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Rhodium catalyzed hydroformylation of 2-phenylsulfonylbicyclo[2.2.1] alkenes: effect of the phenylsulfonyl group

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Abstract—The preliminary results of the hydroformylation of 2-phenylsulfonyl substituted norbornene and norbornadiene derivatives catalyzed by the unmodified $Rh(CO)_2$acac system are presented. The reaction, occurring under standard *oxo* conditions, gives polyfunctionalized *exo* norbornene- and *exo* norbornanecarboxaldehydes. The effect of the phenylsulfonyl group has been evaluated: it has been found that the steric properties of the sulfonyl substituent, more than the electronic ones, influence the regioselectivity of the process.

Polyfunctionalized building blocks are powerful tools in the synthesis of more complex structures. In this field, oxygenate derivatives, such as aldehydes, play a fundamental role. A series of natural and synthetic bridged polycyclic aldehydes has been found to possess a typical fragrance, constituting valuable ingredients for perfumery (Fig. 1).[1]

In the last years, the hydroformylation of bridged polycyclic derivatives has been mainly studied from a mechanistic point of view by using simple unfunctionalized model substrates such as, for instance, β-pinene and camphene,[2] norbornene and norbornadiene.[3] Synthetic applications affording copolymers of 7-functionalized norbornadienes and norbornene have been recently reported by Takahashi.[4] Nevertheless, while the multistep approaches to formulate a bridged polycyclic skeleton are, on the basis of the more recent literature, the most widely employed (for instance retrosynthetic pathways **A**–**B** in Scheme 1),[1b] on the contrary, the potentiality of directly introducing a formyl group (**C**, Scheme 1), despite very attractive, is rarely used for synthetic purposes.

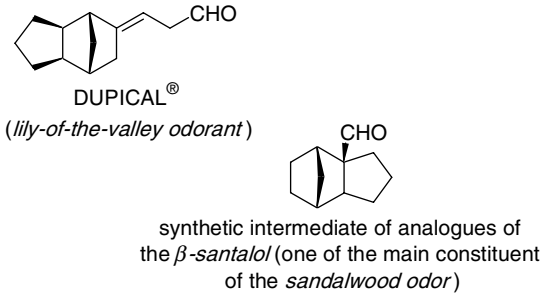
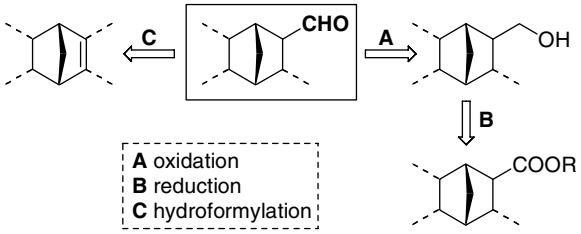


Figure 1.

In a previous letter,[5] we reported the synthesis of bridged phenylsulfonyl substituted bicyclo[2.2.1] polyenes through the conversion of (*Z*)-vinylsulfones to the



Scheme 1.

Keywords: Hydroformylation; Rhodium; Polycyclic compounds; Sulfones; Alkenes.
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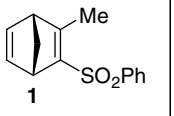
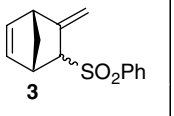
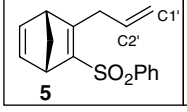
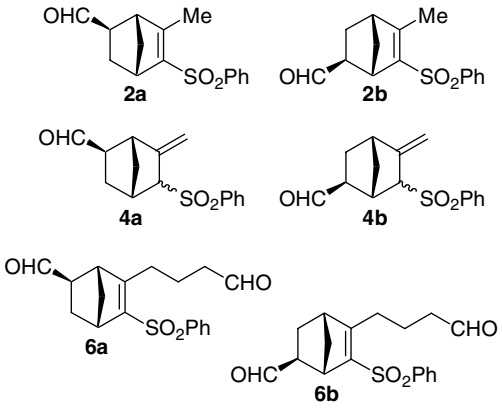
corresponding (*E*)-allylsulfones. In this letter, we describe the results of the hydroformylation of a selection of the aforementioned polyenes catalyzed by the unmodified $Rh(CO)_2acac$ system, directly introducing the –CHO group onto the polycyclic skeleton.

