complexes to α,β -enones. We wish to report herein that this catalyst will, as well, catalyze conjugate addition of terminal alkynyl units to α,β -unsaturated ketones. This procedure is the first one, to the best of our knowledge, which enables this addition to ordinary *S-trans* enones.

A typical procedure for effecting conjugate addition by this route is illustrated as follows. To Ni(acac)₂ in ether at 0 °C is added Dibah in toluene solution. The reaction mixture rapidly turns dark red-brown. To this red-brown solution is then added a dialkylaluminum acetylide (prepared in the usual manner from the lithium acetylide and dialkylaluminum chloride)⁷ as a solution in ether. The reaction mixture is cooled to -5 °C and the unsaturated ketone in ethereal solution is added dropwise over a period of 15 min. The reaction mixture is allowed to stir at -5 °C for several hours. Hydrolysis at 0 °C with saturated KH₂PO₄ (aqueous) solution is then followed by addition of just enough of 10% H₂SO₄ (aqueous) to dissolve aluminum salts. The organic layer is washed with saturated NaHCO₃ and NaCl solutions and is then dried. Removal of solvent and separation of products on silica gel gives the conjugate adduct. Results shown in Chart I demonstrate in part the scope of this reaction.^{8,9} For each case investigated involving the alkoxy-substituted cyclopentenone, the product formed possessed the anti stereochemistry as shown by NMR.¹⁰ Only the acetylide group of the mixed alane was transferred to the enone in a 1,4 manner, and no 1,2 addition was observed in each case examined herein.⁸

Chart I

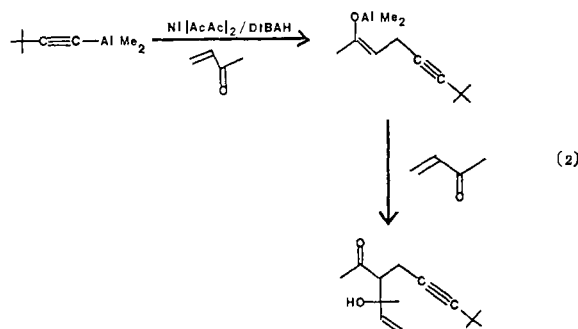


Acetylene	α,β -enone	Product	$\nu(\text{C}\equiv\text{C})$ Raman/cm ⁻¹	Yield % ^a
H-C≡C-			2238	60
H-C≡C-			2236	72
H-C≡C-C ₆ H ₅ ^b			2231	71
H-C≡C-SiMe ₃			2175	60 (vpc)
H-C≡C-H			2060	15 ^b
H-C≡C-			2231	67 ^c
H-C≡C-			2234	49 ^d
H-C≡C-			2238	65
H-C≡C-SiMe ₃			2160	70 ^c
H-C≡C-SiMe ₃			2170	50

^a Yields are isolated except where noted and have *not* been maximized except for that of **8**. ^b **5** can be prepared approximately quantitatively from **4**; ¹⁵ $\nu_{\text{C-H}} = 3313 \text{ cm}^{-1}$. ^c *Cis* ring fusion was assigned by conversion of **9** to the terminal acetylene by cleavage with (CH₃CH₂)₄NF and by subsequent reduction of the terminal acetylene (5% Pd/C, H₂, 1 atm). The resulting ketone was found to be identical by NMR, IR, and gas chromatographic analysis with 9-ethyl-*cis*-2-decalone, prepared by the copper acetate catalyzed addition of ethyl Grignard reagent to $\Delta^{1,9}$ -octalone, a sequence which has been shown to afford *cis* ring fusion (R. F. Church, R. B. Ireland, and D. R. Shredar, *J. Org. Chem.*, **27**, 707 (1962); S. Boatman, T. M. Harris, and C. R. Hauser, *J. Am. Chem. Soc.*, **87**, 82 (1965)). ^d *Cis* ring fusion is based on ¹H NMR (K. L. Williamson, T. Howell, and T. A. Spencer, *J. Am. Chem. Soc.*, **88**, 325 (1966); M. J. T. Robinson, *Tetrahedron Lett.*, 1685 (1965)).

