

SYNTHESIS OF SUBSTITUTED DECALONES BY DIELS-ALDER REACTION
OR BY SEQUENTIAL MICHAEL REACTION - WHICH ONE IS MORE SELECTIVE?

Friedrich Richter and Hans-Hartwig Otto*

University of Freiburg, Department of Chemistry and Pharmacy, Hermann-
Herder-Str. 9, D-7800 Freiburg, West Germany

Abstract: Acetylcyclohexene is transformed into decalones by a two step
Michael reaction with high stereo- and regioselectivity, while the Diels -
Alder reaction in this case shows poor selectivity.

The Diels - Alder reaction is well known to be one of the most versatile methods
for the formation of mono- and poly-cycles containing six-membered rings.
The reaction involves a concerted cycloaddition, and therefore, usually shows
very high stereospecificity¹. However, reactions with dienophiles having an
endo directing group at each end of the double bond often show very poor
regioselectivity. For some reasons, our goal was the development of an
efficient synthetic route to substituted decalones 3 with predictable stereo=
chemistry starting from 1-acetylcyclohexene (1). We had hoped this would
be a very convenient starting material, and we could easily transform it into
the pentadienone system 2. In the following step 2 could then react with
diene 4, which can also be prepared from 1².

Reactions between 1 and aldehydes R-CHO yielded the expected pentadienones
2 in yields ranging from 0 to 57%. As by-products we isolated compounds
3A with yields 10 - 55%³. Careful structure elucidation by NMR spectroscopy -
250 MHz - combined with an X - ray structure analysis of a related com=
pound⁴ established the proposed structure and stereochemistry⁵.

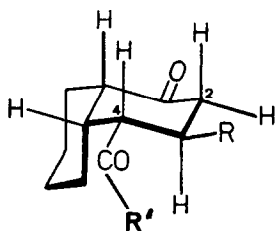


Figure 1.

