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LETTERS

Novel Tandem Diastereoselective Cyclisation Reactions of Dicobalt Hexacarbonyl Complexed Propargyl Cations

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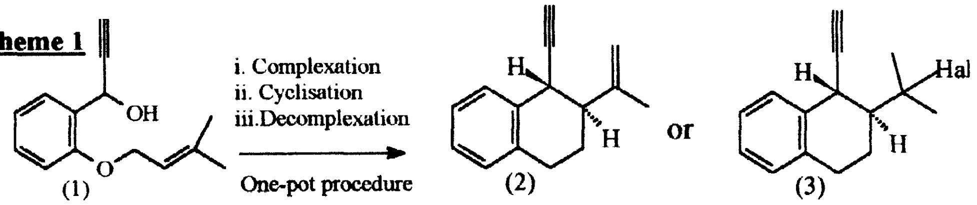
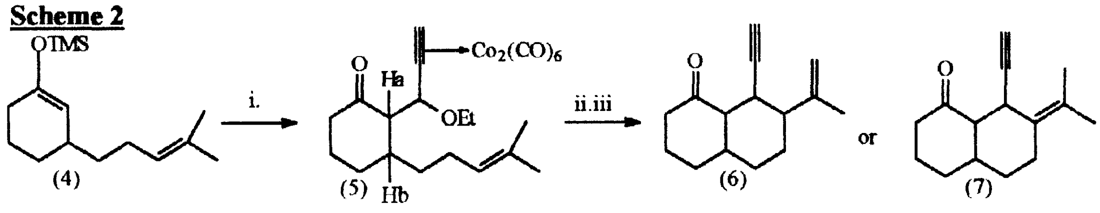
Abstract**: The diastereoselective one-pot synthesis of tricyclic compounds is described that involves a tandem sequence of intermolecular and intramolecular Nicholas reactions followed by a further intramolecular cyclisation process.** © 1998 Elsevier Science Ltd. All rights reserved.

We recently reported the use of non-activated alkenes (1) for quenching dicobalt hexacarbonyl stabilised cations for an intramolecular Nicholas reaction. (2) Using a variety of propynyl alcohols, such as compound **1**, a range of benzopyran derivatives **2** or **3** were synthesised in a diastereoselective process (Scheme 1) using our recently developed one-pot cyclisation procedure. As a continuation of these studies we were keen to apply these novel cyclisation procedures to the corresponding non-aromatic examples as an additional method for the efficient synthesis of decalins and decalones.(3) The rationale is shown (Scheme 2) whereby an intermolecular Nicholas reaction between the O-silylenol ether **4** and a dicobalt hexacarbonyl complex of propiolaldehyde diethyl acetal should afford

Scheme 1



Scheme 2



Reagents: i Hexacarbonyl (propiolaldehyde diethyl acetal) dicobalt./ Lewis acid. ii Lewis acid.
iii. cerium (IV) ammonium nitrate.

the cobalt complexed propynyl ether **5**. A subsequent tandem intramolecular cyclisation followed by an *in situ* decomplexation reaction should then afford a decalone such as **6** or 7.(4) Such tandem/cascade reactions have recently come to prominence as a means of effecting several strategic bond forming reactions in one pot. An important consequence of such developments has been the synthesis of molecules with increased complexity (5) yet maintaining high efficiency during the chemical transformations. Thus apart from the initial synthesis of 4 it was envisaged that all of the subsequent reactions should be effected in one-pot (6) to afford a concise tandem synthesis of these

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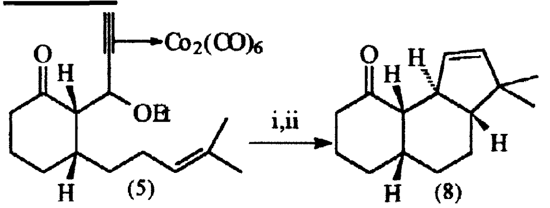
important carbocyclic compounds. We now wish to communicate the preliminary results that have been obtained from these recent studies.