Although phosphorus modified catalysts are more extensively used to hydroformylate alkenes, we have chosen to use the unmodified rhodium catalytic precursor[6] $Rh(CO)_2acac$ because it appeared very advantageous for our purposes. In fact, this catalyst shows to be active even under mild reaction conditions making other possible competitive pathways, such as hydrogenation, isomerization and polymerization negligible. In addition, the correlation between the structural properties of the alkene and the regioselectivity of the reaction can be evaluated without the interference of phosphorus ligands.

The hydroformylation of the polycyclic alkenes **1**, **3** and **5** (Fig. 2) has been carried out in toluene at 60 °C, under 50 atm total pressure ($CO/H_2 = 1:1$), employing $Rh(CO)_2acac$ (molar alkene/rhodium ratio = 125) as the catalyst precursor. The conversion of the substrate and the composition of the reaction mixtures have been evaluated by NMR spectroscopy. All experiments have been carried out to complete substrate conversion (15 h). All the crude reaction mixtures have been purified by flash chromatography on silica gel column affording *exo* aldehydes **2**, **4** and 5-*exo* dialdehyde **6** (Fig. 2) in a chemically pure form (**2**, 35%; **4**, 40%; **6**, 30% yields). In this regard it is well documented that electrophilic reactions to bicyclo[2.2.1]hept-2-enes afford products of *exo* configuration almost exclusively, because the *p*-HOMO has the lobes more developed in the *exo* direction than in the *endo* one.[3b,7] Moreover, the *cis* stereochemistry for the addition of –CHO and –H to the double bond of norbornene or norbornadiene derivatives has been established and documented.[3b] On the basis of the generally accepted mechanism of the rhodium catalyzed hydroformylation, it is reasonable to propose the catalytic cycle shown in Scheme 2. The rhodium hydride species coordinates the endocyclic double bond of the polycyclic substrate generating the π complex ***i***, which is converted to the corresponding alkyl-rhodium species ***ii*** through the insertion of the alkene onto the rhodium hydride bond. The alkyl σ complex ***ii*** evolves to the acyl-rhodium intermediate ***iii*** which in turn provides the final aldehyde as a mixture of regioisomers **a** and **b**. It seems reasonable that the ratio of the regioisomeric alkyl-rhodium species ***ii*** is influenced by the steric properties of the phenylsulfonyl group.

substrate	product	yield %
 **1**	**2a**:**2b** = 2:1	35
 **3**	**4a**:**4b*** = 1:1	40
 **5**	**6a**:**6b** = 2:1	30

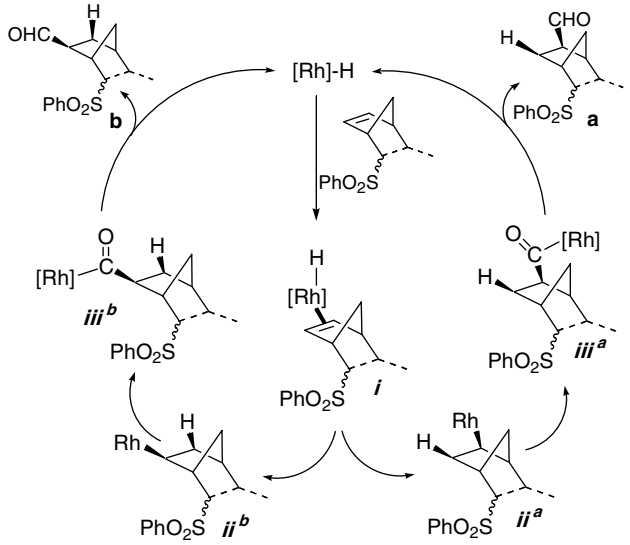
* In aldehyde **4** the 2-*endo*/*exo* ratio remains unchanged in respect of the starting material **3**.



