

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.

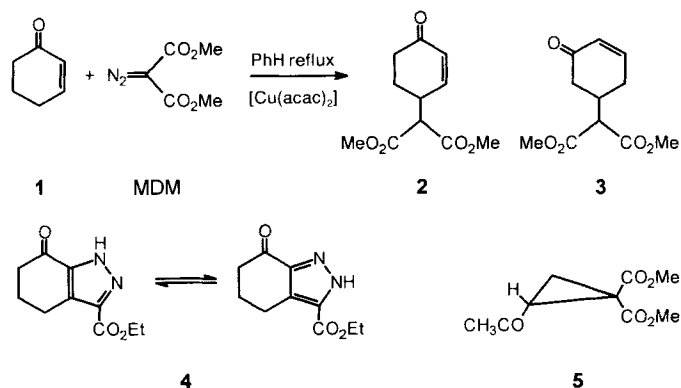
Introduction. – Synthesis of natural products is probably the most popular topic of contemporary organic chemistry. Electrophilic cyclopropanes, which generally have two or more electron-withdrawing substituents, are one of the valuable intermediates in this field; various synthetic methods are currently 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].

Scheme 1



cyclopropane product was detected as expected (Scheme 1). The ratio of the known 2 [8] to 3 was *ca.* 1:1.6. Such C–H insertions are known, mostly in the intramolecular sense, where rhodium(II) carboxylates were employed as catalysts [9]. On the other hand, intermolecular insertions can be found in the pioneering work of the *Wulfsberg* group including the reaction of cyclohexenone, where copper catalysts were used [8] [10]. A Japanese patent [11] reported that the reaction of ethyl diazoacetate with 2-pentylcyclopent-2-en-1-one yielded a vinylic insertion product besides a cyclopropane, at *ca.* 220° and in the absence of a catalyst. Cyclohex-2-en-1-one (1) and ethyl diazoacetate in refluxing CHCl_3 in the absence of catalysts gave the pyrazol 4 (m.p. 160–161°) in 16% yield, whereas the reaction in CH_2Cl_2 in the presence of $[\text{Cu}(\text{acac})_2]$ caused the formation of several C–H insertion products which were difficult to separate [12].

In contrast to the above result, but-3-en-2-one gave cyclopropane 5 under the same conditions, albeit in low (*ca.* 10%) yield²). The known compound 5 [2] could only be purified by prep. GLC. The reactions of this enone with ethyl diazoacetate in the presence of different catalysts were also studied by other research groups [6a, b].

The results of these two reactions allow to draw the conclusion that this sequence is almost absolutely inconvenient for cyclopropane synthesis. Therefore, we directed our attention to the carbonyl-protection method, not only in view of cyclopropane synthesis but also in an exploratory manner.

Reaction of Enone Ethylene Ketals with MDM/ $[\text{Cu}(\text{acac})_2]$. Ethylene ketals of five- and six-membered cycloalk-2-en-1-ones 6 gave the corresponding bicyclic cyclopropane ketals 7 as the only products, after reaction with MDM, in C_6H_6 solution under $[\text{Cu}(\text{acac})_2]$ catalysis (Scheme 2). It was interesting to detect no product resulting from oxonium ylide rearrangement. The bicyclic ketals 7 were successfully cleaved according to *Ford* and *Roskamp* [13] (the method of *Huet et al.* [14] gave erratic results) to yield the ketones 8. This sequence represents a valuable alternative synthetic method for the preparation of 7 and 8 in acceptable yields (7b [3a], 8a [2], and 8b [2] are known compounds). The yields and some data of the products are summarized in Table 1.

²) This reaction gave two other furanoid products also in low yield, due to the high tendency of the enone to polymerize. This reaction is currently being investigated with a variety of enone substrates in our laboratory.

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)	256 (3, <i>M</i> ⁺), 225 (2), 174 (45), 110 (21), 97 (10), 82 (100), 59 (40)
8a	73	11.8 (see 7a)	1740	3.77 (<i>s</i> , 2 MeO); 1.57–2.80 (others)	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)
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)	270 (1, <i>M</i> ⁺), 239 (7), 139 (12), 100 (48), 99 (100), 86 (75), 59 (13)
8b	90	10.1 (see 7b)	1740, 1730	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)

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.

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

REFERENCES

- [1] H. Abdallah, R. Gree, *Tetrahedron Lett.* **1980**, 21, 2239; H. Abdallah, R. Gree, R. Carrie, *ibid.* **1982**, 23, 503; see also: M. Hamaguchi, T. Nagai, *ibid.* **1992**, 33, 1321; D. S. Wulfman, R. S. McDaniel, Jr., *ibid.* **1975**, 4523.
- [2] C. Chen, Y. Liao, Y.-Z. Huang, *Tetrahedron* **1989**, 45, 3011.
- [3] a) P. F. Hudrlik, D. T.-W. Chou, T. David, M. A. Stephenson, *J. Org. Chem.* **1982**, 47, 2987; b) H. Spreitzer, G. Buchbauer, *Helv. Chim. Acta* **1984**, 67, 1112.
- [4] a) E. A. Mash, K. A. Nelson, *J. Am. Chem. Soc.* **1985**, 107, 8256; b) E. A. Mash, K. A. Nelson, *Tetrahedron* **1987**, 43, 679; c) E. A. Mash, D. S. Torok, *J. Org. Chem.* **1989**, 54, 250; d) E. A. Mash, S. B. Hemperly, K. A. Nelson, P. C. Heidt, S. Van Deusen, *ibid.* **1990**, 55, 2045; e) E. A. Mash, S. B. Hemperly, *ibid.* **1990**, 55, 2055.
- [5] 'The Chemistry of the Cyclopropyl Group', Ed. Z. Rappoport, John Wiley & Sons, New York, 1987, Vols. I & II.
- [6] a) M. P. Doyle, W. E. Buhro, J. F. Dellaria, *Tetrahedron Lett.* **1979**, 4429; b) M. Majchrzak, A. Kotelko, *Synthesis* **1983**, 469; c) M. P. Doyle, J. Davidson, *J. Org. Chem.* **1980**, 45, 1538.
- [7] M. P. Doyle, J. H. Griffin, M. S. Chinn, D. Leusen, *J. Org. Chem.* **1984**, 49, 1917.
- [8] B. W. Peace, F. Carman, D. S. Wulfman, *Synthesis* **1971**, 658.
- [9] T. Ye, M. A. McKervery, *Chem. Rev.* **1994**, 94, 1091.
- [10] D. S. Wulfman, B. G. McGibboney, E. K. Steffen, N. V. Thinh, R. S. McDaniel, Jr., B. W. Peace, *Tetrahedron* **1976**, 32, 1257.
- [11] K. Shishido, S. Kurozumi, K. Uchimoto, Jap. Pat. 7000,862 (CA: **1970**, 72, 78526g).
- [12] Ö. Sezer, unpublished results, Istanbul Technical University, 1992.
- [13] K. L. Ford, E. J. Roskamp, *Tetrahedron Lett.* **1992**, 33, 1135.
- [14] F. Huet, A. Lechevallier, M. Pellet, J. M. Conia, *Synthesis* **1978**, 63.
- [15] A. Padwa, S. F. Hornbuckle, *Chem. Rev.* **1991**, 91, 263.
- [16] E. W. Garbisch, Jr., *J. Org. Chem.* **1965**, 30, 2109.
- [17] J. P. Fourneau, S. Chantalou, *Bull. Soc. Chim.* **1945**, 12, 845.