Reaction of Metal–Carbene Complexes with Cyclobutenediones: The First General C–C Bond Insertion Reaction for Fischer Carbene Complexes

Metin Zora and James W. Herndon*

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742-2021

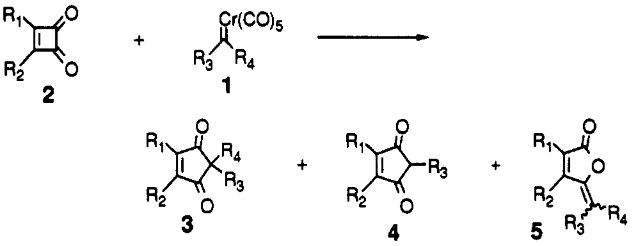
Received November 13, 1992

Summary: Alkylcarbene–chromium complexes react with cyclobutenediones to give 2-alkoxy-4-cyclopentene-1,3-diones in moderate yield, accompanied by varying amounts of 4-cyclopentene-1,3-dione derivatives which result from reduction of the initial product by the chromium byproduct. The reaction is general for a variety of cyclobutenedione derivatives with alkoxy, alkyl, or aryl substituents. The major products of the reaction between arylcarbene complexes and cyclobutenediones are 5-alkylidenefuranone derivatives. A mechanism involving oxidative addition of the acyl–acyl C–C bond, followed by carbene insertion and reductive elimination, is proposed.

Metal–carbene complexes have emerged as very valuable reagents for the preparation of structurally complex organic molecules.[1] Their reactions with various π-bonded substrates such as alkenes and alkynes can lead to diverse array of cyclic compounds, depending upon the structure of the carbene complex and the alkene or alkyne. The subject of this paper is exploration of the reactivity of these complexes with a different type of functional group, cyclobutenediones, which are susceptible to C–C bond insertion.

Reaction of methylmethoxycarbene complex **1A** with cyclobutenedione derivative **2A** led to a mixture of cyclopentenediones **3A** and **4A** (Scheme I). The reaction of complex **1A** with cyclobutenedione **2A** has been examined under a variety of conditions, and the optimal conditions involve heating a 1.3:1 mole ratio of the two reaction species at 100 °C in dioxane at 0.2 M concentration. As can be seen in Table I, the reaction appears to be general for alkylcarbene complexes and oxygen-, alkyl-, and/or aryl-substituted cyclobutenediones. The yield of adducts from non-oxygen-substituted cyclobutenediones was noticeably lower, probably due to instability of the cyclobutenedione. Amino-substituted cyclobutenedione **2C** was not reactive to carbene complexes, and the cyclobutenedione derivative could be completely recovered from the reaction. Aminocarbene complex **1D** was noticeably less reactive and produced cyclopentenedione derivative **3B** in low yield. In the reaction of **1A** and **2A**, the proportion of reduced compound **4A** increased at the expense of compound **3A**. When the compound **3A** was present during the reaction of cyclopropylcarbene complex **1B** and **2A**, partial conversion to **4A** was observed. Similarly, treatment of compound **3A** with chromium hexacarbonyl in dioxane led to very slow reduction to **4A**.[2] Clearly, reduced compound **4** is a secondary product of the reaction, whose formation can be suppressed by keeping the reaction time to a minimum. The mechanism for the reaction is outlined in Scheme II and involves oxidative addition of chromium into the acyl–acyl bond of the cyclobutenedione,[3] followed by carbene insertion[4] and reductive elimination.

Scheme I. Products Obtained from the Reaction of Cyclobutenediones with Carbene Complexes



[a] Compound 1:[5] (**A**) $R_3 = CH_3, R_4 = OCH_3$; (**B**) R_3 = cyclopropyl, $R_4 = OCH_3$; (**C**) $R_3 = Ph, R_4 = OCH_3$; (**D**) $R_3 = CH_3, R_4 = N(CH_3)_2$. Compound 2:[6] (**A**) $R_1, R_2 = i\text{-}OC_3H_7$; (**B**) $R_1 = CH_3, R_2 = i\text{-}OC_3H_7$; (**C**) $R_1 = i\text{-}OC_3H_7, R_2 = N(CH_3)_2$; (**D**) $R_1 = CH_3, R_2 = Ph$. Compounds **3–5**: see Table I.

The reaction of phenylcarbene complex **1C** with diisopropyl squarate (**2A**) produced only 5-alkylidenefuranone derivatives (**5F**), but reaction of alkyl-substituted cyclobutenedione **2B** with complex **1C** led to all three types of products. The formation of compound **5** may not actually represent a different reaction pathway, since the thermal rearrangement of 2-cyclopentene-1,4-diones to 5-alkylidenefuranones is a well-known process.[9,10] This rearrangement typically occurs at 230 °C, but the results in entries F and G imply that the rearrangement can occur in refluxing THF or dioxane. Thermolysis of cyclopen-

---

(1) (a) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984,** *23,* 587–608. (b) Wulff, W. D. In *Comprehensive Organic Synthesis;* Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 1065–1113.

