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RIGID ANALOGS OF 3,3,5,5,-TETRAMETHYLCYCLOHEXANONE : TRICYCLO [5,2,1,$0^{2,7}$] DECANE-5-ONE AND TRICYCLO [5,3,1,$0^{3,8}$]UNDECANE-5-ONE

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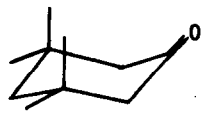
We have previously shown [1] that the secondary kinetic isotope effects in nucleophilic addition reactions to carbonyl compounds are closely related to the nature of the nucleophile and the structure of the ketone. However, using 3,3,5,5-tetramethylcyclohexanone, 1, as a substrate, the values we get for the ratio k^H/k^D in several reactions [2], *are not consistent* with the usually admitted chair-like structure of this compound [3] ; our results compelled us to assume a twist-boat transition state, which raises the question as to know whether the chair conformation is, or is not, the reactive conformation of compound 1 [4].

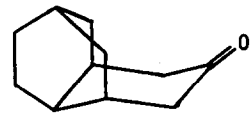
In order to try to shed some light on this problem we have synthesised rigid models of compound 1, having the same steric hindrance as the 3,3,5,5-tetramethylcyclohexanone in the chair conformation.

We have synthesised two such models, - the tricyclo [5,2,1,$0^{2,7}$] decane-5-one, 2, and the tricyclo [5,3,1,$0^{3,8}$] undecane-5-one, 2' - the former compound having been prepared in order to appreciate the effect of the internal strain on the reactivity.

2

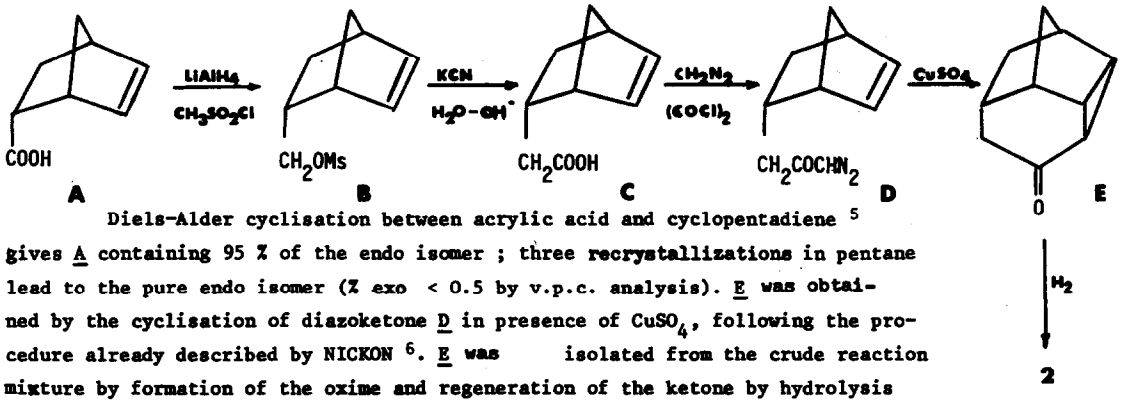


1



2'

Product 2 has been obtained by the reaction sequence shown on the following scheme.



Diels-Alder cyclisation between acrylic acid and cyclopentadiene [5] gives A containing 95 % of the endo isomer ; three recrystallizations in pentane lead to the pure endo isomer (% exo < 0.5 by v.p.c. analysis). E was obtained by the cyclisation of diazoketone D in presence of $CuSO_4$, following the procedure already described by NICKON [6]. E was isolated from the crude reaction mixture by formation of the oxime and regeneration of the ketone by hydrolysis with a sodium bisulfite solution [7].

Column chromatography (C_6H_6) gave us E in a pure state as an odorous liquid. (I.R. CCl_4 : 1700 cm^{-1} ; N.M.R. CCl_4 : cyclopropanic protons at δ : 1.25). D.N.P. (m.p. 210-211° ; Anal. Calcd for $C_{16}H_{16}N_4O_4$: C, 58.50 ; H, 4.90 ; N, 17.10 Found : C, 58.33 ; H, 4.90 ; N, 16.95).

The hydrogenation of E over 10 % Pd/C in Ethyl Acetate yields a white solid 2 (m.p. 111-112°) (I.R. CCl_4 : 1720 cm^{-1} ; N.M.R. CCl_4 ; spectrum shows no cyclopropanic protons). D.N.P. (m.p. 193-193°5 ; Anal : Calcd for $C_{16}H_{18}N_4O_4$: C, 58.18 ; H, 5.49 ; N, 16.96. Found : C, 58.22 ; H, 5.43 ; N, 16.95).

Model compound 2' was prepared in a similar manner, except for the Diels-Alder reaction and the separation of the endo adduct. We used cyclohexadiene and methylacrylate for the cyclisation reaction and we have separated the endo isomer only at the C' stage [8]. Following steps were identical to those used in the synthesis of 2.

Spectral properties of E' are in good agreement with those given for the same product obtained by another method [9].

Semicarbazone (m.p. 212-213°) D.N.P. (m.p. 210-211° ; Anal, Calcd. for $C_{17}H_{18}N_4O_4$: C, 59.64 ; H, 5.30 ; N, 16.36 Found : C, 59.63 ; H, 5.36 ; N, 16.60). Hydrogenation of E' gives a white solid 2' (m.p. 60-61°). I.R. CCl_4 : 1709 cm^{-1} ; N.M.R. CCl_4 δ 0.9 (m) - δ 2.6 (m). D.N.P. (m.p. 199.5-200° ; Anal. Calcd. for $C_{17}H_{20}N_4O_4$: C, 59.29 ; H, 5.85 ; N, 16.27. Found : C, 59.34 ; H, 5.86 ; N, 16.26).

The ^{13}C N.M.R. spectra show respectively seven and eight kinds of carbon atoms for 2 and 2'. This is only consistent with the existence of a plane of symmetry in both molecules and proves unambiguously that the cyclopropyl ring has been opened as indicated on the scheme.

We plan to run on 2 and 2' the same kinetic measurements we have already done on 1 ; moreover the analysis of reduction products of 2' will give us the percent of equatorial and axial attack of metal hydrides on a structurally analogous compound of 3,3,5,5-tetramethyl-cyclohexanone, for which the percent of attack is not directly obtainable for obvious reasons.

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