The First Synthesis of Some Spiro[2,3-Dihydro-2,2-Dimethylbenzofuran-3,1'-Cyclopropanes] through, $Mo(CO)_6$ Catalyzed, One Pot Claisen Rearrangement-Cyclization Reaction of 2-Cyclopropylidene-Aryloxy Alkanes

Angela M. Bernard, Pier P. Piras*

Dipartimento di Scienze Chimiche, Università di Cagliari, Via Ospedale 72, 09100 CAGLIARI (Italy)

Fax (19) 70 6758605; E mail: pppiras@vaxca1.unica.it

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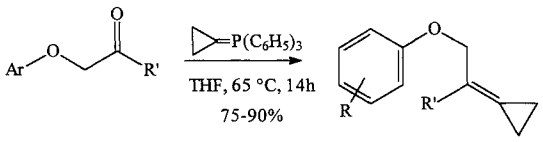
Abstract : $Mo(CO)_6$ effectively transforms the cyclopropylidene aryloxy derivatives **2a-e,g** into the previously unknown spiro[2,3-dihydro-2,2-dimethylbenzofuran-3,1'-cyclopropanes] **3a-e,g**.

Molybdenum hexacarbonyl is a versatile reagent that has been used as an effective catalyst in several reactions. We recently reported[1] that it can be used successfully as a practical alternative to some common Lewis acids ($ZnCl_2$, $AlCl_3$) in the one pot conversion of allyl aryl ethers to dihydrobenzofurans. It was found that the reaction was favoured by the presence of *para* electron donating substituents, while *para* electron-withdrawing substituents decreased the cyclization rate. On the other hand the substitution pattern of the allylic moiety was crucial in determining the amount of $Mo(CO)_6$ to be used to obtain the best conversion. Best yields were obtained with the methallyl ethers while the allyl ethers were much less reactive and the crotyl phenyl ether led to a complex reaction mixture.

As a consequence of our involvement in cyclopropane chemistry,[2] we became aware that no previous report appeared in the literature on the Claisen rearrangement of cyclopropylidene phenoxy derivatives like **2.** Being therefore interested to study if derivatives **2** were suitable substrates for the reaction with $Mo(CO)_6$, we prepared the cyclopropylidene phenoxy derivatives **2a-g** in high yields, by reaction of the phenoxy ketones **1a-g** with the cyclopropylidene triphenyl phosphonium bromide in the McMurry's conditions (Scheme 1).[3]



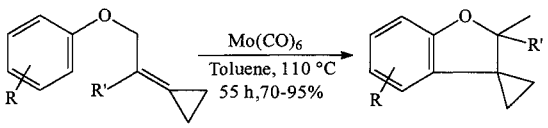
1a-g **2a-g**

a	R = H	R' = Me
b	R = *p*-Me	R' = Me
c	R = *p*-MeO	R' = Me
d	R = *p*-Cl	R' = Me
e	R = *m*-Me	R' = Me
f	R = 2,6-Me	R' = Me
g	R = H	R' = C_6H_5

Scheme 1

We were delighted to discover that, despite the fragility of the cyclopropylidene ring, derivatives **2a-g**, in the presence of $Mo(CO)_6$ in refluxing toluene, gave the corresponding spiro[2,3-dihydro-2,2-dimethylbenzofuran-3,1'-cyclopropanes] **3a-e,g** in excellent yields (70-95%) without opening of the cyclopropane ring.[4] (Scheme 2).

Derivatives **3a-e,g** have been distinguished from their isomers, the spiro-[2,3-dihydro-3,3-dimethylbenzofuran-2,1'-cyclopropanes], actually intensively studied for their antiulcer activity, on the basis of the presence in the ^{13}C NMR of all the derivatives of a signal around 87 ppm. This signal, due to a quaternary carbon, is attributable to a carbon bonded to an oxygen atom and two methyl groups analogously to what we found, in our previous paper,[1] for the 2,3-dihydro-2,2-dimethyl benzofurans. An analogous carbon bonded to an oxygen atom and a cyclopropyl ring should give a signal at higher fields, as reported[5] in the case of the spiro[2,3-dihydro-5-hydroxy-4,6,7-trimethylbenzofuran-2,1'-cyclopropane] (C-2,1': 66.25 ppm).