The conjugate addition of the Grignard derivative of 5-bromo-2-methyl-2-pentene (7) to 2-cyclohexen-1-one and entrapment as the O-silylenol ether gave compound **4** in a yield of 95%. Intermolecular Nicholas reaction gave the cobalt cluster **5** in 90% yield. The stereochemical relationship between the protons Ha and Hb of the decomplexed propynyl ether **5** was established as *cis* by nuclear Overhauser enhancement difference (NOED) experiments. The methine proton Ha, in a position α to the carbonyl group in compound **5**, appeared as an apparent triplet (J 6Hz) at δ 2.54 ppm. Treatment of the cobalt complex **5**, with tetrafluoroboric acid, led to an apparent rapid cyclisation reaction which upon addition of the decomplexation reagent yielded a single product. (8)

In contrast to our previous studies, however, spectroscopic analyses of the product isolated from these chemical reactions were inconsistent with the product being either compound **6** or compound **7**. Extensive nmr studies have led us to conclude that the product from the reaction is the tricyclic compound **8**(9) (Scheme 3). The relevant spectral data in support of this structure are as follows: from the ^{1}H nmr spectrum the presence of a *gem*-dimethyl group at δ 0.66 and 0.85 ppm precludes the methyl groups from being vinylic. Furthermore two sets of resonances were observed that are characteristic of alkenyl protons. These were at a chemical shift δ 5.44ppm (1H, dd, J 6 and 3 Hz) and δ 5.72 ppm (1H, d, J 6 Hz). The ^{13}C DEPT experiments revealed the presence of two =CH carbon atoms at a chemical shifts of δ 131.06 and δ 143.53 ppm and four methine carbon atoms (ring junction carbon atoms) upfield with chemical shifts between δ 46.12 and 89.09 ppm. An HRMS confirmed the structure of the product as being compound **8** .(10) Overall the net effect from these series of reactions has been the formation of three new carbon-carbon bonds, two of which are contiguous to each other (Figure 1).

Scheme 3



Reagents: i Tetrafluoroboric acid. ii. cerium (IV) ammonium nitrate.

From a mechanistic point of view treatment of hexacarbonyl (propiolaldehyde diethyl acetal) dicobalt with a stoichiometric amount of boron trifluoride diethyl etherate followed by addition of **4** would give the propynyl ether **5**. An *in situ* addition of a stoichiometric amount of tetrafluoroboric acid or tin(IV) chloride (11) would then effect a sequential intramolecular cyclisation reaction (12) to afford a second cation **9**. The exact nature of the species **10** that undergoes further cyclisation to afford **8** from **9** has yet to be elucidated (13) however the reaction is the subject of our continued investigations. Addition of the decomplexing reagent, ceric ammonium nitrate (CAN), to the reaction mixture led to the decomplexation of dicobalt hexacarbonyl and the additional intramolecular cyclisation reaction to afford the tricyclic compound **8**(14). The *cis-anti-trans* relative stereochemistry of the tricyclic compound **8** was obtained from appropriate NMR experiments of the 2,4- DNP derivative of **8** (15) (Figure 2). The resonance for proton Hb was found at a chemical shift δ 2.59 ppm and showed two strong couplings ($J_{ab} = J_{bc}$ =14 Hz) and one weaker coupling (J_{bd} =2.5 Hz) suggesting that the protons Ha and Hb are

Figure 1

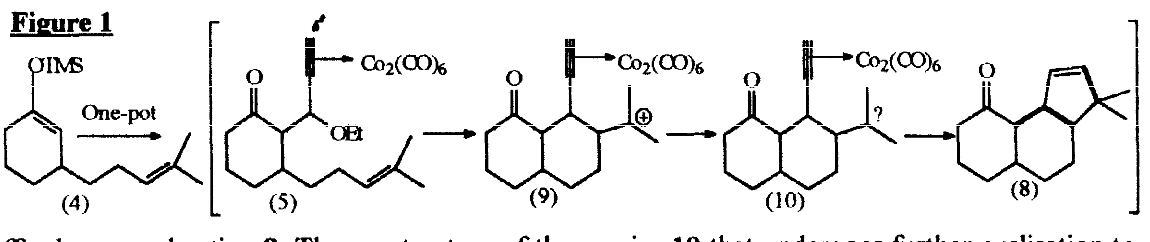
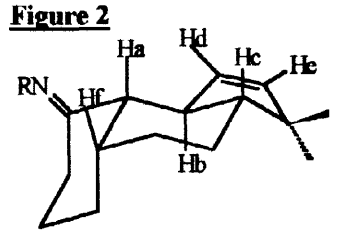