Reaction Conditions: $Rh(CO)_2acac$, toluene, 50 atm H_2/CO = 1/1, 60 °C, 15 h.

Figure 2.

3-Methyl-2-phenylsulfonylnorbornadiene **1** contains a double bond which is deactivated and it has proved to be unreactive under the reported hydroformylation conditions. The regioisomeric ratio (**2a**/**2b** = 2) indicates that the sulfonyl group exerts a control on the regioselectivity favouring the rhodium attack at the position C5 of the polycyclic skeleton (***ii***^{a}, Scheme 2). It is known that remote substituents capable to chelate the metal catalyst can be used to control the regioselectivity of the process. In our case, the phenylsulfonyl moiety exerts a steric control on position 6, partially disfavouring there the attack of the rhodium (***ii***^{b}, Scheme 2). In



Scheme 2.

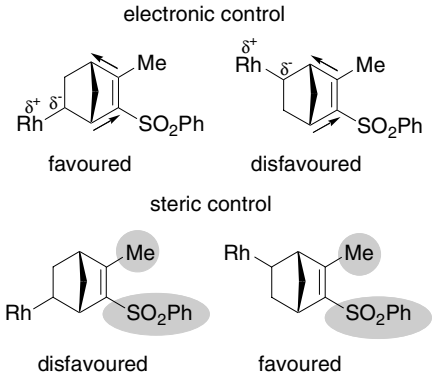


Figure 3.

absence of this sort of steric control, it is reasonable that the electronic effect of the phenylsulfonyl substituent could privilege an opposite regioselectivity (alkyl-rhodium species are represented in Fig. 3).

Considering the hydroformylation of vinylidenic compound **3**, the phenylsulfonyl group does not influence the regiochemistry of the reaction of the endocyclic double bond (regioisomeric ratio **4a**/**4b** = 1) (Fig. 2). This value, compared to the regioisomeric ratio of compound **2**, reveals that the 'planar phenylsulfonyl moiety' can exert in diene **1** a steric influence on C6, whereas, in case of diene **3**, the phenylsulfonyl is situated in *endo*- or *exo*-position and it cannot influence the reactivity of C6. In this regard, it is interesting to note that only diene **1** presents a NOE interaction between the *ortho* H_{Ar} of $PhSO_2$– and the H_6 (Fig. 4).[5]

Interestingly, the $PhSO_2$– prevents the hydroformylation of the exocyclic double bond, acting *non-bonding protecting group*. In the hydroformylation of camphene **7** catalyzed by a platinum complex[2a] as well as by rhodium modified and unmodified catalysts,[2b] the exocyclic double bond reacts affording the linear aldehyde (Fig. 5).

Triene **5** contains two endocyclic double bonds, one is electron-rich and the second is deactivated. A third double bond is located in allylic exocyclic position. The hydroformylation products of **5** are the polyfunctionalized dialdehydes **6a**,**b** (Fig. 2). As shown for compound **1** (Fig. 3), the $PhSO_2$– moiety influences the regioselectivity between the C5 and C6. In addition, the contemporary selective hydroformylatation of the exocyclic double bond occurs so forming the linear aldehyde exclusively. Although for the moment we cannot establish why the branched aldehyde is not formed, it is reasonable that steric interactions can be exerted by the polycyclic skeleton as well as by the phenylsulfonyl group onto the exocyclic position C2′.

