Synthesis of a [5.5.5.5]Fenestrenedione *via* Tandem Pauson–Khand Tetracyclisation

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The first example of formation of a tetracyclic fenestrane from an open-chain ene–diyne *via* the Pauson–Khand reaction is reported.

The intramolecular Pauson–Khand reaction (PKR) is an efficient method for preparation of cyclopent-2-en-1-ones annulated in the 3,4-position.[1] Thus 1,6-ene–ynes give bicyclo[3.3.0]oct-1-en-3-ones, which are important intermediates for the synthesis of tri- and tetra-cyclic hydrocarbons and heterocycles with a cyclopentenone substructure. We have already reported that the fenestrane **2** can be prepared from the bicyclic acetoxyalkene **1a**, which contains a but-3-ynyl side chain in the allylic position.[2] The precursor of **1a**, the enone **1b**, has been prepared by the intramolecular Horner–Emmons reaction.

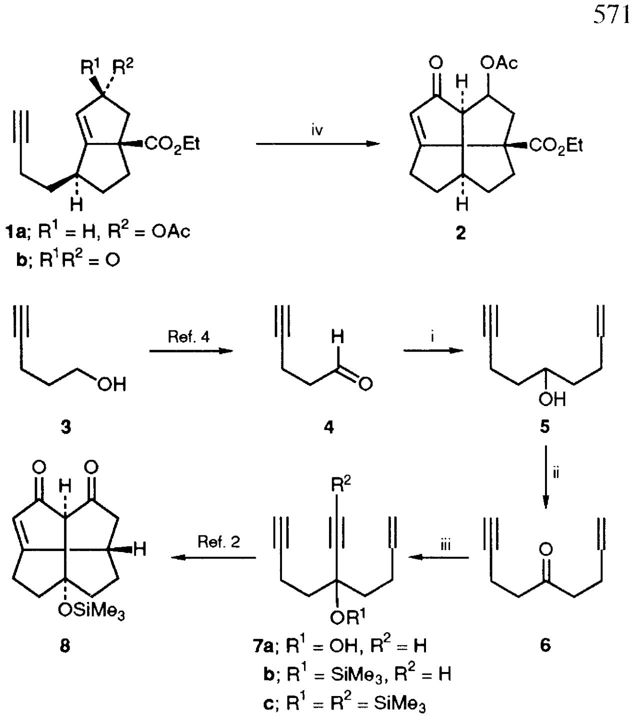
Since cyclopentenone like **1b** may in principle be prepared from an open-chain 1,6-ene–yne, it was of interest to investigate whether fenestranes may be prepared from an ene–diyne by two sequential PKRs. According to the results of Pauson with alkenes in which the double bond is conjugated with a π-acceptor group,[3] it was expected that the CO group of the bicyclo[3.3.0]oct-1-en-3-one, formed by the first PKR, would need to be replaced by a non-conjugating functional group prior to the second PKR. The ene–diyne **7a** needed for this reaction sequence was readily prepared from pent-5-ynol[4] **3** by two pyridinium chlorochromate (PCC) oxidations and two Grignard reactions to give the Me_3Si derivative **7b** in an overall yield of 19% (not optimised). When **7b** was submitted to the PKR under the reaction conditions of Thommen *et al.*,[2] the fenestrenedione **8** was formed directly in a yield of 9.4%.[†]

A mechanistic interpretation of this surprising result suggests that double bonds with π-acceptor substituents might participate in PK cyclisations, if specific structural prerequisites are fulfilled.[5] These aspects will be investigated.[6]

Thus, a six-step synthesis of a fenestrane from a readily available starting material has been achieved. In this tandem PKR tetracyclisation nine new bonds are formed or altered from the ene–diyne **7b**, thereby creating eight new stereogenic centres; it is a reaction of high molecular complexity.[7,8]

This work was performed by A. v. d. W. as part of the thesis required for a diploma at the Catholic University of Nijmegen, The Netherlands. The authors thank the Swiss National Science Foundation and Professor B. Zwanenburg, Nijmegen, for generous support.

Received, 16th December 1991; Com. 1/06304I



Scheme 1 (NMO = *N*-methylmorpholine *N*-oxide) *Reagents and conditions*: i, $H_2C{=}CHCH_2CH_2MgBr$, Et_2O 0 °C, 42%; ii, PCC, CH_2Cl_2, room temp., 58%; iii, $HC{\equiv}CMgBr$ or $Me_3SiC{\equiv}CMgBr$, Et_2O, room temp., 61%; $Co_2(CO)_8$, NMO, CH_2Cl_2.

[†] The spectroscopic data (NMR, IR, mass) for all compounds are compatible with the structures given. Selected data for **8** (NMR, δ, $CDCl_3$, *J*/Hz, sequence according to numbering; NOE results: irradiated at X–H: signal enhancement at Y–H, with 4-H = α). ^{13}C: 189.5 (s), 121.78 (d), 208.75 (s), 68.53 (d), 201.86 (s), 46.50 (t), 42.89 (d), 31.0 (t), 39.76 (t), 87.82 (s), 41.70 (t), 27.32 (t), 76.63 (s) and 1.97 (q, 3C); ^1H: 5.76 (s), 3.34 (approx. s), 2.26 (ddd, *J* 18.1, 4.7, 2.2, 6α-H), 2.69 (dd, *J* 18.1, 9.2, 6β-H), 2.49 (m), 1.57 (m, 8α-H) 2.05 (m, 8β-H, 9-H_2, 11α-H), 2.36 (ddd, *J* 13.6, 9.9, 3.7, 11β-H) and 2.75 (ddd, *J* 15.9, 8.5, 3.3, 12-H_2); NOE: 2-H: 12α-H; 6α-H: 4-H, 8α-H; 6β-H: 7-H; 7-H: 8β-H. 2-H: 12α-H; IR: ν/cm^{-1} 1750, 1700 and 1635. Mass: *m/z* 290 (M^+, 100%), 275 (86), 262 (66), 248 (52), 234 (68), 219 (40), 183 (45) and 75 (48).

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