2a-g **3a-e,g**

Scheme 2

Derivatives **2a,c** gave the corresponding dihydrobenzofurans **3a,c** after 20 h in the presence of 20 mol% of catalyst, while, for **2b,e,g** 40 mol% of catalyst for 55 h was necessary for the complete conversion of the starting material. In these conditions, even with 40% mol of catalyst, 20% of starting material was still present, after 55h, in the case of **2d.** No reaction was observed in the case of derivative **2f** after 55 h with 40 mol% of catalyst. The reaction shows a moderate regiocontrol as, in the case of **2e** the less hindered spiro[2,3-dihydro-2,2,6-trimethylbenzofuran-3,1'-cyclopropane] was preferentially formed (70:30) over the alternative spiro[2,3-dihydro-2,2,4-trimethylbenzofuran-3,1'-cyclopropane]. This ratio was worked out by comparison of the integral of a clear separated triplet at 6.93, in the ^1H NMR spectrum, attributable only to the spiro[2,3-dihydro-2,2,4-trimethylbenzofuran-3,1'-cyclopropane], and the complete integral of the aromatic region. This data was further confirmed by comparison of the integral of the two separate aromatic methyl signals.

This preparation of the spiro dihydrobenzofurans **3a-e,g** represents the first example of synthesis of this previously unknown class of compounds. The only few reported examples[6] of a similar structure are the spiro[benzofuran-3(2*H*),1'-cyclopropan]-2-one derivatives.

The following procedure for the synthesis of the spiro[2,3-dihydro-2,2-dimethylbenzofuran-3,1'-cyclopropane] **3a** is representative. A solution of the cyclopropylidene aryl ether **2a** (3-5 mmol) in toluene (6-10ml) containing $Mo(CO)_6$ (20 mol%), was stirred under argon in a stoppered Schlenk flask at 115 °C (external oil bath) for 55 h. This solution, after cooling, was diluted with Et_2O (10ml), then filtered through Al_2O_3 and concentrated in vacuo. The residue was then chromatographed on a silica gel column using light petroleum-diethyl ether 5:1 as eluent, to give the pure product.

$Mo(CO)_6$ has also recently gained increasing importance as a catalyst in allylic alkylations because of its excellent chemoselectivity and for a regioselectivity that is complementary to that of Pd(O) catalyst. As we have recently published the use of some cyclopropylidene phenoxy derivatives in palladium catalyzed nucleophilic substitutions,[7] we checked also the possibility of carrying out the same reactions using **2a** as a substrate and $Mo(CO)_6$ as a catalyst.[8] The most common leaving groups used in molybdenum-catalyzed allylic alkylations are acetate,

trifluoroacetate, sulfone and tosylate.[8, 9, 2a] Recently one report has appeared where phenyl sulfide and 2-pyridyl sulfide have been used as leaving groups[10] in sulfenylative allylation of carbon nucleophiles, while it appears that a phenoxy group has never been used as a leaving group in this kind of reaction.

Using dimethyl malonate or its sodium salt as nucleophiles in refluxing toluene for 20 h in the presence of 10% mol of $Mo(CO)_6$ we were not able to find, in the reaction mixture, any alkylation product, but we always found the benzofuran **3a** with unreacted starting material (40%). This result seems to confirm, at least in our case, the unsuitability of the phenoxy group as a leaving group in molybdenum catalyzed allylic alkylations because of the concurrent Claisen rearrangement-cyclization reaction.

In conclusion we have reported the first synthesis of some derivatives of the new class of spiro[2,3-dihydro-2-methylbenzofuran-3,1'-cyclopropanes] that present the possibility of introducing functionalities on the C-3 of the dihydrobenzofuran as a consequence of the easy opening of the cyclopropane ring. Moreover the very simple method, based on the new use of $Mo(CO)_6$, is a further confirmation of the possibility of using this product as a catalyst in the synthesis of dihydrobenzofurans.

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References and Notes

(1) Bernard, A. M., Cocco, M. T., Onnis, V., Piras, P. P. *Synthesis* **1997**, 41.

(2) For some of our recent publication in the field see:
a) Stolle,A., Ollivier, J., Piras, P. P., Salaun, J., de Meijere, A. *J.Am.Chem.Soc.* **1992**, 114, 4051; *b*) Aufranc, P., de Meijere, A., Ollivier, J., Piras, P. P.,Salaun, J., Stolle, A. *Tetrahedron Lett.* **1992**, 33, 3307; Bernard, A. M., Piras, P. P. *J.Chem.Soc.Chem.Commun.* **1994**, 257. Ollivier, J., Dorizon, Piras, P. P., De Meijere, A., Salaun, J. *Inorg.Chim.Acta* **1994**, 222, 37; Bernard, A. M., Cocco, M. T., Congiu, C., Franzone, G.L., Piras, P. P. *Synthesis* **1996**, 361.

