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SYNTHESIS OF NITRO-SUBSTITUTED DECALONES BY DOUBLE MICHAEL REACTION, SEQUENTIAL MICHAEL REACTION, AND BY DIELS-ALDER REACTION[1]

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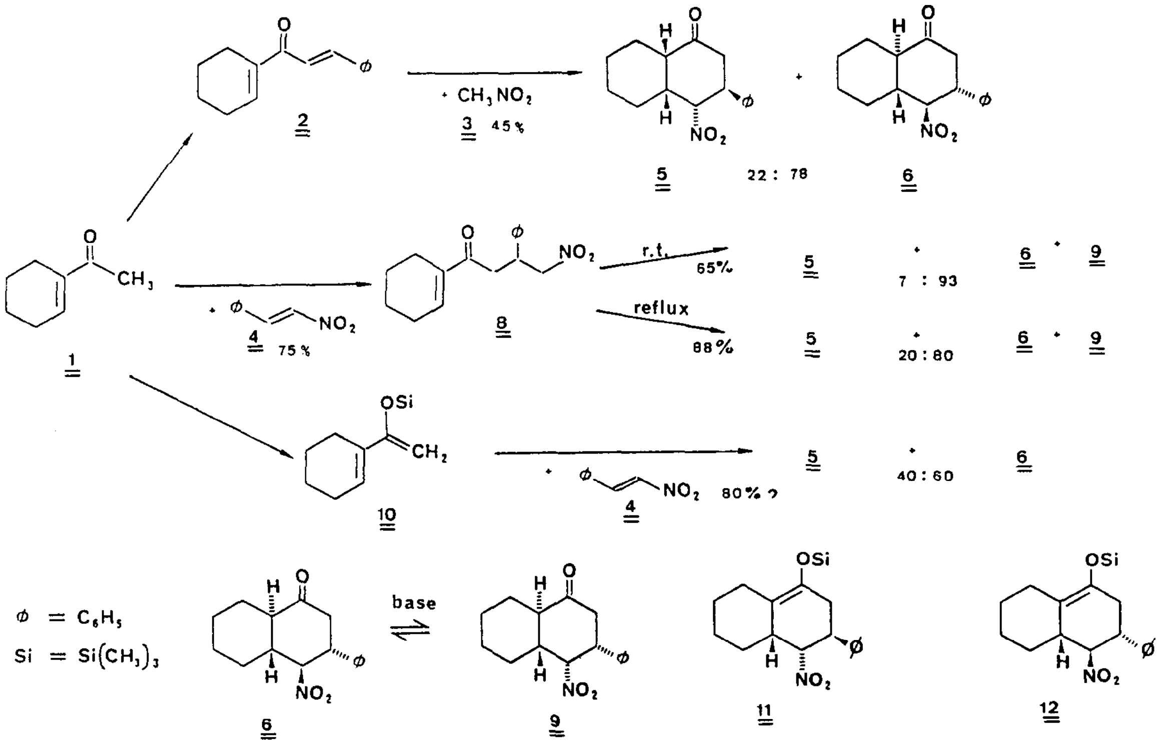
Summary: 4-Nitro-3-phenyl-decalones are obtained from 1-acetylcyclohexene by three different ways. Stereochemistry and reaction pathways are discussed, and, for the first time, an intermediate of a sequential Michael reaction is isolated.

The Michael reaction is of great preparative value for the formation of C-C bonds[2]. We are especially interested in the stereochemistry of the double Michael reaction and its use in drug synthesis[1]. Here we report the synthesis of nitro substituted decalones from 1-acetylcyclohexene 1 by three different ways. 1 was transformed into cyclohexenyl styryl ketone 2 . When 2 was treated with nitromethane 3 in MeONa/MeOH (18 h, reflux) we isolated after acidic workup a 1:4 mixture (45%) of 5 and 6[3]. The structures are deduced from proton NMR data, which are compared with those of cis-4,4-dicyano-3-phenyldecalone 7 (X-ray analysis)[4]. 5 is identical with a product reported by Pitacco et al.[5] from reaction between 1-cyclohexenyl-1-morpholino-ethene and nitrostyrene[6]. As a by-product they have isolated 8 (24%), which we obtained as the only material, when 1 reacted with nitrostyrene at -78°C in THF with LDA. Treatment of 8 with MeONa/MeOH yields a mixture of 5 and 6 (and 9, formed by



isomerisation of 6 in presence of base). Chemical yield and ratio 5:6 are temperature dependent.

The reaction between 1 and nitrostyrene clearly is a sequential Michael reaction with remarkable stereoselectivity. A few other examples are described[7], but authors only have expressed a preference for this way without isolation of any intermediates. Probably, the reported example is the first one, in which an isolated single Michael adduct is transformed into the cyclic product with high stereoselectivity.

The third way is the Diels-Alder reaction between siloxydiene[8,9] 10 and nitrostyrene yielding a 4:6 mixture of 5 and 6 (toluene,15 h reflux,acidic workup,chromatographic separation). This yields primarily the silylated enolates[10] 11 and 12. The nitro group of 11 is endo, and hydrolysis yields the cis decalone 5 with all substituents in equatorial positions. In 12 the aromatic ring prefers endo, and hydrolysis results in the trans decalone 6 with equatorial substituents. The poor selectivity shown by this Diels-Alder reaction seems to be reasonable, as nitrostyrene has an endo directing group at each end of the double bond.

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References and Notes

1 part 28 of Reactions of Pentadienones; part 27 see: F.Richter and H.-H.Otto, Tetrahedron Lett. 26, 4351 (1985).

2 H.O.House, Modern Synthetic Reactions, 2nd ed., W.A.Benjamin Inc., Menlo Park, California 1972.

3 5 : m.p. 139-141° C (MeOH); IR(KBr): 1718(C=O), 1550,1370(NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) $J_{2e/3}$= 6 Hz, $J_{2a/3}$= 12 Hz, $J_{3/4}$= 12 Hz, $J_{4/4a}$= 4 Hz. 6 : m.p. 183°C (MeOH,acetone); IR(KBr): 1720(C=O), 1550,1370(NO_2)cm^{-1}; ^1H NMR (D_6-benzene): $J_{2/2}$= 14 Hz, $J_{2e/3}$= 5Hz, $J_{2a/3}$= 13 Hz, $J_{3/4}$ = 11 Hz, $J_{4/4a}$= 12 Hz.

4 We thank Dr. C. Kratky, Institut f. Physikalische Chemie der Universität Graz, for X-ray analysis of cis-4,4-dicyano-3-phenyldecalone.

5 G.Pitacco, A.Risaliti, M.L.Trevisan and E.Valentin, Tetrahedron 33, 3145 (1977); R.A.Ferri, G.Pitacco and E.Valentin, ibid. 34, 2537 (1978).

6 Repeating their experiments we obtained a 9:1 mixture of 5 and 6.

7 E.G.Gibbons, J.Org.Chem. 45, 1540 (1980) and references therein.

8 C.Symmes,Jr. and L.D.Quin, J.Org.Chem. 41, 238 (1976).

9 C.Veyrat,L.Wartski and J.Seyden-Penne,Tetrahedron Lett.27, 2981 (1986).

10 Mixture of 11 and 12: m.p. 125°C (pentane); IR(KBr): 1670(C=C), 1545,1350(NO_2) cm^{-1}. - All new compounds gave satisfactory microanalyses; all figures show relative configuration.

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