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Note

A short route to cyclopentadienyltricarbonylrhenium substituted derivatives

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Abstract

$CpRe(CO)_3$ substituted derivatives were obtained in good yields (44–96%) from fulvenes and $Re_2(CO)_{10}$ in boiling mesitylene. This new methodology was applied to the synthesis of $CpRe(CO)_3$ substituted steroids with success.

Keywords: Bioorganometallic chemistry; Cyclopentadienyl ligands; Rhenium; Fulvene

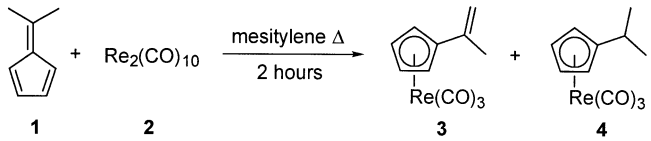
1. Introduction

The access to compounds for use in bioorganometallic chemistry is not always readily achieved by adopting synthetic methods used in classical organometallic chemistry. Our interest in $CpRe(CO)_3$ substituted biomolecules [1] as potential radiopharmaceuticals led us to explore efficient synthesis of these species in the 'cold series'. We thus recently reported a one-pot synthesis of $CpRe(CO)_3$ substituted steroids from the corresponding fulvenes and $BrRe(CO)_5$ under basic conditions [2]. We now present a new procedure using $Re_2(CO)_{10}$ (a precursor of $BrRe(CO)_5$) as the rhenium source which allows direct access to cyclopentadienyltricarbonylrhenium substituted derivatives from fulvenes under neutral conditions.

2. Results and discussion

The commercially available fulvene **1** was chosen as a model substrate for the optimisation process (Scheme 1, Table 1). Mixtures of **1** and **2** (0.2 mmol) were heated at different temperatures, with varying amounts of solvent for 2 h. In these reactions, a relatively small portion of the reduced compound **4** was formed under the conditions used. Even though the reaction occured at 128 °C (run 1), the yields increased upon raising the temperature (runs 2, 3 and 5). The best result was obtained in boiling mesitylene under reflux (run 5). The solvent-free reaction (run 4) gave only 40% yield in comparison with the 62% yield obtained at the same temperature (run 3). Increasing the number of equivalents of **1** relative to **2** (run 6) did not alter significantly the yield while a smaller amount of **1** gave only 60% of **3** and **4** (run 7). The last experiment (run 8) showed that doubling the dilution led to a decrease of the yield. These results can be explained by the relative instability of the fulvene under the conditions used, the best choice thus appearing to be a delicate balance between the formation of the products and degradation of the fulvene **1**. Finally, varying the reaction conditions did not allow us to direct the reaction towards the formation of a sole product, the ratios being quite identical from run 2 to 8.

On the basis of these results and apart from the reaction time, the conditions described in run 5 were used for the synthesis of other cyclopentadienyltricarbonylrhenium derivatives (Scheme 2). A longer reaction



Scheme 1.

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Table 1
Reaction of compound **1** with **2** (0.2 mmol) under selected conditions

Run	**1** (mmol)	Solvent (ml)	*T* (°C)	Yield (%) [a] (**3**/**4**) [b]
1	0.8	1	128	7 (100/0)
2	0.8	1	141	34 (89/11)
3	0.8	1	155	62 (89/11)
4	0.8	0	155	40 (87/13)
5	0.8	1	163	76 (81/19)
6	1.6	1	163	72 (82/18)
7	0.4	1	163	60 (82/18)
8	0.8	2	163	67 (85/15)

[a] Yields are based on rhenium (0.4 mmol).
[b] The ratios were determined on the ^{1}H-NMR spectra of the mixture of compounds **3** and **4** obtained after filtration on silica gel.

time was needed with these fulvenes **5** to give satisfactory yields. The modified steroids **8** were also converted into the corresponding compounds **9** in yields comparable to those obtained by our previous procedure (Scheme 3) [2] based on the use of $BrRe(CO)_5$ and KH. These products are the result of a proton abstraction in the C-6 position. Neither the isomeric products (resulting from the deprotonation of the C-2 position) nor products resulting from reduction of the double bond were isolated.