The structure of either **2a**–**b**, **4a**–**b** and **6a**–**b** has been established by homo (COSY and NOESY) and heteronuclear (HMBC and HMQC) NMR techniques. The assignments of aldehyde **2** are reported in Figure 6.[8]

On the basis of the NOESY maps of **2a** and **2b**, the *exo* position of CHO– group is revealed by the interaction with the apical proton H_{7anti} (dt; **2a**: 1.24 ppm; **2b**: 1.19 ppm). Proton H_{7syn} resonates at lower field (m; **2a**: 1.47–1.53 ppm; **2b**: 1.41–1.47 ppm), because it is situated internally to the smaller shielding zone generated by the double bond bearing a phenylsulfonyl substituent at position 2. The NOESY map of **2a** also evidences appreciable interactions between the formyl proton and both the bridged H_4 and the methyl group (weak); no interaction with the aromatic proton of the phenylsulfonyl group has been observed. Differently, in the case of **2b**, the formyl proton interacts with the bridged H_1 and, in addition, with the aromatic protons while no interaction between formyl and methyl protons is evident. Protons H_4 and H_{5endo} resonate in compound **2a** at lower fields than **2b** (H_4, s_b; **2a**: 3.08 ppm; **2b**: 2.88 ppm; H_{5endo}; **2a**: m, 2.32–2.39 ppm; **2b**: ddd, 1.37 ppm) due to the presence of the vicinal formyl group. Differently H_1 (s_b; **2a**: 3.16 ppm; **2b**: 3.31 ppm) and H_{6endo} (**2a**: ddd, 1.37 ppm; **2b**: m, 2.44–2.51 ppm) of **2b** resonate at lower fields than **2a** because both H_1 and H_{6endo} of **2b** are much more deshielded due to the presence of two electron-withdrawing groups (CHO and $PhSO_2$–). In isomer **2a**, the coupling between the formyl proton (d, 9.74 ppm) and H_{5endo} ($J = 1.6$ Hz) is

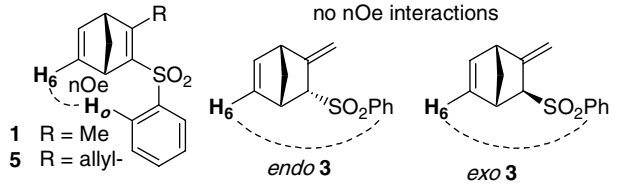


Figure 4.

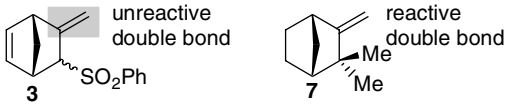


Figure 5.

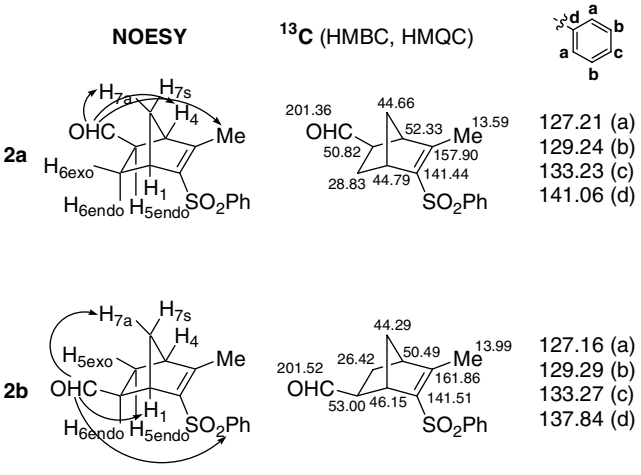


Figure 6.

larger than the analogous coupling between the formyl proton (d, 9.74 ppm) and H_{6endo} of **2b** ($J = 0.8$ Hz). In the latter case, the presence of the electron-withdrawing phenylsulfonyl group decreases the electron density, thus providing a lower spin–spin coupling constant.

In conclusion, the main benefit in the use of functionalized 2-phenylsulfonylbicyclo[2.2.1] alkenes as starting material for the described reaction is represented by the possibility to directly produce mono- and dialdehyde derivatives which are promising synthons in organic synthesis. The regioselectivity of the rhodium catalyzed hydroformylation of the endocyclic double bond in position 5 is influenced by the steric hindrance of the phenylsulfonyl group in vinylic 'planar' position 2, whereas it is not affected when the same substituent occupies either the *endo*- or the *exo*-position. As a relevant result, the 2-phenylsulfonyl group is able to make unreactive the 3-vinylidenic exocyclic double bond in vicinal position.