(3) Stafford, A. J., Mc Murry, E. J. *Tetrahedron Lett.* **1988**, *29*, 2531.

(4) All new compounds have been fully characterized by ^1H NMR (300 MHz), ^{13}C NMR (75.4 MHz) and mass spectra (EI, 70 eV). Spectral data for compounds **2a-g, 3a-e, g** are given.
2a, 2g: ref 7.
2b: ^1H NMR ($CDCl_3$) δ : 1.05 (m, 4H), 1.85 (s, 3H), 2.20 (s, 3H), 4.51 (s, 2H), 6.97 (m, 4H). ^{13}C NMR ($CDCl_3$) δ : 1.82, 2.61, 18.07, 20.45, 71.77, 114.56, 114.69, 121.23, 129.32, 129.75, 156.77. MS (EI) *m/z* : 188 (M^+, 13), 173 (M-Me, 44), 145 (27), 108 (74), 79 (100). **2c:** ^1H NMR ($CDCl_3$) δ : 1.05 (m, 4H), 1.92 (s,3H), 3.68 (s, 3H), 4.54 (s, 2H), 7.22 (m, 4H). ^{13}C NMR ($CDCl_3$) δ : 1.82, 2.60, 18.02, 55.68, 72.34, 114.48, 115.63, 120.71, 121.27, 153.02, 153.64. MS (EI) *m/z* : 204 (M^+, 13), 189 (M-Me, 17), 161 (8), 123 (100), 79 (20). **2d:** ^1H NMR ($CDCl_3$) δ : 1.07 (m, 4H), 1.91 (s, 3H), 4.57 (s, 2H), 7.17-7.31 (m, 4H). ^{13}C NMR ($CDCl_3$) δ : 1.76, 2.60, 17.88, 71.85, 115.91, 120.12, 121.51, 125.24, 129.06, 157.41. MS (EI) *m/z* : 208 (M^+, 7), 193 (M-Me, 10), 173 (M-Cl, 26), 145 (12), 128 (32), 79 (100). **2e** ^1H NMR ($CDCl_3$) δ : 1.09 (m, 4H), 1.93 (s, 3H), 2.31 (s, 3H), 4.59 (s, 2H), 6.71-7.33 (m, 4H). ^{13}C NMR ($CDCl_3$) δ : 1.75, 2.54, 17.99, 21.42, 71.45, 111.45, 115.47, 120.59, 121.13, 121.26, 128.95, 139.14, 158.87. MS (EI) *m/z* : 188 (M^+, 21), 173 (M-Me, 62), 145 (48), 108 (50), 79 (100). **2f:** ^1H NMR ($CDCl_3$) δ : 1.07 (m, 4H), 2.08 (s, 3H), 2.29 (s, 6H), 4.33 (s, 2H), 6.86-6.99 (m, 3H). ^{13}C NMR ($CDCl_3$) δ : 2.03, 2.34, 16.20, 18.55, 75.75, 121.32, 121.61, 123.61, 128.69, 131.03, 155.86. MS (EI) *m/z* : 202 (M^+, 4), 187 (M-Me, 50), 159 (25), 122 (42), 79 (100). **3a:** ^1H NMR ($CDCl_3$) δ : 0.86-1.04 (m,4H), 1.32 (s, 6H), 6.62-7.12 (m, 4H). ^{13}C NMR ($CDCl_3$) δ : 13.08, 25.51, 33.00, 87.37, 109.00, 119.12, 120.14, 127.20, 133.08, 158.13. MS (EI) *m/z* : 174 (M^+, 46), 159 (M-Me, 100), 131 (33). **3b:** ^1H NMR ($CDCl_3$) δ : 0.84- 0.88 (m, 2H), 0.97-1.01 (m, 2H), 1.30 (s, 6H), 2.24 (s, 3H), 6.40-6.87 (m, 3H). ^{13}C NMR ($CDCl_3$) δ : 12.96, 20.80, 25.46, 32.98, 87.25, 108.53, 119.70, 127.51, 129.37,132.96, 156.03. MS (EI) *m/z* : 188 (M^+, 43), 173 (M-Me, 100), 145 (34). **3c:** ^1H NMR ($CDCl_3$) δ : 0.78-1.03 (m, 4H), 1.32 (s, 6H), 3.73 (s, 3H), 6.19-6.67 (m, 3H). ^{13}C NMR ($CDCl_3$) δ : 12.78, 25.20, 33.14, 55.68, 87.17, 105.74, 108.57, 111.36, 134.01, 152.04, 153.93. MS (EI) *m/z* : 204 (M^+, 58), 189 (M-Me, 100), 161 (24). **3d:** ^1H NMR ($CDCl_3$) δ : 0.85-0.92 (m, 2H), 1.03-1.07 (m, 2H), 1.33 (s, 6H), 6.58-7.04 (m, 3H). ^{13}C NMR ($CDCl_3$) δ : 13.32, 25.42, 33.11, 88.60, 109.91, 119.44, 124.86, 126.95, 135.30,156.87. MS (EI) *m/z* : 208 (M^+, 38), 193 (M-Me, 100), 165 (35). **3e:** ^1H NMR ($CDCl_3$) δ: (isomer present in 30%) 0.84-1.12 (m, 4H), 1.27 (s, 6H), 2.12 (s, 3H), 6.49-6.96 (m, 3H); MS (EI) *m/z* : 188 (M^+, 56), 173 (M-Me, 84), 159 (100), 145 (33). (isomer present in 70%) 0.84-1.12(m,4H), 1.30 (s, 6H), 2.28 (s, 3H), 6.49-6.62 (m, 3H). MS (EI) *m/z* : 188 (M^+, 36), 173 (M-Me, 100), 145 (24). ^{13}C NMR ($CDCl_3$) δ: (mixture) 9.29,12.89, 16.59, 21.49, 24.99, 25.52, 32.85, 33.95, 86.40, 87.56, 107.33, 109.84, 118.77, 120.75, 123.06, 126.86, 128.21, 130.11, 132.60, 137.38, 158.30, 158.64. **3g:** ^1H NMR ($CDCl_3$) δ : 0.37-0.45 (m, 1H), 0.60-0.67 (m, 1H), 1.03-1.10 (m,2H), 1.71 (s, 3H), 6.60-7.36 (m, 9H). ^{13}C NMR ($CDCl_3$) δ :11.94, 16.92, 24.10, 35.20, 90.46, 109.11, 119.12, 120.61, 125.19, 127.39, 127.99, 128.16, 132.78, 143.17, 158.48. MS (EI) *m/z* : 236 (M^+, 50), 221 (M-Me, 100), 208 (97), 178 (26), 145 (36), 159 (18).