As can be seen from these examples, different functional groups were found to be compatible with the reaction conditions, including ether, alcohol, ketone, amine, chloride and thioether.

Compounds **7** were synthesized from **6** using an ionic hydrogenation [3] in the presence of triethylsilane and trifluoroacetic acid in nearly quantitative yields (Scheme 4). The amino compound **6a** led to an inseparable mixture of **7a** and a by-product derived from the silane. This reaction thus provides access to the reduced compounds in good yields.

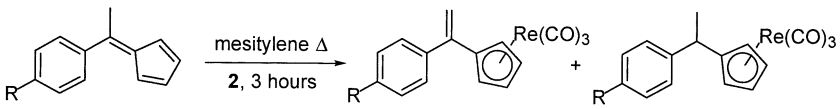
3. Conclusion

In conclusion, we have provided a short and efficient synthesis of several organometallic species bearing a conjugated side chain from fulvenes and $Re_2(CO)_{10}$ as the metallic source. The synthesis of similar species was studied 10 years ago [4,5]. In particular 2-(cyclopentadienyltricarbonylrhenium)propene (**3**) was prepared in a four-step procedure from cyclopentadiene with an overall yield of 32%. Our one-pot synthesis gave the same product in 61% yield. We also showed that the corresponding reduced forms of these compounds were easily obtained in good yields through ionic hydrogenation. In future work, we hope to exploit this method for the discovery of new potential radiopharmaceutical (in the cold series) bearing a $CpRe(CO)_3$ substituted group.

4. Experimental

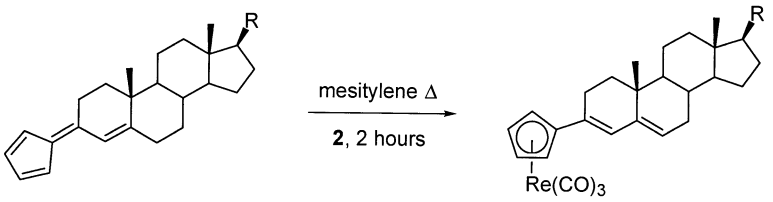
4.1. General

^{1}H- and ^{13}C-NMR spectra were taken on 200 MHz Bruker AC 200 spectrometer. Chemical shifts are reported in ppm and referenced to the residual proton resonances of the solvents. IR spectra were recorded by using a BOMEN MB spectrometer. Mass spectra were obtained on NERMAG R1010C apparatus. HRMS were measured at the Service de Spectrométrie de Masse of the Ecole Normale Supérieure (Paris, France). Melting points were measured on a Büchi B-510 apparatus and were uncorrected. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F 254. Silica gel Merck Gerudan SI (40–63 mm) was used for column chromatography using the Still method [6]. Elemental analyses were measured at the microanalysis laboratory of the Pierre et Marie Curie University (Paris, France) or of the CNRS (Gif sur Yvette, France). Anhydrous MeOH (99.8%) was purchased from Aldrich. Reactions were carried out in flame-dried Schlenk glassware under an inert atmosphere (Ar). 6,6-Dimethylfulvene (98%), 4′-methylthioacetophenone (97%), and 4′-methoxyacetophenone (98%) were purchased from Aldrich; 4′-aminoacetophenone (98%) was purchased from Avocado; 4′-chloroacetophenone was purchased from Fluka; Rhenium carbonyl (98%) was purchased from Strem Chemicals; Mesitylene (99%) and pyrrolidine (99%) were purchased from Acros. These reactants and solvent were used as received.



5a R = NH_2 **6a** (55%) **7a** (25%)
5b R = Cl **6b** (63%) **7b** (25%)
5c R = OMe **6c** (63%) **7c** (28%)
5d R = SMe **6d** (54%) **7d** (35%)

Scheme 2.



8a R = $CHMe(CH_2)_3CHMe_2$ **9a** (44%)

8b R = COMe **9b** (44%)

8c R = OH **9c** (53%)

Scheme 3.