$$J_{2ax/3} = 13.5 \text{ Hz}$$

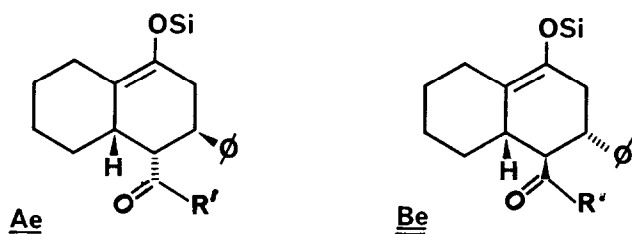
$$J_{2eq/3} = 5.0 \text{ Hz}$$

$$J_{3/4} = 11.0 \text{ Hz}$$

$$J_{4/4a} = 4.5 \text{ Hz}$$

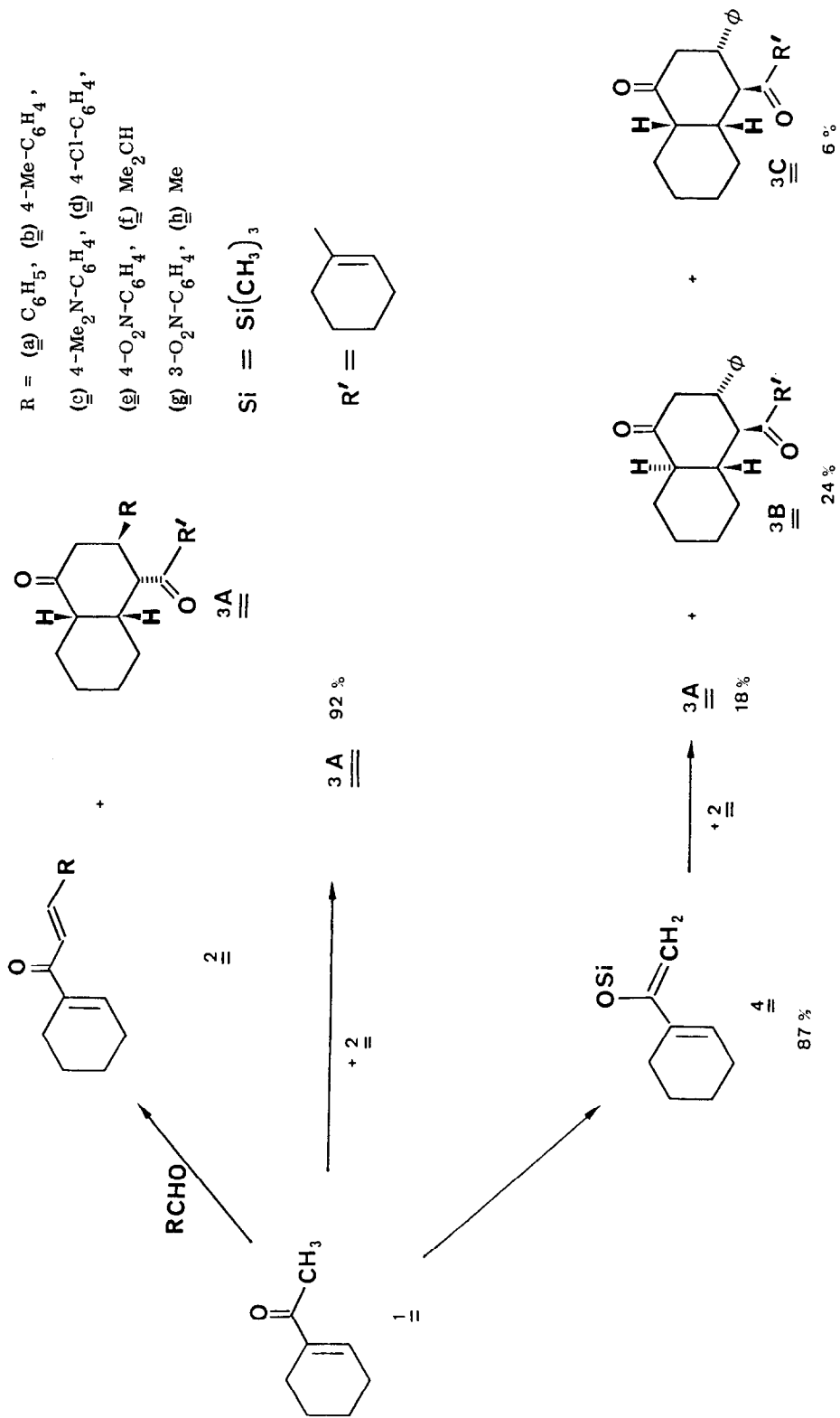
Major coupling constants are shown in figure 1. Furthermore, calculation of relative energies of possible conformers⁶ of 3 is in full agreement with structure 3A.

The Diels-Alder reaction between the diene 4 and 1-(4-methylcinnamoyl)-1-cyclohexene occurred only in the presence of ethylaluminium dichloride at 0°C (1h, CH₂Cl₂). For separation of aluminiumhydroxide we had to hydrolyze the reaction mixture with hydrochloric acid. Thereby we obtained 3 isomers, 3A, 3B, and 3C after chromatographic workup³. Their stereochemistry results from the primary adducts Ae and Be, which we could not isolate under these reaction conditions.



Both products are effected by endo attack: in Ae the cyclohexenylcarbonyl group directs in this position, whereas Be results from an endo orientation of the aromatic ring. Hydrolysis of Ae then gives 3A, and 3B and 3C are formed from Be.

