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NEW ROUTE TO THE SYNTHESIS OF POLYCYCLIC COMPOUNDS BASED ON A STEPWISE Ad_E-REACTION OF DICOBALT HEXACARBONYL COMPLEXES OF CONJUGATED ENYNES WITH A SUBSEQUENT INTRAMOLECULAR KHAND-PAUSON TYPE REACTION.

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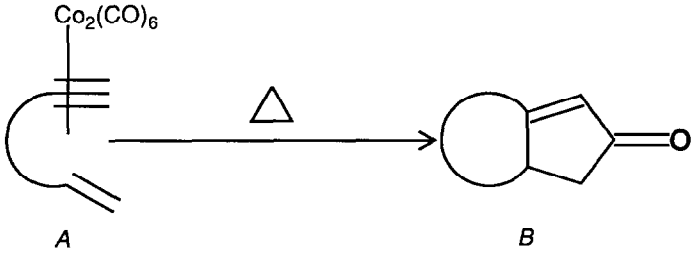
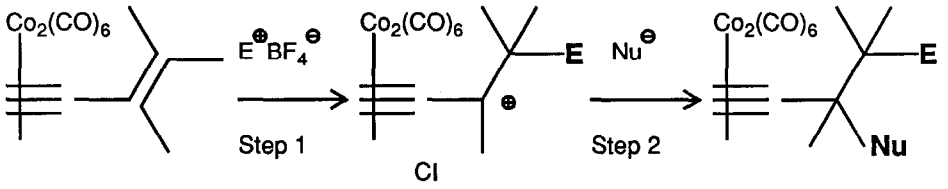
ABSTRACT. The stepwise Ad_E-reaction of dicobalt hexacarbonyl complexes of conjugated enynes has been extended to include unsaturated electrophiles and nucleophiles to produce products with an orientation conducive to a subsequent conversion into polycyclic compounds via an intramolecular Khand-Pauson type reaction.

A promising entry into polycyclic systems is an intramolecular variation of the Khand-Pauson type reaction[1,2] as presented in a general form in *Scheme 1*. Presently the usefulness of this potential route is limited by the availability of the starting substrates of type *A* as well as an optimum method for effecting the conversion of *A* to *B*.

Scheme 1



Scheme 2

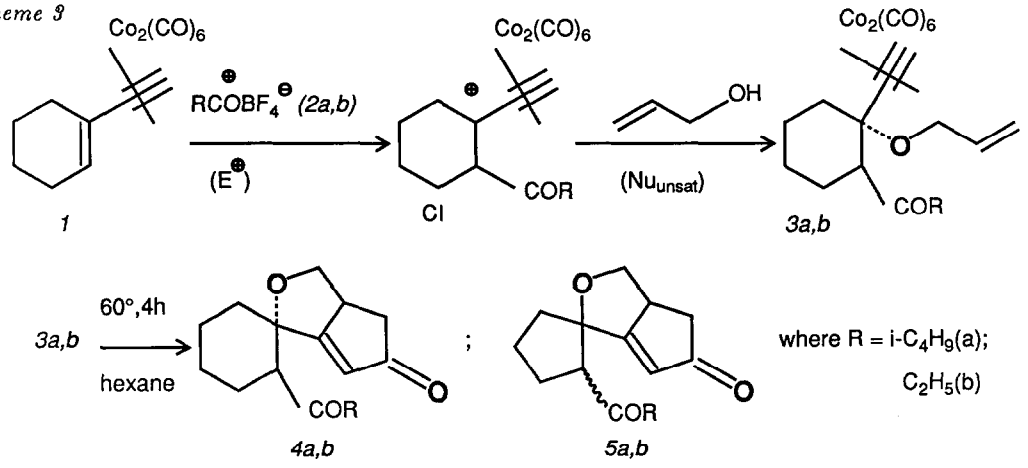


Earlier we described a stepwise Ad_E-reaction of dicobalt hexacarbonyl (DCHC) complexes of conjugated enynes[3] that permits an independent variation of the nature of the electrophile (E) and nucleophile (Nu) that is added to the alkene unit of the starting enyne.

This sequence may be applied in principle to the synthesis of the desired substrates (A) (*Scheme 1*) by using: (a) unsaturated nucleophiles (Nu_{unsat}) in step 2 or, (b) unsaturated electrophiles (E_{unsat}) in step 1 (see *Scheme 2*). In the present work, successful examples of both of these approaches are presented[4].

