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Formal Synthesis of Erythrodiene and Spirojatamol via Rhodium-catalysed Claisen Rearrangement / Hydroacylation

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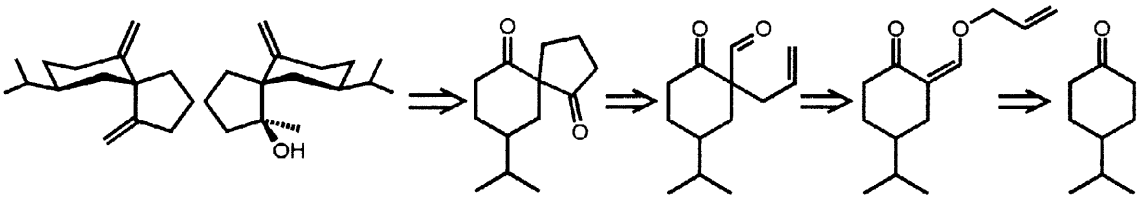
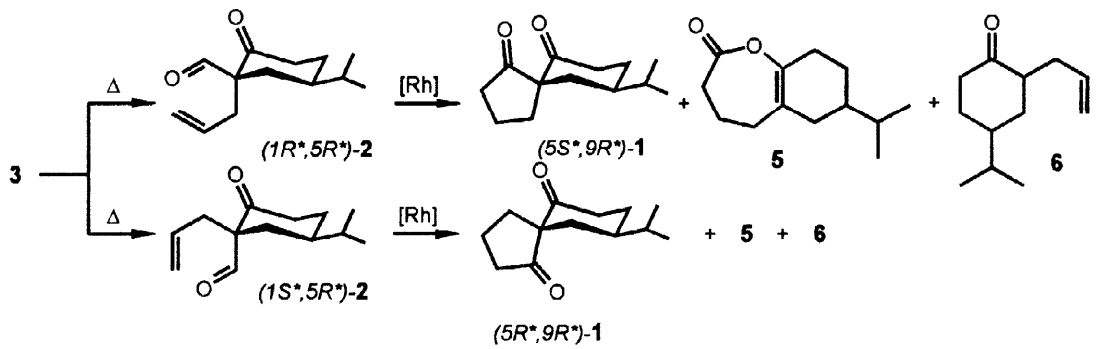
Abstract: A novel procedure allows the synthesis of spiro[4.5]decane-1,6-dione **1**, a key intermediate in the total synthesis of erythrodiene and spirojatamol. The key step is a combination of Claisen rearrangement of allyl vinyl ethers followed by an intramolecular hydroacylation catalysed by RhCl(cod)(dppe).

Keywords: Catalysis, Natural Products, Spiro Compounds

Recently, we introduced a new method for the synthesis of spiro[4.5]decanones using a one-pot reaction sequence of an aliphatic Claisen rearrangement and rhodium catalysed hydroacylation of the resulting 4-pentenals [1]. This procedure was applied to the synthesis of acoradienes [1b] and vetivanes [1c]. We now wish to report on a similar application of this spirocyclopentanellation sequence towards the synthesis of 9-isopropyl-spiro[4.5]decane-1,6-dione (**1**), a diketone which has been used in the total synthesis of erythrodiene [2] and spirojatamol [3] by Fukumoto and co-workers [4].



Interestingly, the similar carbon skeletons of the two natural products are enantiomeric to one another. The retrosynthetic construction of the rare carbon framework of both target compounds applying our method of a combination of Claisen rearrangement and hydroacylation is outlined above. This route requires Claisen rearrangement of allyl vinyl ether **3** followed by the cyclisation of pentenal **2** via intramolecular hydroacylation. Compound **3** is easily prepared from 4-isopropyl-cyclohexanone (**4**) by formylation with alkyl formate [5] and O-alkylation of the resulting enol with propenol. Thermal rearrangement of ether **3** yielded both diastereoisomeric pentenals **2** in an approximately 1:1 ratio along with small amounts of the decarbonylation product **6** [6].



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Only (1*S**,5*R**)-**2** carries the desired relative stereochemistry of the two target molecules. Therefore, we did not use the one-pot combination of Claisen rearrangement and hydroacylation as reported in earlier examples [1], but rather decided to separate the isomers and to perform the cyclisation steps separately. Hydroacylation of the pentenals **2** yielded the desired cyclopentanones **1**, thereby completing a four-step procedure for the formal total synthesis of erythrodiene and spirojatamol in the case of (5*R**,9*R**)-**1** [7,8].

In conclusion this method offers a straightforward approach to a suitable precursor for erythrodiene and spirojatamol. However, using standard reaction conditions in the ring closure step, several unexpectedly byproducts were observed, causing poor yields of isolated **1** [7,8]. The byproducts were identified as the decarbonylation product **6** and the bicyclic lactone **5**. For further optimisation the mechanism of this side product formation has to be clarified. Regarding the reaction mechanism for the formation of **5**, a photochemical rearrangement of spiro[4.5]deca-1,6-dione to give enol lactones has been reported before [9]. However, under the conditions used above, either a rhodium mediated decarbonylation / carbonylation mechanism or an acid mediated ionic rearrangement has to be assumed. Our efforts to simulate reaction conditions enforcing a carbonylating reaction sequence led to completely different products [10]. On the other hand, when **1** is treated with catalytic amounts of hydrochloric acid in methanol, methyl 2-(4-isopropylcyclohexanone)butyrate [11] is formed as the sole product [10]. This ester is based on the same carboxylic acid as lactone **5**. A similar acid-sensitivity is assumed for the side reaction of aldehyde **2**, thereby explaining the unusally high degree of decarbonylation leading to **6** [12]. Therefore we presently are investigating alternative catalytic systems with reduced Lewis- and Brønsted-acidity in order to curtail the formation of the observed byproducts, and thereby improving the yield of the desired spirodiketones [10].