(2) For similar reductions by chromium hexacarbonyl, see: (a) Wulff, W. D.; Kaesler, R. W.; Peterson, G. A.; Tang, P.-C. *J. Am. Chem. Soc.* **1985,** *107,* 1060–1062. (b) Tumer, S. U.; Herndon, J. W.; McMullen, L. A. *J. Am. Chem. Soc.* **1992,** *114,* 8394–8404.

(3) Prior oxidative addition, followed by carbene insertion into preformed metallacyclopentane derivatives, is precedented: (a) Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T. *J. Am. Chem. Soc.* **1987,** *109,* 5025–5026. (b) O'Connor, J. M.; Pu, L.; Rheingold, A. L.; Uhrhammer, R.; Johnson, J. A. *J. Am. Chem. Soc.* **1989,** *111,* 1889–1891.

(4) (a) Oxidative addition into the acyl–acyl bond of cyclobutenediones is well-precedented: Liebeskind, L. S.; Leeds, J. P.; Baysdon, L. S.; Iyer, S. *J. Am. Chem. Soc.* **1984,** *106,* 6450–6451. (b) For another mechanistic proposal involving conversion of maleoyl–chromium complexes to cyclopentenediones, see: Xu, Y.-C.; Challener, C. A.; Dragisch, V.; Brandvold, T. A.; Peterson, G. A.; Williard, P. G.; Wulff, W. D. *J. Am. Chem. Soc.* **1989,** *111,* 7269–7271.

(5) Carbene complexes were prepared from the corresponding organolithium reagents, chromium hexacarbonyl, and methyl trifluoromethanesulfonate. See: Brown, F. J. In *Progress in Inorganic Chemistry;* Lippard, S. J., Ed.; Wiley: New York, 1980; Vol. 27, pp 1–122, and references therein.

(6) (a) Cyclobutenediones **2A,B,D** were prepared according to the procedure of Liebeskind: Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T. *J. Org. Chem.* **1988,** *53,* 2482–2488. (b) Cyclobutenedione **2C** was prepared according to the procedure of Tietze: Tietze, L. F.; Arlt, M.; Beller, M.; Glüsenkamp, K.-H.; Jähde, E.; Rajewsky, M. F. *Chem. Ber.* **1991,** *124,* 1215–1221.

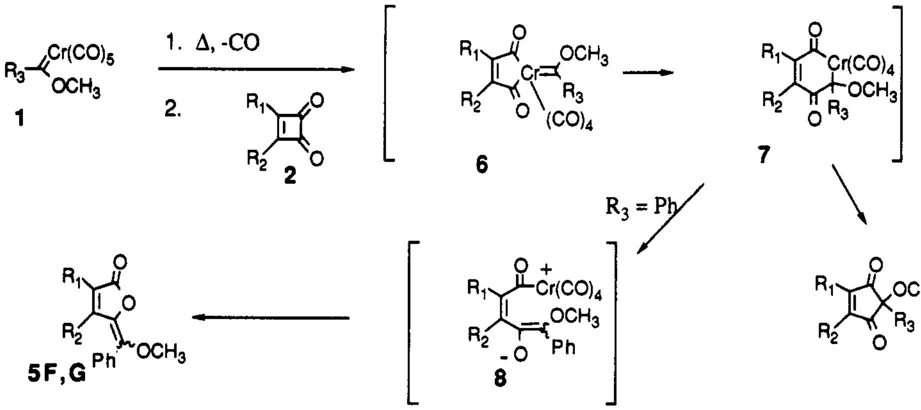
0276-7333/93/2312-0248$04.00/0

Table I. Reaction of Cyclobutenediones with Carbene Complexes[a]

	R groups for 3–5				yield, %		
entry[b]	R_1	R_2	R_3	R_4	**3**	**4**	**5**[c]
A (**1A** + **2A**)	i-C_3H_7O	i-C_3H_7O	CH_3	OCH_3	31	14	0
B (**1D** + **2A**)	i-C_3H_7O	i-C_3H_7O	CH_3	$N(CH_3)_2$	12	0	0
C (**1B** + **2A**)	i-C_3H_7O	i-C_3H_7O	cyclopropyl	OCH_3	34	17	0
D (**1A** + **2B**)	CH_3	i-C_3H_7O	CH_3	OCH_3	25	16	0
E (**1A** + **2D**)	CH_3	Ph	CH_3	OCH_3	20	15	0
F (**1C** + **2A**)	i-C_3H_7O	i-C_3H_7O	Ph	OCH_3	0	0	55 (1.1:1)[d]
G (**1C** + **2B**)	CH_3	i-C_3H_7O	Ph	OCH_3	13	15	21[e] (1.1:1)[d]

[a] For a procedure, see ref 7. [b] The compounds in parentheses are the reacting partners. [c] The numbers in parentheses refer to the E:Z ratio. [d] See the supplementary material for a discussion of the stereoisomer assignment. [e] See ref 8 for a discussion of the regioisomer assignment.

