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Mendeleev Commun., 2008, **18**, 203–204
Mendeleev Communications

Preparation of linearly fused 6-6-5 and 6-5-5 carbotricyclic ring systems related to the natural polyquinanes

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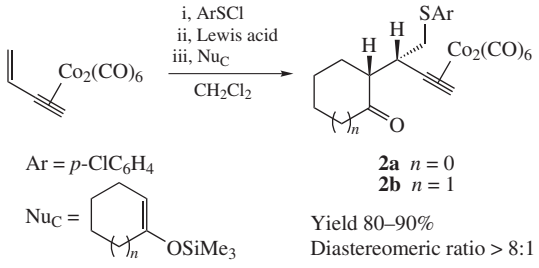
DOI: 10.1016/j.mencom.2008.07.011

A short pathway to the formation of the title framework is elaborated *via* (i) the tandem addition of arylsulfenium chloride and 1-siloxycycloalkenes across the double bond of dicobalthexacarbonyl complex of vinylacetylene, (ii) the diastereoselective Grignard reaction at the carbonyl group of the formed adducts; and (iii) the Pauson–Khand cyclization of 1,6- or 1,7-enyne precursors thus prepared.

Functionalized alkyne derivatives could be prepared using a one-pot protocol of the conjugate addition of arylsulfenium chlorides and various carbon nucleophiles (Nu_C) across the double bond of dicobalthexacarbonyl (DCHC) complexes of conjugated enynes.[1] In particular, it was disclosed[1(*b*)] that a significant diastereoselectivity of the adduct formation could be achieved in the reactions involving the DCHC complex of vinylacetylene **1** provided 1-siloxycycloalkenes are employed as the prochiral Nu_C (Scheme 1).



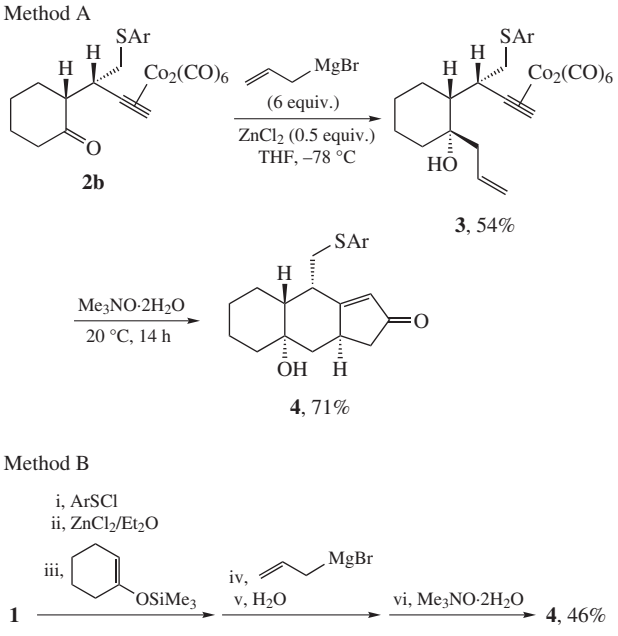
Scheme 1

As the next step, we investigated the use of easily available adducts like **2a**,**b** for the preparation of 1,6- and 1,7-enyne precursors for the intramolecular Pauson–Khand cyclization with the Grignard addition at the carbonyl group. This approach has been checked for the reaction of **2b** with allyl- and vinyl magnesium halides.[†,2]

We have found that the interaction of adduct **2b** with an excess of allylmagnesium bromide in the presence of $ZnCl_2$ proceeds almost instantaneously at –78 °C and furnishes expected carbinol **3** in a satisfactory yield[‡] (Scheme 2). Note that carbinol **3** was isolated as a single diastereomer[§,3] despite of the presence of a minor diastereomer [*ca*. 10%, *cf.* data in ref. 1(*b*)] in starting compound **2b**. The stereochemistry of **3** was firmly established by the results of its further transformations (*vide infra*).

The Pauson-Khand cyclization of the DCHC complex of 1,7-enyne **3** was found to occur easily under the conventional conditions of the oxidative initiation of this reaction with trimethylamine *N*-oxide.[4] It is well known that, in general, the diastereoselectivity pattern of the Pauson–Khand reaction may vary depending on the substitution pattern of the substrate employed.[5] The cyclization of adduct **3** proceeded with a complete control of diastereoselectivity and resulted in the formation of corresponding linearly fused 6-6-5 tricyclic tridecenone derivative **4**[¶] as an individual product in a good yield (Method A). The structure of the product was unambiguously established by single-crystal X-ray analysis.[††]

It was also rewarding to find out that the sequence of (i) the preparation of **2b** from **1**; (ii) the conversion of **2b** into carbinol **3**; and (iii) cyclization to tricyclic adduct **4** could be carried without the isolation of intermediate products as a one-pot transformation with a satisfactory overall yield (Scheme 2, Method B).[¶]



