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Low temperature carbene transfer from alkoxychromium(0) (Fischer) carbene complexes

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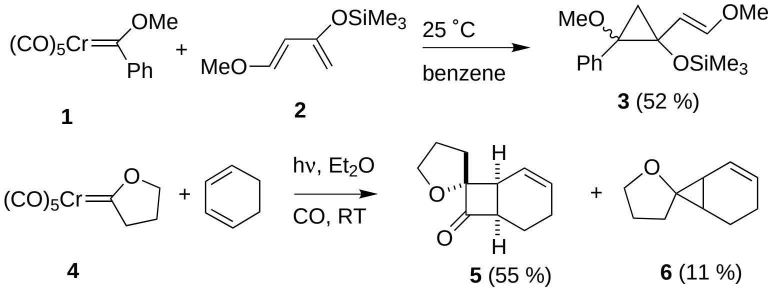
Abstract—Irradiation at low temperatures (0°C) of alkyl-, aryl- and styryl alkoxychromium(0)carbene complexes in the presence of methyl acrylate produces a mixture of diastereomeric cyclopropanes and C–H insertion derivatives. The ratio cyclopropane/C–H insertion product is independent of the reaction conditions, while the cyclopropane *cis*:*trans* ratio strongly depends on the solvent, the selectivity increasing as the polarity of the reaction solvent does. © 2001 Elsevier Science Ltd. All rights reserved.

The use of group 6 (Fischer) carbene complexes as carbene transfer agents is a long standing topic in organic chemistry.[1] In fact, one of the earliest reactions ever reported for these compounds was the cyclopropanation of olefins.[2] The intermolecular cyclopropanation reaction usually required harsh reaction conditions and electron-deficient olefins to occur.[2,3] Nevertheless, alkenes substituted with electron-donor groups,[2c,4] or even neutral alkenes are also intermolecularly cyclopropanated.[5] In most cases, the intermolecular cyclopropanation reaction is carried out at temperatures considerably above rt. On the contrary, intramolecular cyclopropanation reaction happens at rt or below.[6] To the best of our knowledge, there is a single example of the intermolecular cyclopropanation of a diene by an alkoxychromium(0) carbene complex that occurs at rt: the reaction of complex **1** and Danishefsky's diene **2** in benzene to give vinyl cyclopropane **3** with 52% yield after 5 days at rt (Scheme 1).[7] During recent years we have been working in processes leading to the transfer of the carbene ligand from group 6 (Fischer) carbene complexes at rt or below.[8] In the course of this work and related to our long standing research about the photochemical acceleration of processes on chromium–carbene complexes,[9] our attention was attracted by a side product obtained by Hegedus during the photochemical reaction of complex **4** and 1,3-cyclohexadiene to yield cyclobutanone **5**.[10] The isolation of cyclopropane **6** clearly indicates that the carbene transfer reaction can take place under photochemical conditions and at lower temperatures than those reported for thermal processes. We report here the photochemical carbene transfer to electron-poor olefins, which proceeds at temperatures as low as 0°C, a result that has no precedent in the cyclopropanation of deactivated alkenes.

Alkoxychromium(0) carbene complex **7** was irradiated (400 W, medium pressure, Hg-lamp, Pyrex filter and



Scheme 1.

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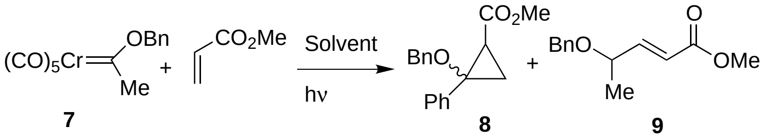
Pyrex well) in MeCN and in the presence of methyl acrylate at 0°C. Mixtures of diastereomeric cyclopropanes **8** (98:2) and methyl 4-benzyloxy-2-pentenoate, **9** (formed by C–H insertion) were consistently obtained in different runs in a 49:51 ratio after 3 h. The reactions were run in parallel experiments under identical conditions (0°C), but in the dark. Chromium complex **7** was recovered unaltered in these conditions. When the reaction was carried out at rt in the dark the complex was slowly consumed to yield benzyl acetate together with unreacted starting material after 86 h.



The ester, that was formed in variable yields, is probably produced by oxidation of the starting material during the long reaction times. Clearly there are significant differences between the thermal and the photochemical reaction. The effect of the solvent in the carbene transfer was studied next. The results obtained are collected in Table 1 and show that the cyclopropane/C–H insertion ratio is hardly sensitive to the change of the solvent. Otherwise, the *cis*:*trans* selectivity for diastereomeric cyclopropanes **8** is very sensitive to solvent polarity with the more polar MeCN giving the highest selectivity. The diastereomeric cyclopropanes were separated and characterized and the stereochemistry assigned by the comparison with related products reported in the literature.[3b,11,12]

Table 1. Effect of the solvent in the product distribution of the reaction of complex **7** and methyl acrylate[a]

Solvent	Time[b] (h)	**8**/**9**[c]	**8** *cis*:*trans*[c]	Yield[d]
Pentane	7	56:44	45:55	69
Benzene	5	54:46	51:49	57
Toluene	3	49:51	30:70	98
DCM	3	59:41	33:77	87
Et_2O	6	46:54	20:80	73
MeCN	3	49:51	2:98	39