4.2. General method for the fulvene synthesis

To a solution of ketone (5 mmol) and cyclopentadiene (1 ml, 12 mmol) in 8 ml of MeOH, pyrrolidine (2 ml, 24 mmol) was added. The mixture was stirred at room temperature (r.t.) for the appropriate time (60 h for **5a**, **5c**, and **5d**; 24 h for **5b**) and diluted with AcOEt/AcOH (50:0.5 ml except for **5a**, the purification being processed on the crude reaction mixture). After stirring for 15 min, the organic layer was washed with brine (3×25 ml), dried over $MgSO_4$ and concentrated. The residue thus obtained was purified via flash chromatography (**5a**: petroleum ether–CH_2Cl_2, 50:50; **5b**: C_5H_{12}; **5c** and **5d**: petroleum ether–CH_2Cl_2, 80:20). Compounds **5a**, **5b** and **5c** are known, and their ^{13}C-NMR spectra are in accord with those reported in the literature [7]. Compounds **8a**, **8b** and **8c** were prepared as previously described [2].

4.2.1. 6-Methyl-6-(4′-aminophenyl)fulvene (**5a**) (25%, orange oil), 6-Methyl-6-(4′-chlorophenyl)fulvene (**5b**) (50%, orange oil), 6-Methyl-6-(4′-methoxy)fulvene (**5c**) (48%, orange solid), 6-Methyl-6-(4′-methylthio)fulvene (**5d**) (56%, orange oil)

4.2.1.1. Compound 5d. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.4–7.2 (m, 4H), 6.7–6.4 (m, 3H), 6.3–6.2 (m, 1H), 2.55 (s, 3H), 2.53 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 149.1, 143.2, 139.2, 138.5, 131.6, 131.4, 129.8, 125.4, 123.4, 121.0, 22.3, 15.4; IR ($CDCl_3$): 3072, 2995, 2925, 2246, 1609, 1592, 1490, 1364; MS (*m*/*z*): 214, 199, 167; Anal. Calc. for $C_{14}H_{14}S$ (214.3): C, 78.45; H, 6.58. Found: C, 78.21; H, 6.59%.

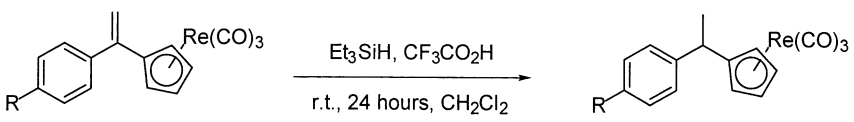
4.3. General method for the $CpRe(CO)_3$ substituted compounds synthesis

The mesitylene was degassed under a stream of Ar (15 min) prior to use. Dirhenium decacarbonyl (0.2 mmol) was added to a solution (or a suspension) of fulvene (0.8 mmol) in mesitylene (1 ml). The reaction mixture was quickly immersed in an oil bath heated to 180 °C and boiled under reflux for 2 or 3 h. After cooling to r.t., the mesitylene was removed under vacuum and the residue was purified via flash chromatography. The spectra of compounds **9a**, **9b** and **9c** are in accord with those previously reported [2].

4.3.1. 2-(Cyclopentadienyltricarbonylrhenium)propene (**3**) and 2-(cyclopentadienyltricarbonylrhenium)propane (**4**)

Purification by filtration (petroleum ether–CH_2Cl_2, 95:5) afforded a mixture of **3** and **4** as a colorless oil (76%). The ^{1}H-NMR spectrum of the mixture shows the presence of **3** according to Ref. [5]. Compound **4** was obtained by reduction of **3** (vide infra).

4.3.1.1. Compound 4. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.3–5.2 (m, 4H), 2.68 (sept, $J = 6.8$ Hz, 1H), 1.17 (s, $J = 6.8$ Hz, 6H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.5, 118.4, 82.7, 82.4, 26.8, 23.9; IR (KBr): 2019, 1911.



6b **7b** (94%)

6c **7c** (92%)

6d **7d** (96%)

Scheme 4.

*4.3.2. 1-Cyclopentadienyltricarbonylrhenium-1-(4′-aminophenyl)ethene (**6a**) and 1-cyclopentadienyltricarbonylrhenium-1-(4′-aminophenyl)ethane (**7a**)*

Purification by flash chromatography (petroleum ether–CH_2Cl_2, 50:50).