Scheme 2

† A successful reaction of organomagnesium or organolithium compounds with cobaltcarbonyl complexed propargylic aldehydes was described previously.[2(*a*),(*b*)] To the best of our knowledge there is no data about the opportunity to carry out Grignard reaction with the ketones containing DCHC complexed alkyne moiety. It is also pertinent to note that according to the initial data of Nicolas *et al.* this moiety generally exhibits a rather low stability toward the action of various carbanionic nucleophiles.[2(*c*)]

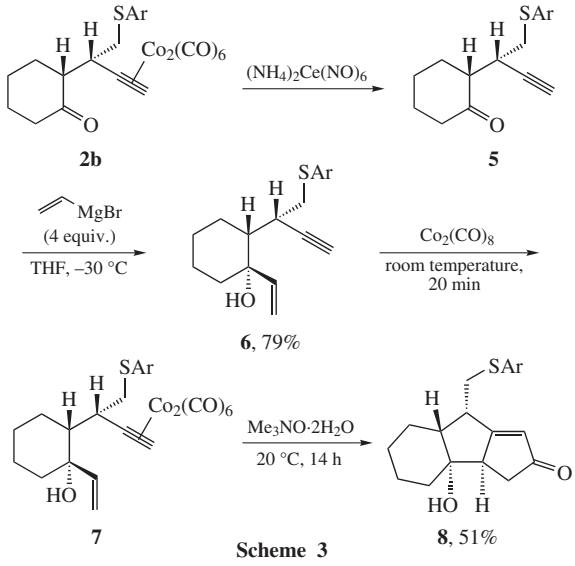
‡ In the absence of $ZnCl_2$ the reaction proceeded less cleanly and furnished the adduct **3** in a substantially lower yield. Additional studies are under way in order to clarify the role of the Lewis acid in this process.

§ The observed highly selective formation of *trans*-1,2-dialkylcyclohexanol derivative **3** is in accordance with the well-known regularities of the Grignard addition to 2-substituted cycloalkanones.[3]

The attempts to perform the Grignard addition of **2b** with vinylmagnesium bromide were unsuccessful [*cf.* data in refs. 1(*a*),2]. In fact, no reaction with ketone **2b** occurred at –78 °C while an intense decomposition was observed at –50 °C. However, we found that the desired transformation could be easily carried out with ketone **5**, prepared in a nearly quantitative yield by the oxidative decomplexation of **2b** upon the treatment with cerium(IV) ammonium nitrate.[6] The reaction of **5** with an excess of vinylmagnesium bromide proceeded uneventfully at –30 °C and resulted in the formation of the expected carbinol as a 12:1 mixture of diastereomers in a good total yield (Scheme 3). The stereochemistry of predominant isomer **6**, which was easily isolated by column chromatography, was deduced from the data on the structure of its cyclization product (see below).

DCHC complex **7** (formed *in situ* from **6**) readily underwent the Pauson–Khand transformation under the action of trimethylamine *N*-oxide to give tricyclic adduct **8** as an individual diastereomer in a good yield. The structure of the latter was accepted by analogy with **4** and is consistent with the ^{1}H and ^{13}C NMR spectra.‡‡

We believe that the above data attest to the promise of the elaborated approach as a new protocol for the synthesis of linearly fused tricyclic compounds and our current studies are aimed at the broadening of its scope and evaluation of its synthetic potential. In this respect it is noteworthy that while a plethora of pathways have been elaborated for the construction of the linearly fused carbotricyclic framework of natural polyquinanes and related compounds they mostly involve the use of a rather laborious and lengthy sequence of steps.[7]



Scheme 3

This work was supported by the Russian Foundation for Basic Research (project no. 03-06-33016).

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Received: 12th December 2007; Com. 07/3059

¶ Experimental details referring to the preparation of the adducts **2b**, **3**, **5** and **6** will be reported in the full paper.