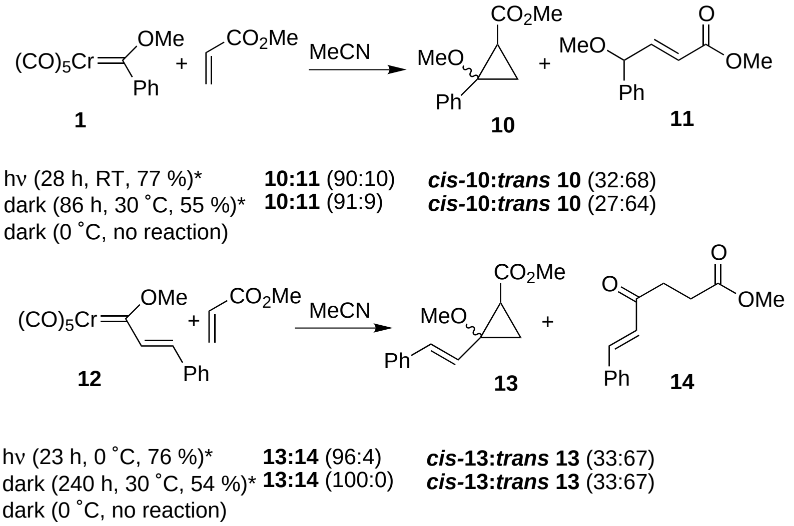
[a] Reaction conditions: $[\mathbf{7}]=10^{-2}$ M; $T=0$°C.

[b] Until complete disappearance of the spot corresponding to the starting carbene complex **7** determined by tlc.

[c] Determined by integration of well resolved signals in the ^{1}H NMR spectra of the crude reaction mixtures.

[d] Combined yields of pure products **8** and **9**.

Once the viability of the photochemical carbene transfer at low temperatures was established, we extended the reaction to complexes **1** and **12**. Compound **1** reacted efficiently with methyl acrylate to yield mixtures of cyclopropanes **10** and C–H insertion product **11**. Complex **12** formed, in turn, a 96:4 mixture of cyclopropanes **13** and α,β-unsaturated ketone **14**. This compound may be derived from the initially formed C–H insertion product by double bond isomerization followed by hydrolysis. However, after submission of this reaction mixture to column chromatography compound **14** was obtained in a 29% (isolated yield of pure material). This pointed clearly to the formation of compound **14** at the expense of cyclopropanes **13**.[13] Although, the reaction of complex **1** and methyl acrylate occurred at 0°C, the competitive oxidation of the complex at this temperature makes the process more efficient if the reaction is carried out at rt (ca. 25–30°C). Both complexes **1** and **12** also reacted at rt (30°C) in the dark but the reaction times were considerably longer. Thus, while complex **1** reacts nicely by irradiation with methyl acrylate after 28 h at rt to yield a 90:10 mixture

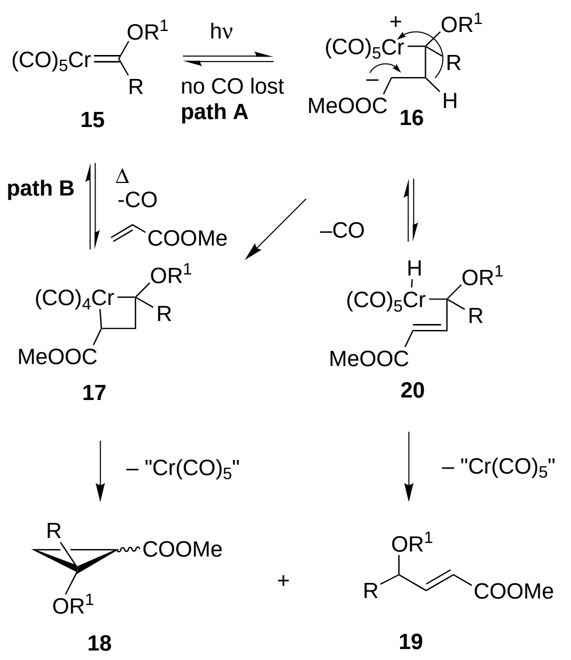


hν (28 h, RT, 77 %)* **10:11** (90:10) ***cis*-10:*trans* 10** (32:68)
dark (86 h, 30 °C, 55 %)* **10:11** (91:9) ***cis*-10:*trans* 10** (27:64)
dark (0 °C, no reaction)

hν (23 h, 0 °C, 76 %)* **13:14** (96:4) ***cis*-13:*trans* 13** (33:67)
dark (240 h, 30 °C, 54 %)* **13:14** (100:0) ***cis*-13:*trans* 13** (33:67)
dark (0 °C, no reaction)

*The given yield is for the combined pure isolated compounds

Scheme 2.



