Cyclopentenones from Carbonylative Cycloaddition of Mackenzie's Allyl Nickel Complexes and Acetylenes

Gabriel García-Gómez and Josep M. Moretó*

Departament de Química Orgànica Biològica
Centre D'Investigació i Desenvolupament, CSIC, C
Jordi Girona 18-26, 08034 Barcelona, Spain

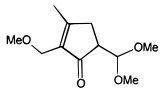
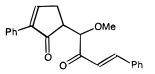
Received June 25, 1998

Transition-metal complexes have proved to be excellent mediators for multicomponent synthetic reactions. In particular, the Pauson−Khand (PK) cycloaddition has attracted the interest of many synthetic chemists[1] since it is able to provide, in a single operation, a variety of cyclopentenone systems for which rings there is no pericyclic reaction equivalent to the Diels−Alder cycloaddition for six-member rings. The efficiency of the metal in such systems stems from both the ability to coordinate either simultaneously or sequentially the different components of the reaction around the metal and their activation toward the required insertion reactions. Since ligand coordination is rather strict in its electronic demand and resulting geometry, a high degree of selectivity is often found in this class of reactions as in the aforementioned PK cycloaddition.

Another formally related process, the Ni-mediated cyclocarbonylation of allyl halides and alkynes, has found much less interest despite displaying a higher degree of regio- and stereoselectivity.[2] The involvement of the hazardous $Ni(CO)_4$ has much to do with its lack of popularity among the chemists' community.

We want to report here that cyclopentenones can be efficiently and selectively obtained in a single operative protocol without any handling of nickel carbonyl,[3] that is, by preparing the required π-allyl Ni complex in the way that Mackenzie et al. do: from $Ni(COD)_2$, acrylaldehydes, and Me_3SiCl.[4] These complexes have found recently extensive application in synthetic chemistry.[5] To the resulting Ni complex, a CO atmosphere is let in at very low temperature (−80 °C), and the acetylene is added. The mixture is allowed to reach approximately −15 °C at which point methanol, as a quencher, is added, and the reaction mixture is kept at this temperature for, at least, 4 h. Further workup and chromatographic separation through triethylamine pretreated silica (to avoid hydrolysis of the products) affords a mixture of two equivalent cyclopentenone derivatives as can be seen in Scheme 1:

Table 1. Products Obtained in the Ni-Mediated Reaction of Acrylaldehydes and Different Alkynes

Entry	R	R_1	R_2	Quenching temperature(°C)	Products (yields %)
1	H	CH_2OMe	Me	RT	**1a**(17) **2a**(26)
					 **3** (17)
2	H	H	Ph	-10	**1b**(3) **2b**(40)
					 **4** (8)
3	H	H	Me_3Si	-5	**1c**(5) **2c**(80)
4	H	CO_2Me	Me	-15	**1d**(3) **2d**(95)
5	H	Me	Me	RT	**1e**(8) **2e**(29)
6	Me	H	Me_3Si	-5	**1f**(5) **2f**(70)

From the results gathered in the Table it can be concluded that high temperatures favor β elimination (formation of the enol ether) and also that the original silyl ether is completely solvolyzed in the final adducts.

The yields (isolated product) can be considered from good to excellent for such a three-component reaction. They have not been optimized, but from the experiments performed with different alkynes it was found that the ideal reaction time and, therefore, the quenching temperature depends on the alkyne ranging from −15 °C (the most activated ones) up to room temperature for nonpolarized alkynes. In the case of entry 2, however, an easy alkyne polyinsertion precludes obtaining a good yield of the discrete cyclopentenone, but the structure of the side product elicits an easy formation of the cyclopentenone ring. Probably the electronic characteristics of the alkyne are to be blamed for this easy polyinsertion.[6]The reaction is regioselective in the same sense as in the one involving conventional π-allyl complexes: the most electronegative end of the alkyne binds the allyl moiety while this inserts by its less impeded end (also the regioisomeric ratios are similar).

Also remarkable here is that terminal alkynes afford only cyclopentenone adducts instead of 3-butenoate esters. This is probably due to the absence of methanol in the reaction mixture until the stage of the cyclopentenone ring closure has already been accomplished. Particular interest offers the reaction of trimethylsilylacetylene able to give a good yield of the corresponding cycloadduct (entries 3 and 6). This can be regarded as the product arising from the parent unsubstituted acetylene.

On the other hand, it is to be noted that in this particular methodology the final product ends up without a further carbonylation but with the formal original aldehyde. That confers versatility to this procedure taking into account the reactivity of the carbonyl group and its character of anchoring point for elongation of the chain. In this context, the convergent hydrolysis of **1d** and **2d** quantitatively affords the corresponding aldehyde **6** which is found to be completely enolized (Scheme 2). In addition, substituted acrylaldehydes efficiently proceed in this reaction to afford the corresponding cyclopentenones (entry 6). However, unlike what was found in the cycloadducts obtained from allyl halides,[2c] the resulting stereochemistry in the cyclopentenone substituents turns out here to be trans.[7]

(1) See leading references on the Pauson Khand cycloaddition in: (a) Schore, N. E, *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G., Wilkinson, G., Eds.; Elsevier: New York, 1995; Vol. 12, p 703. (b) Schore, N. E. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I.. Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, p 1037.