Scheme II. Mechanism for Formation of Compounds 3–5



tenedione **3G** at 100 °C does not lead to **5G**, and thermolysis in the presence of chromium hexacarbonyl slowly produces only cyclopentenedione **4G**. This result implies that alkylidenefuranones are not the products of thermal rearrangement reactions (i.e. kinetic products). Conversion of compound **7** to an enolate, followed by nucleophilic attack on the acylchromium species **8**, would produce compound **5** (Scheme II).[11] This is more likely when R = phenyl due to added stability of the enolate.

In summary, we have discovered a novel and highly predictable C–C bond insertion reaction for chromium carbene complexes.[12] Further investigation of the mechanism and scope and limitations of these processes is currently under investigation, as well as delineation of the factors which influence cyclopentenedione versus 5-alkylidenefuranone formation.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the General Research Board of the University of Maryland for support of this research.

Supplementary Material Available: Characterization data for the products in Table I (4 pages). Ordering information is given on any current masthead page.

OM9207222

---

(7) A solution of cyclobutenedione **2A** (0.198 g, 1.00 mmol) and carbene complex **1A** (0.325 g, 1.30 mmol) in dioxane (5 mL) was heated to reflux under nitrogen for a 6-h period. The mixture was cooled to room temperature, and the solvent was removed on a rotary evaporator. The residue was dissolved in 9:1 hexane–ethyl acetate (25 mL) and the solution filtered through Celite. After removal of the solvent on a rotary evaporator, final purification was achieved by flash chromatography on silica gel using 19:1 hexane–ethyl acetate as the eluent. The compound in the first fraction (0.032 g, 14% yield, R_f 0.31 in 9:1 hexane–ethyl acetate) was identified as compound **4A**. The compound in the second fraction (0.079 g, 31% yield, R_f 0.25 in 9:1 hexane–ethyl acetate) was identified as compound **3A**. Spectral data for **3A**: ^1H NMR ($CDCl_3$) δ 5.48 (septet, 2 H, J = 6.1 Hz), 3.18 (s, 3 H), 1.35 (s, 3 H), 1.32 (d, 6 H, J = 6.1 Hz), 1.31 (d, 3 H, J = 6.1 Hz); ^{13}C NMR ($CDCl_3$) δ 194.9, 150.1, 77.3, 74.8, 53.2, 22.9, 19.2; IR ($CDCl_3$) 1688, 1601 cm^{-1}; MS (EI) m/e 256 (M^+, 25), 214 (59), 172 (100), 143 (24), 115 (21), 97 (13), 84 (10), 75 (10), 69 (10), 55 (30); HRMS calcd for $C_{13}H_{20}O_5$ 256.1311, found 256.1301. Spectral data for **4A**: ^1H NMR ($CDCl_3$) δ 5.41 (septet, 2 H, J = 6.1 Hz); 2.71 (q, 1 H, J = 7.5 Hz), 1.31 (d, 12 H, J = 6.1 Hz), 1.20 (d, 3 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 195.9, 149.9, 74.3, 44.8, 22.9, 11.2; IR ($CDCl_3$) 1685, 1609 cm^{-1}; MS (EI) m/e 226 (M^+, 10), 184 (37), 153 (31), 142 (51), 114 (100), 73 (17), 68 (28); HRMS calcd for $C_{12}H_{18}O_4$ 226.1205, found 226.1220.

(8) The indicated regiochemistry has been assigned on the basis of comparison of ^{13}C NMR spectra in similar systems. In a 4-alkoxyfuranone, the α-carbonyl carbon is unusually upfield, while the β-carbonyl carbon is unusually downfield.[8a] In a 3-alkoxyfuranone (i.e. **5G** if R_1 and R_2 were reversed), considerably less polarization is observed.[8b] In the major stereoisomer of **5G**, the α-carbonyl carbon appears at δ 170, and the β-carbonyl carbon appears at δ 104, which is more consistent with the indicated 4-alkoxyfuranone structure. (a) Anderson, J. R.; Edwards, R. L.; Whalley, A. J. S. *J. Chem. Soc., Perkin Trans. 1* **1982**, 215–221. (b) Raffauf, R. F.; Zennie, T. M.; Onan, K. D.; Le Quesne, P. W. *J. Org. Chem.* **1984**, *49*, 2714–2718.

(9) (a) Campbell, A. R.; Maidment, R. S.; Pick, J. H.; Stevenson, D. F. M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1567–1576. (b) Claisen, L.; Ewan, T. *Justus Liebigs Ann. Chem.* **1895**, *284*, 245–299.

(10) For a citation to the reaction mechanism involving vinylketene intermediates, see: Moore, H. W.; Weigler, W., Jr. *J. Am. Chem. Soc.* **1971**, *93*, 2811–2813.

(11) We thank Prof. Dan Harvey of the University of California at San Diego for this suggestion.

(12) For other examples of insertion of Fischer carbene complexes in σ bonds, see: (a) Wienanad, A.; Reissig, H. U. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1129–1131. (b) Herndon, J. W.; Tumer, S. U. *J. Org. Chem.* **1991**, *56*, 286–294. (c) Cooke, M. D.; Fischer, E. O. *J. Organomet. Chem.* **1973**, *56*, 279–284. (d) Zhao, S.-K.; Knors, C.; Helquist, P. *J. Am. Chem. Soc.* **1989**, *111*, 8527–8528.