

152. Reactions of Enone Ethylene Ketals with Methyl Diazomalonate/Bis(acetylacetonato)copper(II)

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Several cyclic and acyclic enones and their ethylene ketals/acetals were reacted with dimethyl diazomalonate under bis(acetylacetonato)copper(II) catalysis. Cyclohex-2-en-1-one (**1**) yielded only C–H insertion products **2** and **3**, whereas but-3-en-2-one gave a cyclopropane albeit in very low yield. The ethylene ketals **6** of cyclopent-2-en-1-one and cyclohex-2-en-1-one gave the corresponding cyclopropanes **7**, which were in turn cleaved to the ketones **8**. The acetals **9** and **10** of crotonaldehyde ((*E*)-but-2-enal) and cinnamaldehyde ((*E*)-3-phenylprop-2-enal), respectively, yielded C–O insertion and [2,3]-sigmatropic rearrangement products **11b, c** and **12b, c**, as well as cyclopropanes **11a** and **11b**, all of which are polyfunctional and synthetically useful compounds.

Introduction. – Synthesis of natural products is probably the most popular topic of contemporary organic chemistry. Electrophilic cyclopropanes, which generally have two or more electron-withdrawing substituents, are one of the valuable intermediates in this field; various synthetic methods are currently being experimented to obtain these compounds¹). Reactions of the electron-poor enones with diazo compounds as carbene/carbenoid precursors unfortunately do not yield cyclopropanes, although a few successful examples have been described [6]. The idea to temporarily remove the electron-poor character of enones by ketalization, cyclopropanation by a diazo compound, and finally deprotection seems unpromising: Several such reactions studied by the *Doyle* group [7] yielded mainly [2,3]-sigmatropic rearrangement and C–O insertion products, and the cyclopropanes usually were, if formed at all, minor products. On the other hand, the multifunctional major products of this sequence also seem very useful for organic synthesis [7].

Doyle and coworkers performed their study with only two enone-acetal derivatives (acetals of acrolein (prop-2-enal) and cinnamaldehyde ((*E*)-3-phenylprop-2-enal)). We extended this reaction to several other ethylene acetals of acyclic and cyclic enones by exposing them to dimethyl diazomalonate (MDM)/bis(acetylacetonato)copper(II) ([Cu(acac)₂]) in benzene solution.

Results and Discussion. – *Reaction of Unprotected Enones with MDM/[Cu(acac)₂].* We first reexamined the ability of unprotected enones in cyclopropanation with diazo compounds in catalyzed media. Cyclohex-2-en-1-one (**1**), when reacted with MDM in C₆H₆ solution under [Cu(acac)₂] catalysis, yielded the insertion products **2** and **3**, and no

¹) See, e.g., the syntheses *via* dihydropyrazoles [1], *via* enones, dibromomalonates, and Bu₃Sb [2], from bromoesters and enones in the presence of bases [3], and *via* enone threitol ketals and *Simmons-Smith* reagent with high enantiomeric purity [4]; for cyclopropanes in general, see [5].

Table 1. Characteristics of **7** and **8**

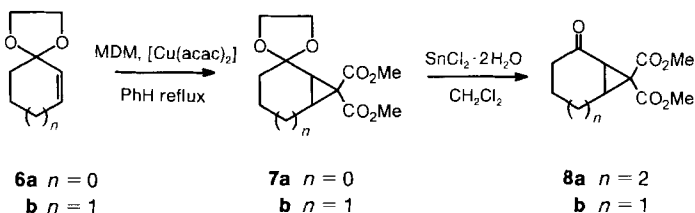
Yield [%]	GC: t_R [min] (temp. program)	IR (neat): $\tilde{\nu}$ [cm ⁻¹]	¹ H-NMR (CDCl ₃): δ [ppm]	MS: m/z (rel. %)
7a 68	12.7 (70° (3.5 min), then 20°/min → 290°)	2965, 2894, 1745, 1440, 1365, 1092, 1025, 945	3.90 (br. <i>t</i> , OCH ₂ CH ₂ O); 3.75, 3.7 (2 <i>s</i> , 2 MeO); 2.3-1.1 (others) 3.77 (<i>s</i> , 2 MeO); 1.57-2.80 (others)	256 (3, <i>M</i> ⁺), 225 (2), 174 (45), 110 (21), 97 (10), 82 (100), 59 (40)
8a 73	11.8 (see 7a)	1740		212 (2, <i>M</i> ⁺), 184 (19), 181 (14), 170 (15), 156 (100), 153 (30), 138 (17), 125 (18), 97 (19), 81 (27), 66 (41), 59 (86) 270 (1, <i>M</i> ⁺), 239 (7), 139 (12), 100 (48), 99 (100), 86 (75), 59 (13)
7b 87	12.7 (155° (10 min), then 10°/min → 290°)	2950, 2880, 1730, 1440, 1340, 1260, 1200, 1160, 1020	3.93 (br. <i>t</i> , OCH ₂ CH ₂ O); 3.79, 3.70 (2 <i>s</i> , 2 MeO); 2.2-1.0 (others) 3.77, 3.76 (2 <i>s</i> , 2 MeO); 2.5 (<i>t</i> , <i>J</i> = 5.4, CH ₂ CO); 2.42 (<i>d</i> , <i>J</i> = 4.74, CHCO); 2.35-1.7 (others)	226 (3, <i>M</i> ⁺), 195 (6), 166 (43), 139 (12), 134 (38), 133 (40), 132 (100), 111 (84), 95 (67), 68 (43), 59 (31)
8b 90	10.1 (see 7b)	1740, 1730		