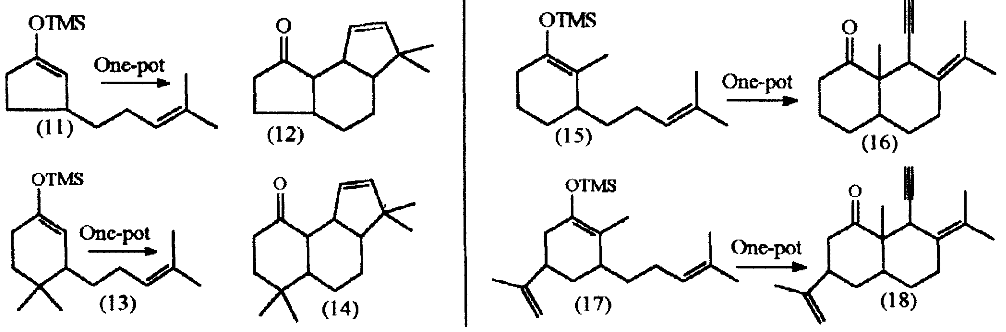
Figure 2



axially orientated.(16) The resonance for proton Ha was found at a chemical shift δ 2.93 ppm and appeared as a doublet of doublets (J_{ab} = 14 Hz and J_{af} = 6 Hz). The ^{13}C nmr spectrum gave resonances for the carbon atoms of the 6-5 ring junction at chemical shifts of 48.62 and 44.31 ppm, shifts characteristic of a *trans* ring junction. (17) The use of NOED experiments established the 6-6 ring junction as *cis* since irradiation of the signal at δ 2.93 (Ha) caused an increase in the intensity of the signals due to Hf and Hc (both signals are coincident at δ 2.01-2.06). When the signal at δ 2.59 ppm (Hb) was irradiated no enhancement in the signals at δ 2.93 ppm, attributed to proton Ha, or between δ 2.01-2.06, attributed to Hc, was observed.

As an extension to these investigations we have been able to effect the complete sequence of four reactions, (i) intermolecular and (ii) intramolecular Nicholas reaction, (iii) decomplexation and (iv) the additional cyclisation step, to afford compound **8**, in an overall yield of 35% from **4** in one-pot.(6) These studies have revealed that the tandem nature of these reactions are quite general and the formation of other tricyclic compounds, analogous to compound **8** are achievable. Additional representative examples are shown (Figure 3). The results show that whereas all of the cyclisation precusors have undergone the one-pot tandem intermolecular (i) and a sequential intramolecular Nicholas reaction (ii) followed by a subsequent *in situ* decomplexation step (iii) the precursors **15** and **17** resisted the additional cyclisation step (iv). It would seem that the presence of an α–methyl group appears to prevent the subsequent cyclisation reaction from occurring. In both of these examples the corresponding *isopropenyl* derivatives **16** and **18** respectively were isolated in yields of 40%-45%. The failure of these examples to undergo the additional intramolecular cyclisation reaction may be a result of steric or stereochemical factors both of which will be the focus of our continued studies. In contrast to these results the O-silylenol ethers **4**, **11** and **13** all underwent the one-pot tandem sequence of reactions to afford the corresponding tricyclic compounds **8**, **12** and **14** as single diastereoisomers in yields of 35%-45%.

Figure 3



One-pot strategy Hexacarbonyl (propiolaldehyde diethyl acetal) dicobalt./ Lewis acid then Tin(IV) chloride then cerium (IV) ammonium nitrate. Final products formed in yields of 35-45%

In addition to CAN we have also investigated the use of other decomplexing reagents such as iodine, iron (III) nitrate nonahydrate and ceric ammonium sulfate. Our results have shown CAN to be the most efficient decomplexing reagent. However in each experiment, the additional cyclisation reaction leading to the synthesis of **8** always prevailed.

In conclusion this letter describes a one-pot tandem series of reactions for an extremely efficient diastereoselective synthesis of tricyclic ring systems. The chemistry involves a novel intermolecular Nicholas reaction followed by a tandem intramolecular Nicholas reaction. During the subsequent *in situ* decomplexation of dicobalt hexacarbonyl a further tandem cyclisation reaction occurs to afford tricyclic compounds.

