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Tandem Deployment of Indium-, Ruthenium-, and Lead-Promoted Reactions. Four-Carbon Intercalation between the Carbonyl Groups of Open-Chain and Cyclic α-Diketones

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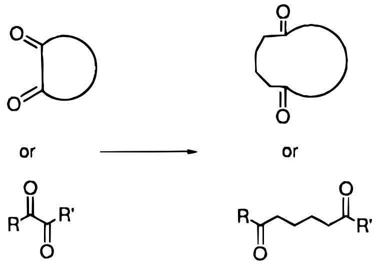
ABSTRACT



An efficient strategy for the conversion of 1,2-diketones into saturated 1,6-diketones and $\Delta^{2,3}/\Delta^{3,4}$-unsaturated congeners thereof is reported.

Chain-extension[1] and ring-enlargement reactions[2,3] play a major role in modern organic synthesis. Although a variety of tactics for achieving such transformations has been reported, little is known about the controlled insertion of carbon chains of differing length between the carbonyl groups of α-diketones. Consequently, we have targeted for investigation a convenient means for achieving four-carbon intercalation. Our results establish that a three-step sequence consisting of diallylation, ring-closing metathesis, and oxidative diol cleavage with Pb(IV) acetate (with or without prior hydrogenation) lends itself conveniently to useful structural modifications of this type.

The protocol was initially investigated with biacetyl (**1**) whose reaction with allyl bromide and indium powder in THF−water (1:4) afforded **2**[4] in a diastereomeric ratio of 3:2 (Scheme 1). Without separation, these diols were converted to **3** by exposure to Grubbs catalyst[5] in CH_2Cl_2 under argon. Direct addition of 1.1 equiv of lead tetraacetate[6] resulted in cleavage of the diol to **4** (66% overall)[7] with effective removal of the highly colored olefin metathesis catalyst impurities by filtration through a pad of silica gel.[8] Prior catalytic hydrogenation of **3** to **5**[9] made possible the analogous conversion to **6**.[10]

Our attempts to effect comparable structural homologation of diketone **7a** and keto aldehyde **7b** again proceed efficiently, but with some notable outcomes (Scheme 2). In

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[1] Ho, T.-L *Polarity Control for Synthesis*; John Wiley and Sons: New York, 1991.

[2] Gutsche, C. D.; Redmore, D. *Carbocyclic Ring Expansion Reactions*; Academic Press: New York, 1968.

[3] Hesse, M. *Ring Enlargement in Organic Chemistry*; VCH Publishers: Weinheim, 1991.

[4] (a) Masuyama, Y.; Tsunoda, T.; Kusuru, Y. *Chem. Lett.* **1989**, 1647. (b) Gewald, K.; Kira, M.; Sakurai, H. *Synthesis* **1996**, 111.

[5] Fu, G.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426.

[6] Mihailovic, M. Lj.; Cekovic, Z. *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Editor -in-Chief; Wiley: Chichester, 1995; Vol. 5, p 2949.

[7] The reported trans isomer exhibits a very different ^1H NMR spectrum: Yasuda, H.; Okamoto, T.; Mashima, K.; Nakamura, A. *J. Organomet. Chem.* **1989**, *363*, 61.

[8] Paquette. A.; Schloss, J. D.; Efremov, I.; Fabris, F.; Gallou, F.; Mendez-Andino, J.; Yang. J. *Org. Lett.* **2000**, 2, 1259.

[9] Hauptmann, S.; Dietrich, K. *J. Prakt. Chem.* **1963**, *19*, 174.