1R,2S*,7R*,9S*-2-(4-Chlorophenylthiomethyl)-9-oxytricyclo[7.4.0.0^{3,7}]-tridec-3-en-5-one* **4**: *Method B*. To a solution of DCHC complex of vinylacetylene **1** (1.39 g, 4.10 mmol) in CH_2Cl_2 (18 ml) at –70 °C a 2.0 M solution of *p*-ClC_6H_4SCl (2.05 ml, 4.10 mmol) in CH_2Cl_2 was added. Then, a 1.47 M solution of $ZnCl_2$/Et_2O in CH_2Cl_2 (0.55 ml, 0.81 mmol) was added with the subsequent addition, after 5 min, of 1-trimethylsilyloxycyclohex-1-ene (1.04 g, 6.12 mmol). The reaction mixture was kept at –30 °C for a day and then cooled to –78 °C. A 3.3 M solution of allylmagnesium bromide (7.50 ml, 24.7 mmol) in THF was added dropwise to the mixture. After 5 min, the solution was quenched with saturated aqueous NH_4Cl (6 ml) at –78 °C and warmed up to room temperature. The water layer was carefully removed, the organic layer was treated with $Me_3NO·2H_2O$ (2.72 g, 24.5 mmol) and stirred at room temperature for 14 h. The mixture was filtered through a plug of silica gel (ethyl acetate–hexane, 1:1) and evaporated. Column chromatography (silica gel) of the residue furnished product **4** (680 mg, 46%) as a colourless solid, mp 133–134 °C (from benzene), R_f 0.34 (Et_2O–hexane, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.09–1.33 (m, 6H), 1.51–1.64 (m, 5H), 1.70–1.85 (m, 3H), 1.71 (d, 1H, *J* 15.0 Hz), 2.02 (dd, 1H, J_1 6.1 Hz, J_2 13.4 Hz), 2.47 (dd, 1H, J_1 6.1 Hz, J_2 19.5 Hz), 2.83 (m, 1H), 3.15 (m, 1H), 3.26 (dd, 1H, J_1 3.7 Hz, J_2 13.4 Hz), 3.46 (dd, 1H, J_1 10.0 Hz, J_2 13.4 Hz), 5.81 (s, 1H), 7.18 (s, 4H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 21.1, 25.5, 26.1, 33.0, 33.6, 40.2, 41.5, 44.1, 46.8, 48.7, 71.1, 128.8, 129.0, 130.8, 131.8, 134.7, 184.8, 208.9. Found (%): C, 66.39; H, 6.41. Calc. for $C_{20}H_{23}ClO_2S$ (%): C, 66.19; H, 6.39.

†† *X-ray data for* **4**. Crystals of **4** ($C_{20}H_{23}ClO_2S$, M = 362.89) are monoclinic, space group $P2_1/c$, at 100 K: a = 13.919(3), b = 8.9032(13) and c = 16.272(3) Å, β = 112.834(6)°, V = 1858.5(6) Å^3, Z = 4 (Z' = 1), d_{calc} = 1.297 g cm^{-3}, μ(MoKα) = 3.27 cm^{-1}, F(000) = 768. Intensities of 10387 reflections were measured with a SMART 1000 CD diffractometer [λ(MoKα) = 0.71073 Å, ω-scans, $2\theta < 56°$] and 4481 independent reflections [R_{int} = 0.0249] were used in the further refinement. The structure was solved by a direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation. The positions of hydrogen atoms were calculated from the geometrical point of view and refined in the isotropic approximation in a riding model. For **4**, the refinement converged to wR_2 = 0.1222 and GOF = 0.930 for all independent reflections [R_1 = 0.0455 was calculated against F for 2528 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0. X-ray diffraction investigation has been performed by K. A. Lyssenko (X-ray Structural Centre, Institute of Organoelement Compounds, Russian Academy of Sciences).

CCDC 691808 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2008.

‡‡ *1R*,2S*,7R*,8S*-2-(4-Chlorophenylthiomethyl)-8-oxytricyclo[6.4.0.0^{3,7}]-dodec-3-en-5-one* **8**. To a solution of ketone **5** (209 mg, 0.71 mmol) in THF (6 ml) at –70 °C a 1.2 M solution of vinylmagnesium bromide (2.30 ml, 2.76 mmol) in THF was added and the mixture was kept at –30°C for 1.5 h. After standard quenching with saturated aqueous NH_4Cl, extraction with hexane and filtration through silica gel, the solvent was removed. The residue was dissolved in CH_2Cl_2 (5 ml) and treated with $Co_2(CO)_8$ (252 mg, 0.74 mmol). After stirring for 1 h at room temperature $Me_3NO·2H_2O$ (380 mg, 3.40 mmol) was added and the reaction mixture was stirred overnight. Isolation of the product was carried out as described above. Yield 101 mg (40%) overall, mp 156–157 °C (from benzene), R_f 0.35 (ethyl acetate–hexane, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.33 (m, 1H), 1.44–1.80 (m, 6H), 1.88 (m, 2H), 2.15 (m, 1H), 2.30 (dd, 1H, J_1 3.4 Hz, J_2 17.7 Hz), 2.36 (dd, 1H, J_1 6.2 Hz, J_2 17.7 Hz), 2.91 (m, 2H), 3.05 (m, 1H), 3.22 (dd, 1H, J_1 4.6 Hz, J_2 12.9 Hz), 6.43 (s, 1H), 7.28 (s, 4H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 20.7, 22.5, 25.9, 29.7, 35.6, 36.1, 39.7, 52.0, 56.9, 76.3, 126.3, 129.2, 130.8, 132.3, 134.6, 192.0, 211.5. Found (%): C, 65.10; H, 6.38. Calc. for $C_{19}H_{21}ClO_2S$ (%): C, 65.41; H, 6.07.