We find that optimal yields of conjugate adduct are obtained when an excess of dialkylaluminum acetylide is employed. For example, using 0.22 equiv of Ni(acac)₂, 0.20 equiv of Dibah, 2.2 equiv of dimethylaluminum(*t*-butylacetylide) and 1 equiv of cumyloxycyclopentenone gave compound **8** (after 1.5-h reaction) in 85% isolated yield. Using a smaller excess of the aluminum acetylide results in a decreased yield of the desired product. In each of these sequences we find that most of the unused aluminum acetylide is converted on workup back to the

starting terminal acetylene which can be recovered by chromatography. We believe that it is important to employ an excess of the aluminum acetylide because the initial product of conjugate addition is an aluminum enolate which can react with additional unsaturated ketone to give the aldol adduct. In the presence of excess aluminum acetylide, the added unsaturated ketone in the presence of the nickel catalyst preferentially reacts with it. If less aluminum acetylide is employed, then the desired product and oligomers are observed. Specifically, we could isolate, in addition to the desired product, the compound formed by aldol condensation¹¹ of the aluminum enolate derived from conjugate addition to methyl vinyl ketone with another equivalent of methyl vinyl ketone.



Lewis basic solvents such as THF are not effectively employed and reduced yields in this solvent are observed. Adding oxygen functionality to the unsaturated ketone also slows down the rate of conjugate addition. Thus cyclohexenone and cyclopentenone react more rapidly with this conjugate addition reagent system than does 4-cumyloxycyclopentenone.

We have examined the use of other acetylides in this conjugate addition procedure. However, we find that lithium, magnesium, zinc, and bis(cyclopentadienyl)zirconium acetylides give rise to no or only trace amounts of desired conjugate adduct. We have observed that Ni(acac)₂ in the absence of added DIBAL will catalyze conjugate addition of dialkylaluminum acetylides to α,β -enones;⁸ however, here, a yield approximating an equimolar amount (based on nickel) of coupled diacetylene is obtained. An investigation into the use of other nickel species as possible catalysts revealed that NiCl₂(PEt₃)₂, Ni(PPh₃)₄, and Ni[P(OPh)₃]₄, in conjunction with aluminum acetylides, gave rise only to trace amounts of the desired conjugate adduct at best.

As shown in Chart I, we have observed that direct addition occurs of acetylide to α,β -enones via dimethylaluminum acetylide.¹² Here yields were found to suffer from product destruction over a relatively short period of time in the presence of the catalytically reactive nickel species. We attribute this to side reactions involving the product, a terminal acetylene.¹³ As indicated in Chart I, this difficulty can be easily circumvented by the use of the (trimethylsilyl)acetylide reagent shown.¹⁴ Silylated products obtained could be cleanly and easily converted to terminal acetylenes through cleavage with KF.¹⁵

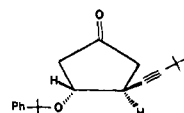
We are currently investigating the structure of the catalytically active species formed from Ni(acac)₂ and DIBAL and are also investigating alkylation chemistry of the dialkylaluminum enolates¹⁶ formed by these conjugate addition routes.

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Raman spectra, and Professor B. B. Snider for helpful comments and suggestions.

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- (9) A small amount of the diyne product of dimerization of RC≡CH is observed (<5%).
- (10) NMR spectral data (CCl₄): δ 1.05 (s, 9, H-7), 1.5 ("d", 6, H-2, 3.5-Hz separation), 1.9-2.4 (m, 3, H-5 and H-6), 2.8 (m, 2, H-4), 3.85 ("q", 1, J = 5.2 Hz, H-3), 7.2 (m, 5, H-1).



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Cyanoketenes. Mechanism of Cycloaddition of Chlorocyanoketene to Imidates

Sir:

The most widely employed synthetic route to 2-azetidinones (β -lactams) involves the reaction of an acid halide with an imine in the presence of an amine base.¹ It is generally assumed that this transformation is actually a nonconcerted [2 + 2] cycloaddition of a ketene with the imine and that a dipolar zwitterionic intermediate is the penultimate precursor to the β -lactam. However, little unambiguous evidence has appeared to substantiate this mechanism. Evidence for the nonconcerted nature of the reaction comes primarily from the facts that the cycloadditions are often nonstereospecific when prochiral reagents are employed, and, in some cases, adducts are formed in which the ratio of ketene to imine is 2:1. Even though such data are consistent with a ketene precursor, a mechanism which is as reasonable would be an initial acylation of the imine by the acid halide followed by proton abstraction to give the zwitterion and its subsequent ring closure to the β -lactam.² That preformed ketenes do cycloadd to imines has been es-