(a) Nu_{unsat}. Allyl alcohol was used as a model nucleophile in this variant. Thus acylation of the DCHC complex of cyclohexenylacetylene (1) with isovaleryl tetrafluoroborate (*2a*[3c]), with a subsequent work-up of the carbenium ion intermediate (CI) with allyl alcohol, gave the anticipated adduct *3a* in a 71% yield. Thermal cyclization under normal conditions [2a] lead to the formation of the tricyclic product 4*a* in a 45% yield. Likewise, 1 was transformed into 3*b* (69%) and finally into 4*b* (31%)[5,6]. With the DCHC complex of cyclopentenylacetylene the corresponding tricyclic products 5*a* and 5*b* were formed in 43% and 43% yields, respectively[5,7].

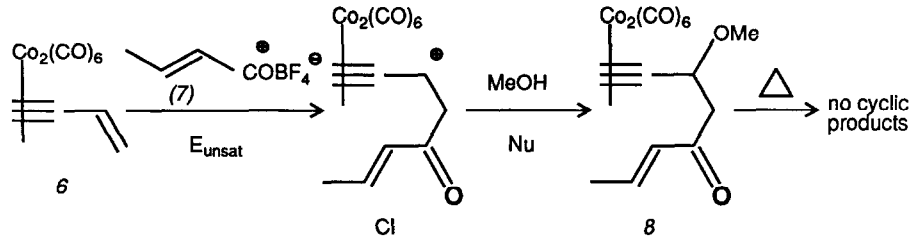
Scheme 3



(b) E_{unsat}. The viability of this approach was examined by the synthesis of 8 via the acylation of the DCHC Complex of vinylacetylene 6 with E-crotonyl tetrafluoroborate 7 and a subsequent quenching with methanol (98% yield)[3c]. Unfortunately, all attempts at cyclization of 8 under a range of different thermolysis conditions did not lead to the desired result[8].

Therefore, 8 was further transformed by reaction with MeMgI into a mixture of stereoisomers of the tertiary alcohols *9a,b* (combined yield of 55%), which could be separated by chromatography over SiO_2 into the individual isomers 9*a* and 9*b*. Although the structures of these alkenes appear ideally suited for an intramolecular cyclization of the Khand-Pauson type[2b], attempts to effect this reaction by thermolysis in solution (60°, 4*h*) into the expected bicyclic compound 10*a*, *b* (see below) led only to considerable tarring

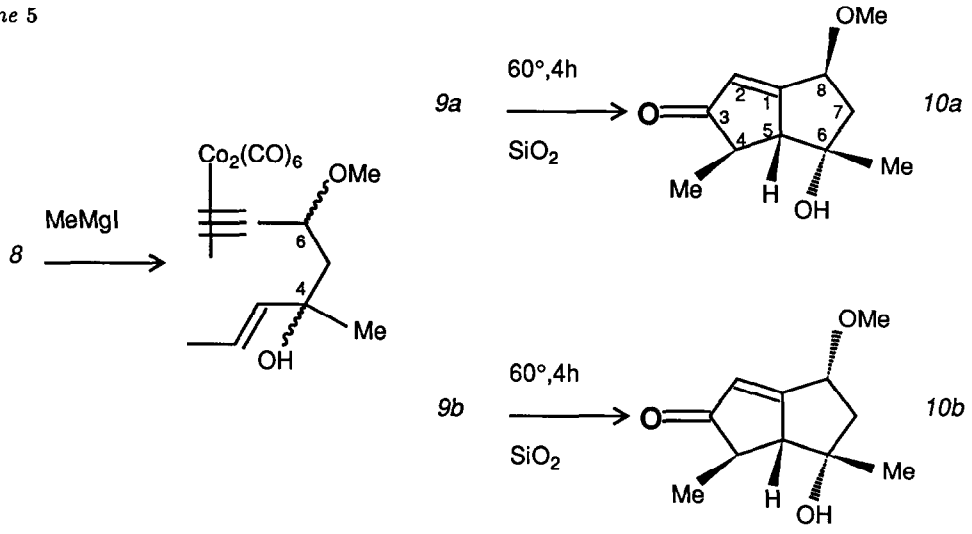
Scheme 4



and an insignificant quantity (5%) of product.