*4.3.2.1. Compound **6a** (55%, white solid).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.17 (d, $J = 8.5$ Hz, 2H), 6.66 (d, $J = 8.5$ Hz, 2H), 5.48 (t, $J = 2.2$ Hz, 2H), 5.43 (s, 1H), 5.30 (t, $J = 2.2$ Hz, 2H), 5.18 (s, 1H), 3.74 (bs, 2H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.2, 146.4, 140.3, 129.9, 129.1, 114.6, 114.2, 107.7, 83.9, 83.6; IR ($CDCl_3$): 2023, 1931; HRMS Calc. for $C_{16}H_{13}NO_3^{185}Re$: 452.0425. Found: 452.0428; HRMS Calc. for $C_{16}H_{13}NO_3^{187}Re$: 452.0453. Found: 452.0442.

*4.3.2.2. Compound **7a** (25%, white solid).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.00 (d, $J = 8.4$ Hz, 2H), 6.65 (d, $J = 8.4$ Hz, 2H), 5.4–5.1 (m, 4H), 3.75 (q, $J = 7.2$ Hz, 1H), 3.63 (bs, 2H), 1.47 (d, $J = 7.2$ Hz, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.5, 145.1, 134.7, 127.8, 116.5, 115.1, 84.0, 83.8, 83.6, 81.6, 37.5, 22.7; IR (KBr): 2017, 1910; HRMS Calc. for $C_{16}H_{15}NO_3^{187}Re$: 456.0611. Found: 456.0610.

*4.3.3. 1-Cyclopentadienyltricarbonylrhenium-1-(4′-chlorophenyl)ethene (**6b**) and 1-cyclopentadienyltricarbonylrhenium-1-(4′-chlorophenyl)ethane (**7b**)*

Purification by flash chromatography (petroleum ether–CH_2Cl_2, 96:4).

*4.3.3.1. Compound **6b** (63%, colorless oil).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.4–7.3 (m, 4H), 5.57 (s, 1H), 5.45 (t, $J = 2.3$ Hz, 2H), 5.32 (t, $J = 2.3$ Hz, 2H), 5.22 (s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 193.8, 139.8, 138.2, 134.1, 129.5, 128.6, 116.0, 106.1, 84.0, 83.7; IR ($CDCl_3$): 2021, 1939; HRMS Calc. for $C_{16}H_{11}ClO_3^{185}Re$: 470.9926. Found: 470.9914; HRMS Calc. for $C_{16}H_{11}ClO_3^{187}Re$: 472.9946. Found: 472.9957.

*4.3.3.2. Compound **7b** (25%, colorless oil).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.30 (d, $J = 8.4$ Hz, 2H), 7.15 (d, $J = 8.4$ Hz, 2H), 5.4–5.1 (m, 4H), 3.84 (q, $J = 7.1$ Hz, 1H), 1.50 (d, $J = 7.1$ Hz, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.1, 143.1, 132.6, 128.7, 128.3, 114.8, 84.2, 83.9, 83.6, 81.9, 37.8, 22.6; IR (KBr): 2020, 1913; HRMS Calc. for $C_{16}H_{13}ClO_3^{185}Re$: 473.0083. Found: 473.0082; HRMS Calc. for $C_{16}H_{13}ClO_3^{187}Re$: 475.0102. Found: 475.0106.

*4.3.4. 1-Cyclopentadienyltricarbonylrhenium-1-(4′-methoxyphenyl)ethene (**6c**) and 1-cyclopentadienyltricarbonylrhenium-1-(4′-methoxyphenyl)ethane (**7c**)*

Purification by flash chromatography (C_5H_{12}–CH_2Cl_2, 85:15).

*4.3.4.1. Compound **6c** (63%, slightly yellow oil).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.30 (d, $J = 8.8$ Hz, 2H), 6.89 (d, $J = 8.8$ Hz, 2H), 5.49 (s, 1H), 5.47 (t, $J = 2.3$ Hz, 2H), 5.31 (t, $J = 2.3$ Hz, 2H), 5.20 (s, 1H), 3.84 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.0, 159.5, 140.1, 132.1, 129.2, 114.9, 113.6, 107.3, 83.8, 55.2; IR ($CDCl_3$): 2031, 1928; Anal. Calc. for $C_{17}H_{13}O_4Re$ (467.5): C, 43.68; H: 2.80. Found: C, 43.60; H, 2.92%.