(5) Gilbert, J.C., Pinto, M. *J.Org.Chem.* **1992**, *57*, 5271.

(6) Nakano, Y., Hamaguchi, M., Nagai, T. *J.Chem.Res., Synop.* **1991**, *7*, 170; Appendino, G., Ghilardi, E., Cravotto, G., Gariboldi, P. *Collect.Czech.Chem.Commun.* **1991**, *56*, 1052 (C.A., **1991**, *115*, 92637g); Vilsmaier, E., Baumheier, R., Lemmert, M. *Synthesis* **1990**, 995; Kalsi, P. S., Chhina, K. *Indian J.Chem., Sect. B* **1987**, *26B*, 11 (C.A. **1988**, *108*, 112758h); Setsune, J., Ueda, T., Shikata, K., Matsukawa, K., Iida, T., Kitao, T. *Tetrahedron* **1986**, *42*, 2647; Delabar, J. M., Goldgaber, D., Lamour, Y., Nicole, A., Huret, J. L., Sinet, P. M. *Science* (*Washington, D.C.* **1883-**) **1987**, *235*(4794), 1390; Kalsi, P. S., Sood, V. B., Masih, A. B., Gupta, D., Talwar, K. K. *Phytochemistry* **1983**, *22*, 1387; Ali, S. M., Lee, T. V., Robertsw, S. M., Newton, R. F. *J.Chem.Soc.Perkin Trans.1* **1979**, 708.

(7) Bernard, A. M., Piras, P. P. *Synth.Commun.* **1996**, in press.

(8) Trost, B.M., Merlic, C.A. *J.Org.Chem.* **1990**, *55*, 1127; Trost, B.M., Lautens, M. *J.Am.Chem.Soc.* **1987**, *109*, 1469.

(9) Silverman, G.S., Strickland, S., Nicholas, K.M. *Organometallics* **1986**, *5*, 2117.

(10) Masuyama, Y.,Yamada, K., Kurusu, Y. *Tetrahedron Lett.* **1987**, *28*, 443.