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References and Notes:

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2) Nicholas, K.M. *Acc. Chem. Res.*, **1987**, 20, 207.
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5) Parsons, P.J.; Penkett, C.S.; Shell, A.J. *Chem. Rev.* **1996**, 96, 195.
6) As the cobalt clusters are all coloured they are readily visualised by thin layer chromatography. This feature coupled with the significant R_f differences between complexed precursors such as (5) and the decomplexed products facilitates a one-pot protocol.
7) Aldrich Chemicals Ref: 26,250-1
8) As determined from both tlc analyses and from the corresponding nmr spectra for instance the ^{13}C nmr spectrum of compound **8** contained 15 peaks with no evidence to suggest that another compound was present.
9) All new compounds, with the exception of metal complexes, gave satisfactory ^1H and ^{13}C NMR spectra as well as IR and mass spectra that were consistent with the assigned structures. In most cases infrared spectra only were recorded for the metal complexes.
10) Spectroscopic data for compound **8**
Found (EI): (M^+), 218.1671, $C_{15}H_{22}O$ requires M^+, 218.1668: ν_{max} (cm^{-1}): 3067.9, 3029.6, 1710.6, 1640.7, 1484.4: δ_H ($CDCl_3$, 300MHz): 5.72-5.74 (1H,d J 6Hz, =CH), 5.43-5.46 (1H, dd, J 4 and 6Hz, =CH), 2.16-2.19 (3H, m, 3 X C-H), 1.74-1.87 (3H, m, C-H,CH_2), 1.62-1.63 (1H, m, C-H), 1.44-1.47 (3H, m, C-H, CH_2),1.28-1.30 (2H, m, CH_2), 1.01-1.07 (2H, m, CH_2), 0.85 (3H, s, Me), 0.66 (3H, s, Me), δ_C ($CDCl_3$, 75.45MHz): 215.14 (s), 143.53 (d), 131.06 (d), 69.10 (d), 57.17 (d), 47.60 (d), 46.12 (d) 43.99 (s), 42.03 (t), 34.93 (t) 32.68 (t), 27.11 (t), 27.02 (q), 24.08 (t), 19.35 (q).
11) A range of Lewis acids have been studied for suitability in effecting the intramolecular Nicholas reaction and tin (IV) chloride was found to be a superior reagent to tetrafluoroboric acid which gave reduced yields.
12) In the absence of the cobalt cluster a reduced yield and a mixture of products was observed. For the importance of the cobalt cluster in maintaining both the efficiency and the selectivity in cyclisation reactions of this type see Ganesh, P.J.; Nicholas, K.M. *J.Org. Chem.*, **1997**, 62, 1737.
13) The presence of a cobalt hexacarbonyl complexed alkyne with an intermediary alkenyl group (see nmr data associated with ref 14) may offer the possibility of a variant of a Pauson Khand reaction taking place to establish the third ring system.
14) In a separate experiment an ^1H nmr spectrum was obtained from a quenched sample of the complex **9**. This revealed a characteristic downfield shift for the alkynyl proton which appeared as a doublet (J2Hz) at a chemical shift δ 4.81 ppm. Furthermore two groups of signals, characteristic of vinylic methyl moieties, were observed at chemical shifts δ 1.405 and 1.414ppm and downfield at 1.597 and 1.601 ppm.
15) The protons Ha and Hb (Fig.2) were well separated in the ^1H nmr spectrum of the DNP-derivative.
16) The complexation of dicobalt octacarbonyl to alkynes is known to be accompanied by a change in the geometry of the linear alkynyl group. The bond angle for the linear C-C-H is reduced from 180° to 138°.(18)
17) The use of ^{13}C nmr spectroscopy to establish the stereochemistry of fused ring systems is not without precedent. See:Kalinowski, H-O.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy;* John Wiley & Sons-Interscience, New York, **1988**, 129. In compound **8** these resonances were at δ 47.60 and 46.12 ppm, for a *cis* stereochemistry the chemical shifts are typically δ 38-39 ppm.
18) Sly, W.G. *J. Am. Chem. Soc.*, **1959**, 81,18.