(2) (a) Chiusoli, G. P.; Cassar, L. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 124. (b) Camps, F.; Coll, J.; Moretó, J. M.; Torras, J. *J. Org. Chem.* **1989**, *54*, 1969−1978. (c) Camps, F.; Moretó, J. M.; Pagès,- Ll. *Tetrahedron* **1992**, *48*, 3147−3162. (d) Pagès, Ll.; Llebaria, A.; Camps, F.; Molins, E.; Miravitlles, C.; Moretó, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 10449−10461. (e) Oppolzer, W. *Pure Appl. Chem.* **1990**, *62*, 1941−1948 and references therein.

(3) In most of the cases, $Ni(COD)_2$ can also efficiently replace $Ni(CO)_4$ in the preparation of cyclopentenones through the initial formation of the π-allyl Ni complex from an allyl halide. This work is in progress.

(4) Johnson, J. R.; Tully, P. S.; Mackenzie, P. B.; Sabat, M. *J. Am. Chem. Soc.* **1991**, *113*, 6172−6177. Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 5160−5165.

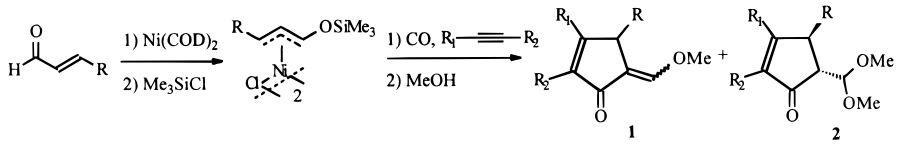
(5) Montgomery, J.; Savchenko, A. V.; Zhao, Y. *J. Org. Chem.* **1995**, *60*, 5699−5701. Montgomery, J.; Savchenko, A. V. *J. Am. Chem. Soc.* **1996**, *118*, 2099−2100. Montgomery, J.; Oblinger, E.; Savchenko, A. V. *J. Am. Chem. Soc.* **1997**, *119*, 4911−4920. Oblinger, E.; Montgomery, J. *J. Am. Chem. Soc.* **1997**, *119*, 9065−9066.

(6) Polyinsertion is also frequent in the conventional methodology. Sometimes it may be supressed to a large extent by the presence of acetate. See ref 2d. The effect of additives in this reactions or optimization of this precise reaction has not been undertaken.

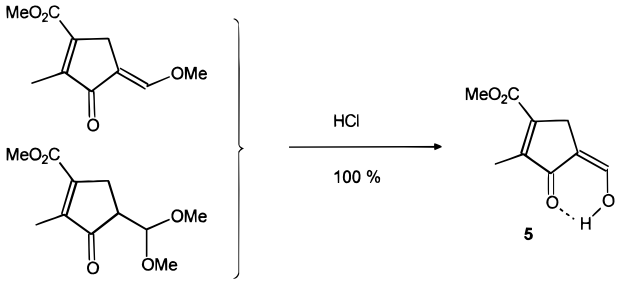
(7) Mutual coupling contants $J = 3$ Hz and NOE experiments are in agreement with the proposed stereochemistry.

10.1021/ja982207m CCC: $18.00
Published on Web 01/16/1999

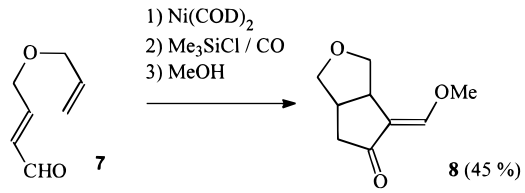
Scheme 1



Scheme 2



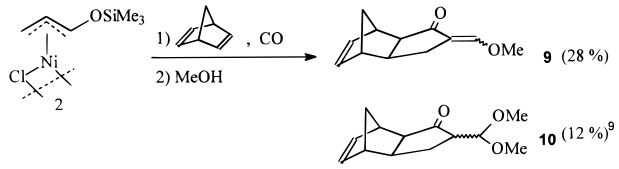
Scheme 3



The attempted intramolecular version of this process on enyne 5-oxaoct-2-en-7-ynal (**6**) failed, probably owing to the interfering presence of a triple bond during the formation of the π-allyl complex. This assumption was further supported by the surprising intramolecular cyclization of the corresponding diene **7** (Scheme 3). Further in this line, a strained olefin-like norbornadiene is found to undergo the intermolecular cycloaddition; albeit, the cycloadducts (formal cyclopentenones) are obtained in a rather low yield.[8] (Scheme 4).

Since many bioactive compounds (prostaglandins, antitumorals, antibiotics, perfumes, etc.) include a cyclopentenone moiety in their structure, the study of the scope of this reaction, especialluy toward the application of activated olefins, and that of the resulting stereoselectivity in the building up of more complex structures seems promising and will be pursued.

Scheme 4



Acknowledgment. We thank DGICYT and Generalitat de Catalunya (Project PB97-0407-C05-05 and Grant 5GR95-0439) for financial support. G.G.-G. thanks CIRIT for a fellowship. We thank also J. Roget and BASF Española S.A. for their support.

Supporting Information Available: Details of the experimental procedures and characterization data for all the products reported are described (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA982207M

(8) Ni(0) species are active catalysts for (carbonylative) oligomerizations of both alkynes and strained olefins, see: P. W. Jolly; G. Wilke. *The Organic Chemistry of Nickel*; Vol. II Academic Press: New York, 1974; Vol. II, pp 39−54, 94−103, 306−313).

(9) Estimated yields from the ^{1}H NMR spectrum of the product mixture.