When we tried to run the reaction between 1 and the pentadienone 2 in the presence of lithium diisopropylamide in THF at -78°C, we isolated only the stereo isomer 3A in high yield after warming up to room temperature and acidic workup. The yield was even higher (up to 100%), when we added stoichiometric amounts of 1,3-dimethyltetrahydro-2(1H)-pyrimidinone⁷ to the reaction mixture before adding of 2. From the reaction conditions evidence is provided that the best way of understanding this reaction is assuming a sequential Michael reaction⁸ instead of an anion accelerated Diels-Alder reaction. This is supported by isolation of an open chained intermediate in a similar reaction with β -nitrostyrene⁹. The high selectivity of this sequential Michael reaction probably can be explained by the "lithium effect". That means lithium is fixing the product of the first addition step resulting only



isomer 3A. As the diene in the Diels-Alder reaction has two directing groups, the selectivity in this case is much lower.

References and Notes

- 1 T.Clark and M.A.McKervey in *Comprehensive Organic Chemistry*, ed. H.D.Barton and W.D.Ollis, Pergamon Press, Oxford 1979, Vol.1, p. 1o1f.
- 2 C.Symmes, Jr. and L.D.Quin, *J.Org.Chem.* 41, 238 (1976).
- 3 Conditions: THF, lithium diisopropylamide, -78°C to 0°C , acidic workup, fractional crystallization. 2 : IR 165o (C=O), 162o-163o (C=C) cm^{-1} ;
a m.p. 66°C (methanol), lit^{1o} 68°C ; b m.p. $1o7^{\circ}\text{C}$ (petrolether); c m.p. $1o9^{\circ}\text{C}$ (cyclohexane); d m.p. 119°C (ethanol); e m.p. 162°C (ethanol);
f b.p. $o.15$ $1o6-1o9^{\circ}\text{C}$; g m.p. $1o3^{\circ}\text{C}$ (methanol); h b.p. 12 $122-125^{\circ}\text{C}$.
3Aa m.p. 191°C (ethanol), IR 1715,165o (C=O),163o (C=C) cm^{-1} . 3Ab m.p. 216°C (CHCl_3 /acetone), IR 172o,1655 (C=O), 1635 (C=C) cm^{-1} .
3Bb m.p. 171°C (methanol), IR 172o,165o (C=O), 1635 (C=C) cm^{-1} .
3Cb m.p. $136-8^{\circ}\text{C}$ (methanol),IR 17o5,165o (C=O), 164o (C=C) cm^{-1} .
3Ac m.p. 234°C (ethyl acetate), IR 1715,165o (C=O), 163o (C=C) cm^{-1} .
3Ad m.p. $2o9^{\circ}\text{C}$ (cyclohexane), IR 171o,165o (C=O), 163o (C=C) cm^{-1} .
3Ae m.p. 218°C dec. (methanol), IR 171o,165o (C=O), 163o (C=C) cm^{-1} .
3Af m.p. 147°C (ligroin), IR 172o,1655 (C=O), 164o (C=C) cm^{-1} .
3Ag m.p. $2o9^{\circ}\text{C}$ (ethyl acetate), IR 17oo,165o (C=O), 163o (C=C) cm^{-1} .
3Ah m.p. 117°C (ligroin), IR 171o,165o (C=O), 1635 (C=C) cm^{-1} .
 All new compounds gave satisfactory microanalyses.
- 4 We thank Dr.C.Kratky, Institut für Physikalische Chemie der Universität Graz (Austria), for the X-ray analysis of *cis*-4,4-dicyano-3-phenyldecalone, which will be published elsewhere.
- 5 All figures show relative configurations.
- 6 We are indebted to Dr.H.Burghard, Farbwerke Hoechst AG, Frankfurt, for this calculation using the program SCRIPT; see N.C.Cohen et al., *Tetrahedron* 37, 1711 (1981).
- 7 Commercial material from E.Merck AG, Darmstadt, Nr. 818 214.
- 8 E.G.Gibbons, *J.Org.Chem.* 45, 154o (198o).
- 9 F.Richter, Thesis, Freiburg 1985.
- 1o R.E.Christ and R.C.Fuson, *J.Am.Chem.Soc.* 59, 893 (1937).

(Received in Germany 28 May 1985)