*4.3.4.2. Compound **7c** (28%, slightly yellow oil).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.14 (d, $J = 8.5$ Hz, 2H), 6.86 (d, $J = 8.5$ Hz, 2H), 5.4–5.1 (m, 4H), 3.81 (q, $J = 7.2$ Hz, 1H), 3.80 (s, 3H), 1.49 (d, $J = 7.2$ Hz, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.4, 158.5, 136.9, 128.0, 116.2, 114.0, 84.1, 83.9, 83.6, 81.8, 55.3, 37.6, 22.8; IR (KBr): 2018, 1917; HRMS Calc. for $C_{17}H_{16}O_4^{185}Re$: 469.0578. Found: 469.0581; HRMS Calc. for $C_{17}H_{16}O_4^{187}Re$: 471.0607. Found: 471.0600.

*4.3.5. 1-Cyclopentadienyltricarbonylrhenium-1-(4′-methylthiophenyl)ethene (**6d**) and 1-cyclopentadienyltricarbonylrhenium-1-(4′-methylthiophenyl)ethane (**7d**)*

Purification by flash chromatography (petroleum ether–CH_2Cl_2, 85:15).

*4.3.5.1. Compound **6d** (54%, white solid).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.4–7.2 (m, 4H), 5.53 (s, 1H), 5.47 (t, $J = 2.1$ Hz, 2H), 5.32 (t, $J = 2.1$ Hz, 2H), 5.23 (s, 1H), 2.51 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.0, 140.2, 138.8, 136.4, 128.5, 126.2, 115.5, 106.8, 83.8, 15.6; IR ($CDCl_3$): 2022, 1940; Anal. Calc. for $C_{17}H_{13}O_3ReS$ (483.6): C, 42.23; H, 2.71. Found: C, 42.85; H, 2.91%.

*4.3.5.2. Compound **7d** (35%, white solid).* ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.4–7.1 (m, 4H), 5.4–5.1 (m, 4H), 3.84 (q, $J = 7.2$ Hz, 1H), 2.50 (s, 3H), 1.52 (d, $J = 7.2$ Hz, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$): δ 194.3, 141.6, 136.8, 127.5, 126.9, 115.4, 84.2, 83.9, 83.6, 81.8, 37.9, 22.6, 15.8; IR (KBr): 2014, 1912.

*4.4. General method for the reduction of compounds **6***

To a solution of **6** (1 mmol) and Et_3SiH (232 mg, 2 mmol) in CH_2Cl_2, trifluoroacetic acid (2 ml) was added. After stirring at r.t. for 24 h, the mixture was diluted in CH_2Cl_2 (100 ml) and poured in a saturated solution of $NaHCO_3$ (100 ml). The organic layer was dried over $MgSO_4$, concentrated and flash chromatographied ac-

cording to the conditions previously used (vide supra). Yields are given in Scheme 4.

References

[1] F. Le Bideau, M. Salmain, S. Top, G. Jaouen, Chem. Eur. J. 7 (2001) 2289.
[2] F. Le Bideau, A. Pérez-Luna, J. Marrot, M.-N. Rager, E. Stéphan, S. Top, G. Jaouen, Tetrahedron 57 (2001) 3939.
[3] D.N. Kursanov, Z.N. Parnes, N.M. Loim, Synthesis (1974) 603.
[4] E.J. Miller, C.A. weigelt, J.A. Serth, R. Rusyid, J. Brenner, L.A. Luck, M. Godlewski, J. Organomet. Chem. 440 (1992) 91.
[5] T.E. Bitterwolf, X. Dai, J. Organomet. Chem. 440 (1992) 103.
[6] W.C. Still, M. Khan, A.J. Mitra, J. Org. Chem. 43 (1978) 2923.
[7] D.J. Sardella, C.M. Keane, P. Lemonias, J. Am. Chem. Soc. 106 (1984) 4962.