Table 2. Characteristics of **11** and **12**

Yield [%] ^{a)}	GC: t_R [min] (temp. program)	¹ H-NMR (CDCl ₃): δ [ppm]	MS: m/z (rel. %)
11a 3	15.5 (50° (5 min), then 20°/min → 250°)	4.62 (<i>d</i> , <i>J</i> = 7, H-C(2)); 3.96 (br. <i>t</i> , OCH ₂ CH ₂ O); 3.83, 3.87 (2 <i>s</i> , 2 MeO); 1.18 (<i>d</i> , <i>J</i> = 7.16, Me); 1.3-1.4 (<i>m</i> , H-C(2), H-C(3))	244 (2, <i>M</i> ⁺), 229 (1), 185 (11), 174 (63), 83 (53), 69 (100), 59 (94)
11b 4	15.6 (see 11a)	5.93 (<i>dd</i> , <i>J</i> = 8.76, 1, H-C(8)); 4.9 (<i>dd</i> , <i>J</i> = 8.76, 5.75, H-C(7)); 3.98 (br., OCH ₂ CH ₂ O); 3.85, 3.86 (2 <i>s</i> , 2 MeO); 1.84 (<i>m</i> , H-C(6)); 1.75 (<i>d</i> , <i>J</i> = 7.2, Me-C(6))	229 (2, [<i>M</i> - Me] ⁺), 174 (13), 132 (16), 113 (39), 69 (100), 59 (11)
11c 30	15.3 (see 11a)	5.7-5.9 (<i>m</i> , 2 olef. H); 3.98-3.86 (<i>m</i> , OCH ₂ CH ₂ O, H-C(3)); 3.82, 3.85 (2 <i>s</i> , 2 MeO); 1.89 (<i>dd</i> , <i>J</i> = 7, 1.3, MeCH=CH)	244 (2, <i>M</i> ⁺), 229 (4), 185 (17), 174 (99), 113 (11), 83 (55), 69 (95), 59 (100)
12a 3	12.45 (150° (5 min), then 20°/min → 290°)	7.3-7.2 (<i>m</i> , Ph); 4.9 (<i>d</i> , <i>J</i> = 6.3, H-C(2)); 4.0-3.6 (<i>m</i> , OCH ₂ CH ₂ O); 3.5, 3.4 (2 <i>s</i> , 2 MeO); 2.75 (<i>d</i> , <i>J</i> = 6.55, H-C(3)); 1.28 (<i>dd</i> , <i>J</i> = 6.3, 6.6, H-C(2))	306 (1, <i>M</i> ⁺), 233 (7), 173 (6), 115 (11), 73 (100), 59 (3), 45 (12)
12b 10	12.63 (see 12a)	7.5-7.2 (<i>m</i> , Ph); 6.41 (<i>dd</i> , <i>J</i> = 5.75, 1, H-C(8)); 5.6 (<i>dd</i> , <i>J</i> = 5.77, 8.86, H-C(7)); 3.95 (<i>dd</i> , <i>J</i> = 8.83, 1.1, H-C(6)); 3.9-3.6 (<i>m</i> , OCH ₂ CH ₂ O); 3.67, 3.56 (2 <i>s</i> , 2 MeO)	306 (1, <i>M</i> ⁺), 247 (6), 215 (24), 174 (18), 131 (100), 115 (19), 104 (28), 103 (26), 91 (3), 59 (27)
12c 32	13.15 (see 12a)	7.4-7.2 (<i>m</i> , Ph); 6.71 (<i>d</i> , <i>J</i> = 16, PhCH=CH); 6.57 (<i>dd</i> , <i>J</i> = 16, 6.76, PhCH=CH); 4.82 (<i>d</i> , <i>J</i> = 6.76, H-C(3)); 4.1-3.9 (<i>m</i> , OCH ₂ CH ₂ O); 3.83, 3.73 (2 <i>s</i> , 2 MeO)	306 (2, <i>M</i> ⁺), 247 (5), 215 (21), 174 (13), 131 (100), 115 (19), 104 (27), 103 (26), 91 (6), 77 (13), 59 (24)

^{a)} According to GC, **11a**/**11b**/**11c** 1:2:14 and **12a**/**12b**/**12c** 1:2:6.5.

