Tetrahedron Letters, Vol.32, No.4, pp 491-494, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

# STEREOSELECTIVE SYNTHESIS OF CIS RING FUSED ENDO OR EXO OCTAHYDROPYRINDIN-4 ONES BY IMINO-DIELS-ALDER REACTION.

Renée PAUGAM and Lya WARTSKI

Laboratoire des Carbocycles
Unité Associée au CNRS 0478
Institut de Chimie Moléculaire d'Orsay
Université de Paris-Sud, 91405 ORSAY Cedex (France)

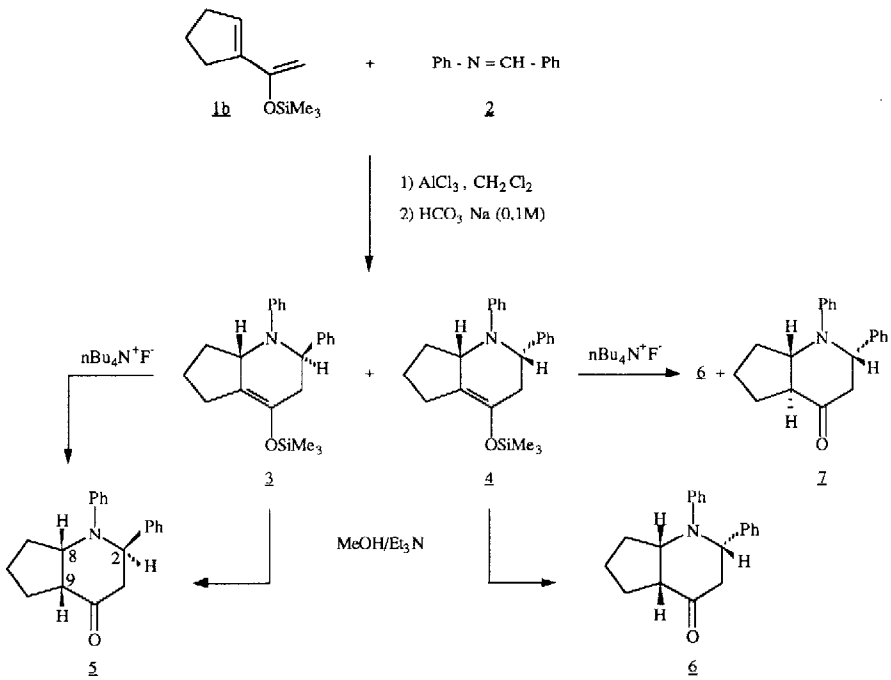
***Abstract :*** The Diels-Alder reaction of trimethylsilylenolether of 1-acetylcyclopentene 1b with benzylideneaniline 2, catalyzed by $AlCl_3$, occurred with high **exo** or **endo** selectivity, depending upon kinetic or thermodynamic control. MeOH/$Et_3N$ treatment of the intermediate cycloadducts 3 and 4 gave stereospecifically the *cis* ring fused **exo** or **endo** octahydropyrindin-4 ones 5 and 6 while α,β unsaturated ketones 8 or 9 were formed after acidic treatment. Basic isomerization of 6 afforded the corresponding *trans* ring fused **endo** ketone 7.

The cycloaddition reactions between silyloxydienes and different dienophiles were extensively studied in the last decades (1-3). We have recently reported that the reaction of trimethylsilylenolether of 1-acetylcyclohexene 1a and various imines led to *cis* and *trans* ring fused decahydroquinolin-4 ones (4). The recent obtention of only *trans* ring fused **endo** compounds , starting from 5-menthyloxy-2 [5H]-furanone and the diene 1a or the analog 1b derived from 1-acetylcyclopentene (5), prompted us to publish our results related to the condensation of the diene 1b with benzylideneaniline 2 focusing on the peculiarity of this system.

The reaction of 1b (1,2 eq.) and 2 (1 eq.) took place under Lewis acid catalysis ($AlCl_3$, 1 eq.) in $CH_2Cl_2$ at various times and temperatures. After aqueous $HCO_3Na$ (0,1 M) treatment, carefully controlled, two enoxysilanes 3 and 4 were only detected next to starting materials by $^1H$ NMR analysis of the crude product (6). They were formed in good yield (75%).

Under kinetic control (-40°C, 15mn), the cycloadduct 3 was favoured (3/4 = 87/13) while under thermodynamic control (r.t., 2hrs) 4 was strongly privileged (3/4 = 2/98).

MeOH/Et3N treatment of 3 and 4 mixtures led stereospecifically and quantitatively to the corresponding ketones 5 and 6. Furthermore, $nBu_4N^+ F^-$ treatment of 3 gave only 5 as previously mentioned (4) while a mixture of ketones 6 and 7 in a 70/30 ratio, was obtained starting from 4. The same 6/7 ratio was observed when submitting 6 to these conditions.