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References and Notes

[1] (a) P. Eilbracht, A. Gersmeier, D. Lennartz, T. Huber, *Synthesis* **1995**, 330-334. (b) T. Sattelkau, C. Hollmann, P. Eilbracht, *Synlett* **1996**, 1221-1223. (c) T. Sattelkau, P. Eilbracht, *Tetrahedron Lett.* **1998**, *39*, 1905-1908.

[2] C. Pathirana, W. Fenical, E. Corcoran, J. Clardy, *Tetrahedron Lett.* **1993**, *34*, 3371-3372.

[3] A. Bagchi, Y. Oshima, H. Hikino, *Tetrahedron* **1990**, *46*, 1523-1530.

[4] (a) Y. Tokunaga, M. Yagihashi, M. Ihara, K. Fukumoto, *J. Chem. Soc., Chem. Commun.* **1995**, 955-956. (b) Y. Tokunaga, M. Ihara, K. Fukumoto, *J. Chem. Soc., Perkin Trans.1* **1997**, 207-209. (c) Y. Tokunaga, M. Yagihashi, M. Ihara, K. Fukumoto, *J. Chem. Soc., Perkin Trans. 1* **1997**, 189-190. For a different approach see: (d) H. Huang, C.J. Forsyth, *J. Org. Chem.* **1995**, *60*, 2773-2779. (e) H. Huang, C.J. Forsyth, *Tetrahedron Lett.* **1993**, *34*, 7889-7890.

[5] C. Ainsworth, *Org. Synth. Coll.* **1963**, *4*, 536-539.

[6] 5.00g (24mmol) 2-allyloxymethylene-4-isopropyl-cyclohexanone (**3**) are heated in 3.0g tetradecane for 8h at 174°C. The reaction mixture is chromatographed on silica gel (hexanes/MTBE), yielding 0.34g (2mmol, 8%) *cis*-2-allyl-4-isopropyl-cyclohexanone (**6**), 1.85g (9mmol, 37%) (1*S**,5*R**)-1-allyl-2-oxo-5-isopropyl-cyclohexanecarbaldehyde (**2**) and 2.22g (10mmol, 44%) (1*R**,5*R**)-**2**. Relative stereochemistry was established by NOESY spectroscopy and confirmed by the known products **1** from the next reaction step.

[7] 0.97g (4.62mmol) (1*R**,5*R**)-**2** and 152mg RhCl(cod)(dppe) [16] (0.24mmol, 5mol%) are heated in 1.5ml dry benzonitrile under Ar atmosphere for 36h at 140°C. The crude product is filtered through alumina. Benzonitrile along with **6** [11] is removed by kugelrohr distillation and the residues chromatographed on silica gel (hexanes/MTBE), yielding 0.27g (1.3mmol, 28%) (5*S**,9*R**)-9-isopropyl-spiro[4.5]decane-1,6-dione (5*S**,9*R**-**1**) and 0.08g (0.4mmol, 8%) of lactone **5**. (1*S**,5*R**)-**2** was converted by essentially the same method, yielding 19% of (5*R**,9*R**)-9-isopropyl-spiro[4.5]decane-1,6-dione. Spectroscopic data for 7-isopropyl-4,5,6,7,8,9-hexahydro-3*H*-benzo[*b*]oxepin-2-one (**5**): MS (EI, 70eV): m/z (%)= 208 (42), 190 (29), 180 (33), 137 (43), 124 (36), 110 (65), 93 (60), 80 (51), 67 (52), 55 (79), 41 (100); IR (Film, NaCl): $\tilde{\nu}$ [cm^{-1}]= 2960, 2872, 1740, 1451, 1437, 1368, 1261, 1217, 1158, 1119, 1033; ^{1}H NMR (400MHz, $CDCl_3$): δ[ppm]= 2.55 (m, 2H), 2.3-1.9 (8H), 1.85 (m, 1H), 1.56 (m, 2H), 1.37 (m, 1H), 0.93 (d, *J*=6.8Hz, 3H), 0.92 (d, *J*=6.7Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ[ppm]= 173.3 Cq, 145.8 Cq, 119.0 Cq, 40.3 CH, 32.5 CH_2, 32.3 CH_2, 31.7 CH, 27.6 CH_2, 27.1 CH_2, 26.4 CH_2, 26.1 CH_2, 20.0 CH_3, 19.7 CH_3

[8] The use of [Rh(dppe)(nbd)]ClO_4 as a catalyst precursor, an effective system reported to yield only minimum or no decarbonylation products, here leads to quantitative decarbonylation of **2**. See D.P. Fairlie, B. Bosnich, *Organometallics* **1988**, *7*, 936-945.

[9] (a) H.J. Wüthrich, A. Siewinski, K. Schaffner, O. Jeger, *Helv. Chim. Acta* **1973**, *56*, 239-258. (b) J.-M. Bessiere, H. Christol, Z. Vossough, M. Mousseron, *C.R. Acad. Sc. Paris Ser. C* **1973**, *276*, 307-310.

[10] C. Hollmann, C. Mersch, T. Sattelkau, P. Eilbracht, unpublished results.

[11] (a) A. Uehara, J.C. Bailar Jr., *J. Organomet. Chem.* **1982**, *239*, 11-15. (b) T.A. Stephenson, G.J. Wilkinson, *Inorg. Nucl. Chem.* **1966**, *28*, 945.

[12] **6** is accompanied by various isomers resulting from double-bond migration.