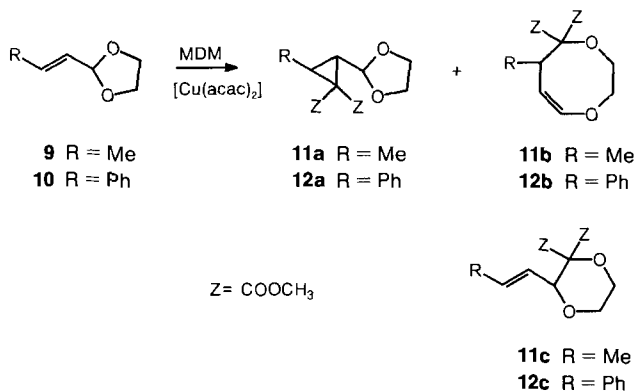
Scheme 2



Unfortunately, attempts on extension of the scope of this procedure to an enantioselective synthesis of **8a, b** using enantiomerically pure threitol ketals [4b] failed: The threitol ketal of **1** was almost quantitatively recovered, and tetramethyl ethylenetetracarboxylate was isolated as the only product. The formation of this ‘carbene dimer’ in all the other reactions can be avoided by very slow addition of MDM to the reaction mixture.

The success of this procedure led us to examine the reactivities of several open-chain enone ethylene acetals, namely the acetals **9** and **10** of (*E*)-but-2-enal (crotonaldehyde) and (*E*)-3-phenylprop-2-enal (cinnamaldehyde), respectively (Scheme 3). These reactions

Scheme 3



were not as clean as their predecessors, yielding [2,3]-sigmatropic rearrangement and C–O insertion products to a greater extent than cyclopropanes (Table 2). Yields of the cyclopropanes **11a** and **12a** were very low due to the formation of several other products, and serious difficulty was experienced in the purification steps. On the other hand, all products **11b, c** and **12b, c**, obviously arising from carbene-oxygen ylides³⁾, have the polyfunctionality required for their use in multi-step organic syntheses. We believe that this attenuates the draw-back of the low yields and the purification problems encountered in the transformations of **9** and **10**.

The products **7, 8, 11**, and **12** might have applications in perfumery, cosmetics, and fragrance industries.

³⁾ This interesting topic was the subject to an excellent review [15].

153. The Directionality of d-Orbitals and Molecular-Mechanics Calculations of Octahedral Transition-Metal Compounds

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A novel approach to modeling the angular geometry about the metal centre in transition-metal complexes, using a variation of classical molecular-mechanics calculations, is presented. The approach is based on the combination of 1,3-nonbonded interactions around the metal centre and a harmonic sine function with a ligand-field-dependent force constant for the $L-M-L'$ terms. Force-field parameters for four-, five-, and six-coordinated first-row transition-metal coordination centres and a variety of ligands containing N-, S-, and O-donor sets are given. The new 'electronically doped' force field is shown to generally lead to computed structures with higher accuracy than those obtained when the coordination geometries are modeled with 1,3-nonbonded interactions alone.

Introduction. – The relatively slow development of molecular-mechanics modeling of metal complexes is mainly due to the great variety of oxidation states, coordination numbers, and coordination geometries that are accessible for transition-metal centres, and this is a result of the partly filled d-orbitals [1]. Even with a given oxidation state and coordination number, and with systems where more pronounced effects such as *Jahn-Teller* distortions or *trans*-influences are absent, modeling of coordination geometries is not trivial. The problem that the angular distribution of the ligand atoms around a metal centre requires a function with various minima (*e.g.* 90/180° for square-planar and octahedral geometries, and 90/180/120° for trigonal bipyramidal coordination) has been solved with four fundamentally different approaches: *i*) representation of ligand–metal–ligand valence-angle bending by purely electrostatic or *van der Waals* terms [2] [3]; *ii*) search procedures based on the starting geometry followed by the assignment of a particular function and/or force field to the coordination angle [4]; *iii*) modeling of coordination angles with trigonometric potential-energy functions having multiple minima, similar to those used for torsional angle potentials [5]; and *iv*) computation of the angular geometry with models involving valence bond [6] or ligand-field [7] approaches.

We have developed force fields for a large series of transition-metal compounds including primarily first transition-metal-row centres and N-, S-, and O-donor groups, using 1,3-nonbonded interactions to model the coordination geometries [3b]. This parameterization has been tested successfully with many problems involving the modeling of structural, thermodynamic, and spectroscopic features [1b] [8]. However, we have recently found that the agreement between experimental and computed angular geometries of metal complexes may be unacceptably poor for applications involving

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