Cobalt-Mediated [3 + 2]-Annulation Reaction of Alkenes with α,β- Unsaturated Ketones and Imines

Jennifer M. Schomaker, F. Dean Toste,* and Robert G. Bergman*

Department of Chemistry, University of California, Berkeley, California 94720
rbergman@berkeley.edu; fdtoste@berkeley.edu

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ABSTRACT

The utility of cobalt dinitrosyl complexes for the [3 + 2]-annulation of alkenes with unsaturated enones and ketimines has been demonstrated. Reaction of a series of cobalt dinitrosyl/alkene adducts with conjugate acceptors in the presence of Sc(OTf)3/LHMDS formed two new C–C bonds at the carbons α to the nitrosyl groups of the substrate, leading to unusual tri- and tetracycles. Retrocycloaddition of these products in the presence of norbornadiene yielded functionalized tetrasubstituted bicyclic olefins.

Vinyl anion synthons (e.g., A in eq 1) provide versatile partners for the formation of new carbon–carbon bonds at alkenyl centers.1 In contrast, the generation of the corresponding dianion equivalent B, which would allow for the one-pot formation of two carbon–carbon bonds on adjacent carbons of the alkenyl substrate, is a much more challenging task.2 We recently reported that in the presence of base, cobalt dinitrosyl/alkene adducts behaved as vinyl anion (A) equivalents and were capable of Lewis acid-mediated conjugate addition reactions to enones (eq 1).3,4 Thermal retrocycloaddition of these alkylated intermediates produced organic products in which the unactivated alkene C–H bond had been functionalized. Herein, we report that sequential deprotonation of these cobalt complexes provides access to vinyl dianion equivalents (B, eq 2), allowing for the overall [3 + 2]-annulation reaction of alkenes with enones.


Treatment of the tetrahydrofuran-containing cobalt dinitrosoalkane adduct 1 with 2-cyclohexen-1-one 2 in the presence of 1.0 equiv of Sc(OTf)₃ and 2.1 equiv of LHMDS gave a 2.6:1 mixture of the polycyclic tertiary alcohol 3 and the Michael adduct 4. Both compounds were isolated and their structures confirmed by X-ray diffraction (Scheme 1).

We were pleased to find that the annulation reaction was not limited to the tetrahydrofuran-containing complex 1. Cobalt dinitrosopyrrolidine (5) and cyclobutane (10) complexes also underwent reaction with 2 to furnish the [3 + 2] annulated adducts 7 and 11 respectively (eqs 3 and 4). We thus turned our attention to the use of 1,2-unsaturated ketimines as partners in the annulation reaction. Unsaturated N-tert-butylsulfinyl ketimines proved to be viable electrophiles in the annulation reaction, yielding tertiary amines 8, 9, and 12 in 54–69% yield and modest diastereoselectivity (up to 2.6:1 dr). An additional benefit imparted by the use of a chiral auxiliary was the ability to separate the product diastereomers.

The strained cobalt dinitrosoalkane complexes synthesized by this simple conjugate addition/aldol annihilation reaction serve as useful precursors for a number of synthetic building blocks (eq 5). For example, treatment of the tricyclic fused-ring product 3 with norbornadiene under microwave conditions gave the expected tetrasubstituted bicyclic olefin 13 in 72% yield. Alternatively, the syn-1,2-diamine 14 could be prepared by treatment of 3 with LiAlH₄. Since both nitrogen-bearing carbons are fully substituted, epimerization at these carbons is not possible and the stereochemistry installed by means of the [3 + 2] annulation reaction remains intact.

Given that cobalt complex 1 was prepared from 2,5-dihydrofuran, the sequence leading to 13 illustrated in eqs 2 and 5 constitutes the overall [3 + 2]-annulation of this alkene with 2-cyclohexen-1-one. Therefore, the cobalt dinitrosoalkane complex 1 was treated with several enones to determine the scope of the new cobalt-mediated annihilation reaction (eq 6). Several acyclic conjugate acceptors underwent the first step of the sequence in 44–58% yield. In contrast to our previous work using cobalt dinitrosoalkanes, 1,2-unsaturated aldehydes were now viable substrates for the annihilation reaction, giving rise to secondary alcohols 15 and 16. Unsaturated methyl ketones also underwent successful annihilation with 1 to yield the tertiary alcohols 17 and 18. Moreover, the thermal retrocycladdition liberated the newly

(5) 2-Cyclopenten-1-one afforded only the conjugate addition product, and 2-cyclohepten-1-one gave a 22% yield of fused-ring product and 48% of the acyclic product (see Supporting Information).
(6) Structure confirmed by X-ray structure analysis (see Supporting Information).
(8) (a) Becker, P. N.; Bergman, R. G. Organometallics 1983, 2, 787.
(9) Reaction of 18 with LiAlH₄ furnished the corresponding diamine in 66% yield (see Supporting Information for details).
formed cyclopentenols (19–22) in greater than 90% yield in most cases. Notably, aliphatic enones and those conjugated to an aromatic or heteroaromatic group underwent the both steps of the sequence with equal efficiency.

Additionally, the two-step synthesis of aminated cyclopentenes can be achieved using α,β-unsaturated imines as electrophiles. For example, the use of the N-tert-butylenesulfamide imine 23, derived from cis-4-(2-furyl)-3-buten-2-one, allowed for the preparation of enantiomerically pure tertiary amine 25, after separation of the diastereomers of 24 (eq 7).

A proposed mechanistic pathway is outlined in Scheme 2 for the formation of annulated adduct 3. We postulate that 3 is formed by a tandem reaction involving deprotonation of an α-nitrosyl hydrogen and formation of initial diastereomeric Michael adducts 26a and 26b. Both diastereomers are susceptible to further deprotonation at the remaining α-NO hydrogen leading to diastereomeric anions 27a and 27b. In 27a, the carbanion is in close proximity to the carbonyl group; therefore, rapid ring closure ensues, affording 3 in 58% yield. In contrast, the anion of 27b cannot readily approach the carbonyl moiety, and therefore 27b leads to 4 in 22% yield on protonation during workup. To explore this hypothesis, we subjected compound 26b to further treatment with base and Lewis acid and found that it does not undergo cyclization.

In conclusion, we have demonstrated a facile [3 + 2]-annulation reaction of cobalt dinitrosalkane complexes with α,β-unsaturated carbonyls and ketimines that leads to unusual tri- and tetracyclic ring systems. The cycloannulated tetrasubstituted olefins can be prepared by a thermally induced olefin exchange reaction of the fused-ring product with norbornadiene. Diamines are also accessible via a LiAlH₄ reduction of the aforementioned complexes. Future work will focus on the identification of other difunctionalized electrophiles that undergo the annulation reactions. Efforts to develop enantioselective, cobalt-catalyzed variants are ongoing and will be reported in due course.

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Supporting Information Available: Experimental procedures and spectral information are available for all new compounds. X-ray crystal structure data are available for compounds 3, 4 and 7. This material is available free of charge via the Internet at http://pubs.acs.org.

Scheme 2. Proposed Mechanism for the Annulation Reaction