Acknowledgements

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References and notes

1. (a) Fráter, G.; Bajgrowicz, J. A.; Kraft, P. *Tetrahedron* **1998**, *54*, 7633–7703; (b) Buchbauer, G.; Stappen, I.; Pretterklieber, C.; Wolschann, P. *Eur. J. Med. Chem.* **2004**, *39*, 1039–1046.
2. (a) Soulantica, K.; Sirol, S.; Koïnis, S.; Pneumatikakis, G.; Kalck, P. *J. Organomet. Chem.* **1995**, *498*, C10–C13; (b) Azzaroni, F.; Biscarini, P.; Bordoni, S.; Longoni, G.; Venturini, E. *J. Organomet. Chem.* **1996**, *508*, 59–67; (c) Gusevskaya, E. V.; dos Santos, E. N.; Augusti, R.; Dias, A. O.; Foca, C. M. *J. Mol. Cat. A: Chem.* **2000**, *152*, 15–24; (d) Barros, H. J. V.; Ospina, M. L.; Arguello, E.; Rocha, W. R.; Gusevskaya, E. V.; dos Santos, E. N. *J. Organomet. Chem.* **2003**, *671*, 150–157.
3. (a) Parrinello, G.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7122–7127; (b) Botteghi, C.; Paganelli, S.; Perosa, A.; Lazzaroni, R.; Uccello-Barretta, G. *J. Organomet. Chem.* **1993**, *447*, 153–157.
4. Zhang, S. W.; Kaneko, T.; Takahashi, S. *Macromolecules* **2000**, *33*, 6930–6936.
5. Cossu, S.; Peluso, P.; Moretto, F.; Marchetti, M. *Tetrahedron Lett.* **2006**, *47*, 2253–2256.
6. Lazzaroni, R.; Settambolo, R.; Caiazzo, A. Hydroformylation with unmodified rhodium catalysts. In *Rhodium Catalyzed Hydroformylation*; Van Leeuwen, P. W. N. M., Claver, C., Eds.; Kluver Academic: Dordrecht, The Netherlands, 2000; pp 15–33.
7. Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4054–4061.
8. Compound **2a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (dt, 1H, $J = 9.6$ Hz, $J = 1.2$ Hz, H_{7anti}), 1.37 (ddd, 1H, $J = 12.0$ Hz, $J = 8.8$ Hz, $J = 2.0$ Hz, H_{6endo}), 1.47–1.53 (m, 1H, H_{7syn}), 1.97 (dt, 1H, $J = 12.0$ Hz, $J = 4.4$ Hz, H_{6exo}), 2.29 (*s*, 3H, Me), 2.32–2.39 (m, 1H, H_{5endo}), 3.08 (s_b, 1H, H_4), 3.16 (s_b, 1H, H_1), 7.48–7.68, 7.88–7.95 (series of m, 5H, Ar), 9.74 (d, 1H, $J = 1.6$ Hz, CHO); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.59, 28.83, 44.66, 44.79, 50.82, 52.33, 127.21, 129.24, 133.23, 141.06, 141.44, 157.90, 201.36. Compound **2b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (dt, 1H, $J = 9.2$ Hz, $J = 1.2$ Hz, H_{7anti}), 1.37 (ddd, 1H, $J = 12.4$ Hz, $J = 8.8$ Hz, $J = 2.8$ Hz, H_{5endo}), 1.41–1.47 (m, 1H, H_{7syn}), 2.13 (dt, 1H, $J = 12.4$ Hz, $J = 4.0$ Hz, H_{5exo}), 2.28 (*s*, 3H, Me), 2.44–2.51 (m, 1H, H_{6endo}), 2.88 (s_b, 1H, H_4), 3.31 (s_b, 1H, H_1), 7.52–7.65, 7.88–7.93 (series of m, 5H, Ar), 9.74 (d, 1H, $J = 0.8$ Hz, CHO); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.99, 26.42, 44.29, 46.15, 50.49, 53.00, 127.16, 129.29, 133.27, 137.84, 141.51, 161.86, 201.52.