Scheme 3.

of cyclopropanes **10** and ester **11**, the same reaction in the dark requires 86 h and takes place in lower yield. The reaction of complex **12** under thermal conditions requires also longer reaction times (240 versus 23 h) leading to a distribution of products analogous to the photochemical reaction (Scheme 2). Complexes **1** and **12** remained unaltered after several days in the presence of methyl acrylate and in the dark at 0°C.

The clear acceleration of the reactions above under irradiation may be explained by activation of the MLCT band of the metal that promotes one-electron from a metal d-centered HOMO to a π^*-carbene centered LUMO, which is formally one-electron oxidation. Since the activated species resulting from the irradiation of the chromium–carbene complex **15** are nucleophile, it should be able to add to one deactivated olefin in a Michael fashion (path A) to yield the zwitterionic intermediates **16**.[14,15] This intermediate may then evolve to metallacyclobutane **17** by ring closure involving CO extrusion. Metallacyclobutane **17** is the key intermediate in the thermal reaction of carbene complexes and electron-poor olefins formed from **15** by sequential CO lost, coordination of the metal to the double bond and final intramolecular cycloaddition (path B, Scheme 3).[16] In the absence of CO the photochemical reaction of complexes **15** and deactivated olefins should follow path A with intermediate **16** evolving to metallacyclobutane **17**. In these conditions little differences in the distribution of cyclopropanes **18** and C–H insertion products **19** are expected because photochemical and thermal reactions join in intermediate **17**. However, the *cis*:*trans* ratio of the cyclopropanes should be strongly dependent on the solvent polarity since this ratio is determined during the evolution of the charged species **16** to **17**. Experiments above clearly show that the ratio cyclopropane/C–H insertion is nearly the same in both thermal and photochemical conditions. However, Table 1 shows the strong dependence of the *cis*:*trans* selectivity in the cyclopropanation reaction with the solvent, the more polar solvents giving the highest selectivities. Zwitterions **16** can also produce compounds **18** by direct ring closure and C–H insertion derivatives **19** through intermediate **20**.[17] This last intermediate would be formed by migration of the β-hydrogen to the metal center assisted by the electron pair α-to the carbonyl carbon. This mechanism may also explain the fact that the thermal, intramolecular cyclopropanation in group 6 carbene complexes occurs under moderated CO-pressures.[6c,9]

In conclusion, the carbene transfer from chromium-(0)carbene complexes to electron-poor olefins can be effected at low temperatures (0°C) by irradiation. The ratio cyclopropane/C–H insertion product is mostly independent of the reaction conditions, while in photochemical conditions the cyclopropane *cis–trans* selectivity depends strongly on the solvent. Based on these results we proposed the formation of a zwitterionic intermediate **16** as the key step for the photochemical reaction. Efforts to extend this photochemical carbene transfer to other Michael-acceptors are underway in our laboratories.

Acknowledgements

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12. The following experimental procedure is representative: All photochemical reactions were conducted by using a 400 W, medium pressure mercury lamp through a Pyrex filter. All the reactions were carried out in dry degassed CH_3CN or Et_2O in a sealed Pyrex tube filled with argon. In a typical experiment a 2×10^{-2} M solution of the carbene complex and the corresponding olefin (1:5 ratio, respectively) was irradiated at 0°C or rt for the time specified for each case. The solvent was removed in vacuo and the residue was dissolved in a mixture of hexane:AcOEt (1:1) and exposed to direct sunlight until a clear solution was obtained. The solution was filtered through a short pad of Celite, the solvent eliminated and the products were purified by flash column chromatography.
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15. Zwitterionic intermediates have been proposed by Wulff in the thermal cyclopropanation of Danishefsky's diene **2** by alkoxychromium(0)- and tungsten carbene complexes. However, the formation of these zwitterions is essentially inverse to the proposed by us in Scheme 3. In Wulff's case the carbene carbon behaves as an electrophile and the addition of the diene as nucleophile leads to the corresponding zwitterions. See Ref. 7 and pertinent references therein. For the isolation of a zwitterionic intermediate in the cyclopropanation of electron-rich alkenes, see: Barluenga, J.; Ballesteros, A.; Santamaría, J.; Bernardo de la Rúa, R.; Rubio, E.; Tomás, M. *J. Am. Chem. Soc.* **2000**, *122*, 12874.
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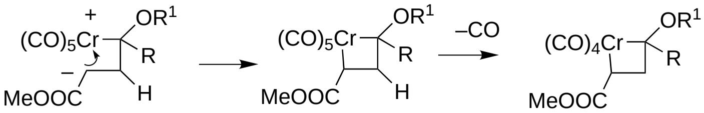
17. Intermediate **16** may alternatively evolve to metallacyclobutane **17** through a hepta-coordinated metallacyclobutane **21** by ring-closure followed by CO extrusion (Eq. (1)). The overall result as well as the influence of the solvent in the cyclopropane stereochemistry would be, in principle, identical to the mechanism proposed in Scheme 3. Although with data in hand this possibility cannot be ruled out, the formation of hepta-coordinated complexes of group 6 metal carbenes is rare. See: Jaeger, M.; Stumpf, R.; Carsten, T.; Fischer, H. *Chem. Commun.* **2000**, *1*, 931 and the pertinent references cited therein.



16 **21** **17**

(1)