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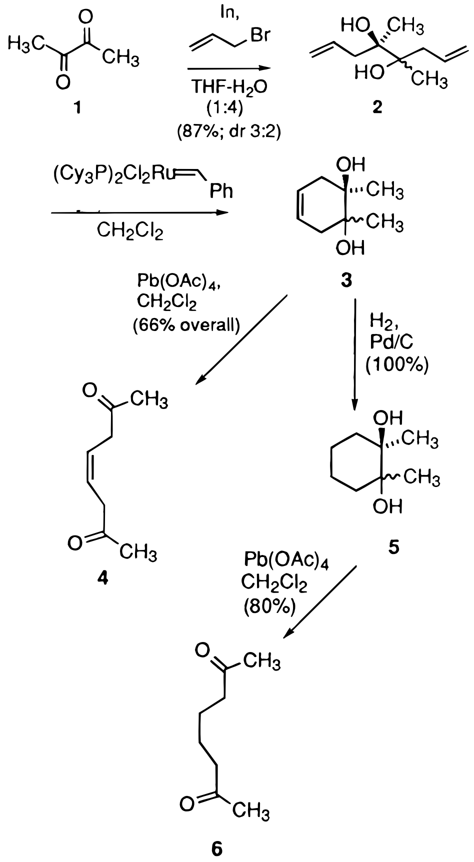
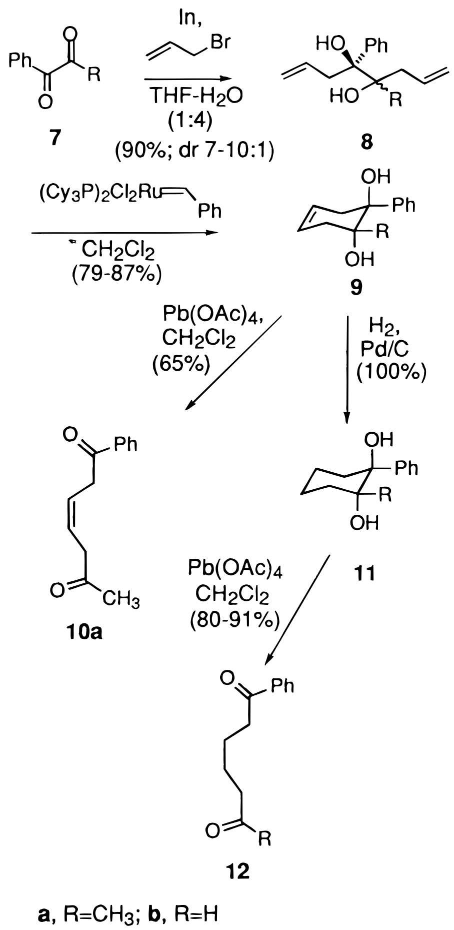
Scheme 1



Scheme 2



both of these examples, the diastereomeric ratios of allylated diols (7:1 and 10:1, respectively)[4b,11] were significantly more elevated than in the case of **2**. An increased bias for formation of the anti diols was deduced by analysis of the relevant chemical shifts exhibited by **9a** and **9b**.[12,13] This phenomenon may be indicative of a significantly greater preference for adoption of chelated transition states.[14] Although **10a**, **12a**,[15] and **12b**[16] were obtained with ease, **10b** could not be characterized because of its marked sensitivity to polymerization.

A pair of cyclic substrates has been studied in detail. The 2-fold allylindation of 1,2-cyclohexanedione under the predescribed aqueous conditions proceeded rapidly at the 0.08 M level to furnish **13** in 92% yield (Scheme 3). Exposure of **13** to the Grubbs catalyst in CH_2Cl_2 provided bicyclic diol **14**[17] as a 3:1 mixture of diastereomers. Sequential catalytic hydrogenation afforded **15**[18] from which 1,6-cyclodecanedione (**16**)[19] was derived. Once again, the introduction of lead tetraacetate immediately after completion of the ring-closing metathesis was found to be optimal in providing **17** and **18** as a 3:2 mixture in 69% overall yield. In **17** where no double bond migration occurs, the olefinic linkage must necessarily be cis. When conjugation does materialize as in **18**, the favored double bond geometry is trans ($J_{2,3} = 11.9$ Hz).

Implementation of the allylindation of **19**[20] was met with exclusive monoaddition. The second 1,2-addition occurred uneventfully when recourse was made to the allyl Grignard reagent in anhydrous ether. These conditions gave rise in 83% yield to a single diasteriomer of **20** (Scheme 4). Activation of the terminal vinyl groups in this diol with the Grubbs catalyst elaborated **21** in essentially quantitative yield. From this point, it proved an easy matter to generate pure **22**[21] or a mixture of **23** and **24**, which could be readily separated by chromatography.

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(10) Barbot, F.; Aidene, M.; Miginiac, L. *Synth. Commun.* **1998**, *28*, 3279.

(11) Kobayashi, S.; Hachiya, I. *J. Org. Chem.* **1993**, *58*, 6958.

(12) The methyl protons of **9a** (δ 1.05) experience significant shielding as a consequence of their position relative to the phenyl ring.

(13) (a) Diol **11a** is known: Fujiwara, T.; Tsuruta, Y.; Arizono, K.; Takeda T. *Synlett* **1997**, 962. (b) For **11b**, see: Berti, G.; Bottari, F.; Macchia, B.; Macchia, F. *Tetrahedron* **1965**, *21*, 3277. (c) Delgado, A.; Granados, R.; Mauleon, D.; Soucheiron, I.; Feliz, M. *Can. J. Chem.* **1985**, *63*, 3186.

(14) Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931.

(15) Nishinaga, A.; Rindo, K.; Matsuura, T. *Synthesis* **1986**, 1038.