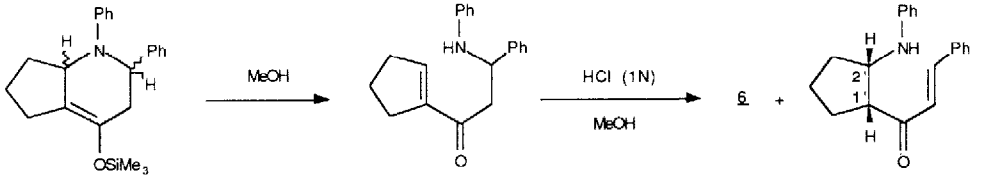

The octahydropyrindine-4 ones were characterized by IR, MS and $^1H$ NMR analysis. It is well known that the stereochemistry at ring junction in hydrindan analogs is difficult to assign from the $^1H$ NMR data (7,8,9). However, the $^3J_{H8H9}$ coupling constant values for 5 (J = 7.1 Hz) and 6 (J = 6.0 Hz) are in agreement with a *cis* ring fused structure. For 5, this assignment was confirmed by X-ray analysis which also indicated a *trans* relationship between C2-H2 and C8-H8 bonds (10).

It appeared thus that the cycloaddition reaction of 1a (4) and 1b with benzylidene aniline 2 in the presence of Lewis acid is highly regioselective as well as the condensation of the same dienes with 5-menthyloxy-2 [5H]-furanone under thermal conditions (5).

In the case of imine 2, a higher **exo** selectivity is observed with 1b than with 1a, under kinetic control while under thermodynamic control the **endo** approach is strongly favoured with both dienes. On the other hand, with 5-methyloxy-2 [5H]-furanone, the **endo** ketone is the only one formed whatever the diene but there is no information on the intermediate species (5).

Protonation by MeOH/$Et_3N$ at the ring junction of **exo** 3 or **endo** 4 enoxysilanes having a cyclopentyl group, led only to *cis* ring fused ketones as those derived from 1a. In the same way, $nBu_4N^+ F^-$ treatment of **exo** enoxysilanes furnished the corresponding *cis* ring fused ketones with both dienes. On the contrary, the $nBu_4N^+ F^-$ treatment of **endo** cyclo adduct 3 afforded a mixture of *cis* and *trans* ring fused ketones while from analog adduct having a cyclohexyl group only the *trans* one was formed under these epimerizing conditions. These results differ also from those of Feringa who obtained only a *trans* ring fused ketone starting either from 1a or 1b (5).

Cycloadducts 3 and 4 treated by MeOH led to one α,β unsaturated ketone 8 by acid catalyzed ring opening, a behaviour different from cyclohexyl analogs (4) which were stable in this condition.




3 or 4 8 9

Furthermore, 8 gave bicyclic ketone 6 next to an other α,β unsaturated ketone 9 by aqueous HCl (1N)/MeOH treatment. The two opened ketones have been characterized by IR, MS, and $^1H$ NMR analysis (11). The $^3J_{H1'H2'}$ coupling constant value of 4.6 Hz for 9 corresponds probably to a *cis* disubstituted cyclopentane. In cyclohexyl analog such a ring closure did not take place in these conditions and required $TiCl_4$ catalysis while it was observed in other related systems (1b,2,12). Moreover, the cyclohexyl analog of 9 has never been evidenced (4).

Nevertheless, the pericyclic mechanism of the reaction between 1b and 2 is ascertained since ketone 8 was never detected in the crude product obtained after hydrolysis by aqueous hydrogenocarbonate.

In conclusion, the control of the stereoselectivity of the cyclocondensation of 1b and 2 and the protonation of the enoxysilanes was realized as previously with 1a and allowed the synthesis of unknown *cis* ring fused **exo** and **endo** ketones and *trans* ring fused **endo** ketone. On the other hand, it turned out that these dienes may give different stereochemical behaviour according to the 2π component, in connection with the discrepancy between Feringa's results and ours. Interpretation of this fact requires further investigations.

**Acknowledgments:**

We thank Dr. J.Seyden-Penne for helpful discussions, Mrs N. Platzer for her contribution to the 500MHz $^1$H NMR analysis of 6 and Mrs M. Nierlich for X-ray analysis of 5

***References and notes***

1. (a) Boger, D.L.; Weinreb, S.N. *"Hetero Diels-Alder Methodology in Organic Synthesis"*, Academic Press, New-York, **1987**. (b) Pfrengle, W.; Kunz, H. *J. Org. Chem.* **1989**, 54, 4261. (c) Danishefsky, S.J.; Kerwin, J.F. *Tetrahedron Lett.* **1982**, 23, 3739. (d) Danishefsky,S.J. ; Myles,D.C. ; Harvey,D.F., *J.Am.Chem.Soc.* **1987**, 100, 862 and references therein.