In searching for a method for effecting the conversion *9* ⟶ *10* we unexpectedly discovered that the reaction sharply accelerates if it is carried out not in solution, but in an absorbed state on the surface of some adsorbent. Thus, warming 9*a* (0.3g,0.86 mmol) applied to SiO_2 (Silpearl, Czechoslavakia, 15 ml) in a sealed ampoule (60°, 3*h*) lead to the complete conversion of *9a* into 4,6-dimethyl-6-hydroxy-8-methoxybicyclo[3.3.0]oct-1-en-3-one (10*a*) as the major product[9] which could be isolated in pure form (0.125 g, 74%)[5], mp 77-78°, by washing the adsorbent with ether, removal of the solvent, additional purification on SiO_2 and recrystallization (ether-hexane)[10]. Under similar conditions 9*b* was transformed into 10*b* (40% yield, mp 109-110°)[11]. The structures of the major products 10*a* and 10*b* (and the corresponding configurations at C-4 and C-6 in 9*a* and 9*b*) were unambigously established by X-ray analysis[12].

Scheme 5



The results presented in *Schemes* 3 – 5, graphically illustrate the synthetic possibilities generated by our route to the production of bicyclic compounds by an initial assemblage as indicated in *Scheme* 2 followed by a subsequent Khand-Pauson type of cyclization (*Scheme* 1).

It is important to notice that in the sequence of conversion 1 ⟶ 4 and 6 ⟶ 10 the fragment corresponding to the original enyne served as a C_4-component, in which in turn all four carbons were functionalized. In all of this the DCHC complex secures the protection of the triple bond, provides the stabilization for the CI, and, finally, serves as the reagent for the cyclization.

The possible ramifications of utilizing the two-step Ad_E-reaction of conjugated enynes for creating substrates useful in this reaction, as well as in related intramolecular cyclizations such as [4 + 2], [2 + 2] and [2 + 2 + 2] cycloadditions, is presently being investigated. The potential of the unusually mild procedure for promoting the Khand-Pauson cyclization is discussed in the following paper.

LITERATURE AND NOTES

1. For intermolecular variations of this reaction see P. L. Pauson and I. U. Khand, *Ann. N. Y. Acad. Sci., 295*, 2 (1977) and subsequent work of these authors.
2. For examples of intramolecular reactions see: (a) D. C. Billington, D. Willison, *Tetrahedron Lett., 25*, 4041 (1984), (b) C. Exon, P. Magnus, *J. Amer. Chem. Soc., 105*, 2477 (1983), (c) N. E. Shore, M. C. Croudace, *J. Org. Chem., 46*, 5436 (1981), (d) M. J. Knudson, N. E. Shore, *J. Org. Chem., 49*, 5025 (1984).
3. (a) A. A. Schegolev, W.. A. Smit, Y. B. Kalyan, M. Z. Krimer, and R. Caple, *Tetrahedron Lett., 23*, 4419 (1982), (b) G. S. Mikaelian, A. S. Gybin, W.. A. Smit, and R. Caple, *Tetrahedron Lett., 26*, 1269 (1985), (c) W. A. Smit, A. A. Schegolev, A. S. Gybin, G. S. Mikaelian, and R. Caple, *Synthesis*, 887 (1984), and references cited therein.
4. For a preliminary communication see G. S. Mikaelian and W. A. Smit, *Izvestia Acad. Nayk, SSSR*, Ser. Khim, 2652 (1984).
5. Yields are for purified adducts (chromatography on $Si0_2$) and the structures were confirmed by elemental analyses, 250 MH_Z ^{1}H NMR, and mass spectroscopy.
6. The stereochemistry shown is based on the previously established steric course of alkoxyacylation of *1*.[3c]
7. The stereochemistry of *5a,b* remains undefined since the configuration of the corresponding alkoxyacyl adducts has not been determined.
8. The inability of compounds containg a double bond in conjugation with an electron attracting group to form cyclopentenones in this reaction has been noted.[1]
9. The completion of the reactions can be checked by the disappearance of the characteristic dark-red color of the Cobalt complex.
10. The mother liquor contained, in addition to *10a*, a minor isomer (yield 10%) with the same gross structure (PMR, glc-MC data).
11. In this case the reaction is less selective and PMR analysis of the crude product revealed the presence of two additional by-products of unknown structure (total content 20-30%).
12. Crystal data *10a*. Monoclinic, a - 9,5917(7), b = 13,1204(7) A, β = 112,396(5)°, V = 1098,3(1) $Å^3$, Z = 4, sp.gr. $P2_1/c$, λ Mo, 1284 ref., R = 0,052 Crystal data *10b*. Triclinic, a = 5,9535(4), b = 9,2227(7), c = 10,0304(8) A, α = 69,844(6), β = 83,721(6), γ = 88,464(6)°, V = 513,88(7) $Å^3$, Z = 2, sp.gr.PI, Mo, 1811 ref., R = 0.045.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2, 1EW, UK.

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