(16) (a) Yamaguchi, M.; Takada, T.; Endo, T. *J. Org. Chem.* **1990**, *55*, 1490. (b) Kabalka, G. W.; Yu, S.; Li, N.-S. *Can. J. Chem.* **1998**, *76*, 800.

(17) The trans isomer of **14** has been reported: Hueckel, W. *Chem. Ber.* **1956**, *89*, 2098, 2102.

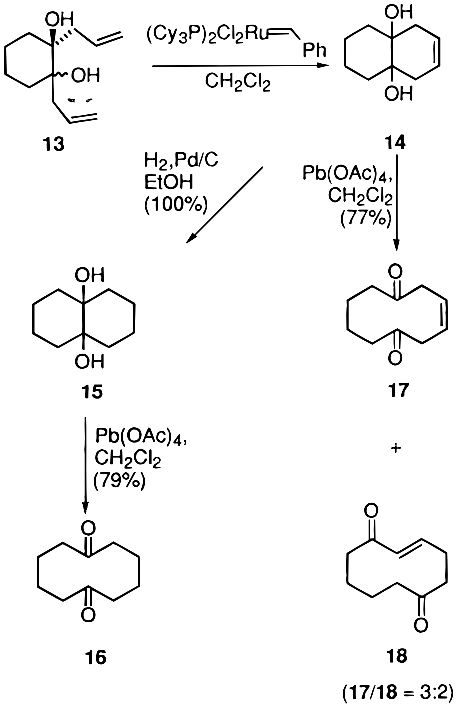
(18) (a) Dev, S. *J. Ind. Chem. Soc.* **1954**, *1*, 5. (b) Betzemeier, B.; Lhermite, F.; Knochel, P. *Synlett* **1999**, 489.

(19) House, H. O.; Lee, J. H. C.; Van Deveer, D.; Wassinger, J. E. *J. Org. Chem.* **1983**, *48*, 5285.

(20) Kawada K.; Gross, R. S.; Watt, D. S. *Synth. Commun.* **1989**, *19*, 777.

(21) Leriverend, P.; Conia, J.-M. *Bull. Soc. Chim. Fr.* **1970**, 1040.

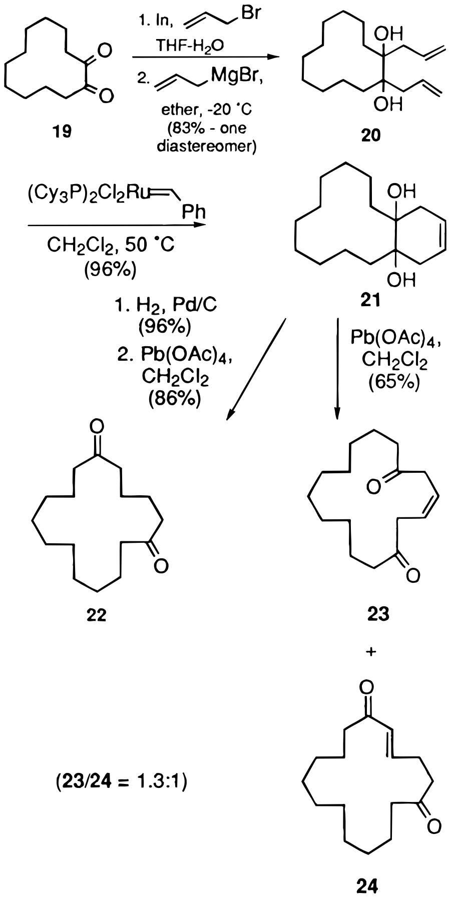
Scheme 3



It was at this point that the diminished reactivity of **19** toward the allylindium reagent was briefly probed. These ancillary studies make clear that other α-diketones share this reluctance to enter into 2-fold addition in an aqueous environment. Included in this group are 1,2-cyclooctanedione, 5-cyclooctene-1,2-dione, camphorquinone, and dimethyl squarate. The exceptionally high enol character of 3-methyl-1,2-cyclopentanedione deterred even simple monoaddition.

The ease of obtaining systems such as **2**, **8**, **13**, and **20**, the very mild conditions required for their cyclization via ring-closing metathesis, and the capability to access 1,6-diketones by direct treatment of the metathesis reaction mixtures with $Pb(OAc)_4$ render this protocol of demonstrable synthetic merit. Considerable potential lies beyond the realm of allylation, where longer chains having terminal double bonds would give rise to diketone products having carbonyl groups separated by 6–20 carbons or more on demand. It is our intention to explore in greater detail various aspects of these intercalation processes.

Scheme 4



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Supporting Information Available: Representative examples of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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