2. Midland, M.M.; McLoughlin, J.I. *Tetrahedron Lett.* **1988**, 29, 4653.

3. Lamy-Schelkens, H.; Giomi, D.; Ghosez, L. *Tetrahedron Lett.* **1989**, 30, 5887.

4. Le Coz, L.; Veyrat-Martin, C.; Wartski, L.; Seyden-Penne, J.; Bois, C.;Philoche-Levisalles, M. *J. Org. Chem.*. **1990**,55,4870.

5. DeJong, J.C.; Jansen, J.F.G.A.; Feringa, B.L. *Tetrahedron Lett.* **1990**, 31, 3047.

6. For 3 : $^1$H NMR (200 MHz, $CDCl_3$) δ 0.30 (s, 9H, $SiMe_3$), 1.40-2.70 (m, 7H, cyclopentyl and H31), 3.09 (m, 1H, H32, $^2J_{H31H32}$ = 16.5 Hz), 3.57 (m, 1H, H8), 4.85 (d, 1H, H2, $^3J_{H2H31}$ = 7.3 Hz), 6.60-7.60 (m, 10H, phenyl).
   For 4 : $^1$H NMR (200 MHz, $CDCl_3$) δ 0.05 (s, 9H, $SiMe_3$), 1.00-2.60 (m, 7H, cyclopentyl and H31), 2.72 (m, 1H, H32, $^2J_{H31H32}$ = 15.6 Hz), 4.07 (m, 1H, H8), 4.72 (t, 1H, H2, $^3J_{H2H31}$ = $^3J_{H2H32}$ = 5.2 Hz), 6.70-7.50 (m, 10H, phenyl).
   The relative configuration of the C2H2 and C8H8 bonds in the adducts 3 and 4 is determined from that of the corresponding ketones 5 and 6.

7. Fuchs, B. *Top. Stereochem.*. **1979**, 10, 1.

8. Lo Cicero, B.; Weisbuch, F.; Dana, G. *J. Org. Chem.* **1981**,46, 914.

9. Prasad, C.V.C.; Chan, T.H. *J. Org. Chem.* **1988**, 54, 3242.

10. For 5 : m.p. 129.3°C; $^1$H NMR (200 MHz, $C_6D_6$) δ 2.56 (td, 1H, H9), 3.86 (m, 1H, H8, $^3J_{H8H9}$ = 7.1 Hz), 4.74 (t, 1H, H2).
    For 6 : Rf (cyclohexane/ether : 50/50) = 0.58; $^1$H NMR (500 MHz, $CDCl_3$) δ 2.84 (qd, 1H, H9), 4.01 (q, 1H, H8, $^3J_{H8H9}$ = 6.0 Hz), 4.74 (dd, 1H, H2).
    For 7 : Rf (cyclohexane/ether : 80/20) = 0.33; $^1$H NMR (250 MHz, $CDCl_3$) δ 2.50-3.15 (m, 3H, H31, H32 and H9), 3.28 (m, 1H, H8, $^3J_{H8H9}$ = 10.3 Hz), 4.58 (dd, 1H, H2).
    Details of the $^1$H NMR data of the octahydropyrindin-4 ones 5, 6 and 7 will be published elsewhere with the crystal and molecular stucture determination by X-ray analysis for 5 and molecular modeling (molecular mechanistics and ab initio calculations) for the three products.

11. For 8 : m.p. 134.9°C; $^1$H NMR (200 MHz, $CDCl_3$) δ 1.90 (td, 2H, H4'), 2.50 (m, 4H, H3' and H5'), 3.17 (ddd, 2H, H2), 4.84 (dd, 1H, H3), 6.50-7.50 (m, 11H, phenyl and H2').
    For 9 : Rf (cyclohexane/ether : 80/20) = 0.27; $^1$H NMR (250 MHz, $CDCl_3$) δ 1.50-2.30 (m, 6H, cyclopentyl), 3.18 (m, 1H, H1'), 4.27 (td, 1H, H2', $^3J_{H1'H2'}$ – 4.6 Hz), 6.54-6.74 (m, 3H, phenyl), 6.80 (d, 1H, H3), 7.07-7.50 (m, 7H, phenyl), 7.60 (d, 1H, H2, $^3J_{H2H3}$ = 16.0 Hz).

12. Le Coz,L. and Wartski,L., unpublished results.

(Received in France 26 July 1990)