SYNTHESIS OF TRANS-(35,45)-DIBENZYLOXYCYCLOPENTANONE

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Abstract : The 1-cyano-1-thiophenylcyclopentane derivative 1, obtained from (R,R)-(+)-tartaric acid, has been converted into a number of derivatives including the important trans-(3S,4S)dibenzyloxycyclopentanone 2 in 45% overall yield.

In a preceeding Letter¹ we described the synthesis of 1-cyano-1-thiophenyl-3,4dibenzyloxycyclopentane <u>1</u> from (R,R)-(+)-tartaric acid. The preparation of the title compound is disclosed in this communication.

Having obtained the desired masked cyclopentanone 1, we examined first the transformation of 1 to 2. During these studies, a variety of potentially useful cyclopentanoids were prepared as shown in the Scheme. Among these intermediates the nitrile 3, the sulfone 10 and the hydroxy-amide 15 were particularly interesting. We anticipated that they could undergo oxidative decyanation, 2 oxidative desulfonylation³ and oxidative rearrangement to the elusive cyclopentanone 2.

Compound <u>3</u> was first obtained inefficiently (Scheme) by Raney nickel desulphurization. However, treatment of α -(phenylthio)nitrile <u>1</u> with n-butyl-lithium in ether (1 eq.) at -70°C over 5 min gave the intermediate lithiocyclopentane <u>5</u> and <u>n</u>-butyl phenyl sulphide. Quenching the carbanion <u>5</u> with acetic acid or allyl bromide yielded the cyanide 3 or allyl derivative 6 in 75% and 55% yield respectively.

The ready formation of $\underline{3}$ and $\underline{6}$ suggested that the transformation of $\underline{1}$ to $\underline{2}$ could be effected in a "one pot" procedure.

Accordingly 5 was treated with molecular oxygen and the resulting α -hydroperoxy nitrile was reduced to the cyanohydrin 7. With aqueous base the desired ketone 2 was formed in 17% overall yield from 1; $[\alpha]_D^{25}$ -11° (0.8, CHCl₃), its <u>p</u>-nitrophenylhydra-zone; m.p. 89-90°C, $[\alpha]_D^{25}$ -29° (c 1.14, CHCl₃).

No significant improvement in the yield (20% of 2) was observed on replacing molecular oxygen by the Mimoun reagent. $\!\!\!\!\!\!^4$

Due to the low yield for the conversion of $\underline{1}$ to $\underline{2}$, we decided to examine the oxidative desulphonylation of the readily accessible sulphone $\underline{10}$, efficiently prepared in an overall yield of 95% from 1 (Scheme).



 $\frac{\text{Scheme.}}{\text{PhCH}_3}, \text{ 80°C, 15h; } \text{ 0} \text{ H}_0, \text{NaHCO}_3, \text{PhCN, 20°C, 18h; } \text{ e} \text{ NBu-Li, 1}_{eq}, \text{ eher, -70°C, 5} \text{ min;} \\ \text{PhCH}_3, \text{ 80°C, 15h; } \text{ d} \text{ H}_0, \text{ NaHCO}_3, \text{PhCN, 20°C, 18h; } \text{ e} \text{ nBu-Li, 1}_{eq}, \text{ eher, -70°C, 5} \text{ min;} \\ \text{f) acetic acid; } \text{g} \text{ 0}_2, \text{ 30 min, -30°C, SnCl}_2/\text{HCI 2M, 0°C, 30 min; } \text{ h} \text{ aq. NaOH, ether, 15 min;} \\ \text{i) allyl bromide; } \text{j} \text{ MCPBA 3.5 eq, CH}_2(\text{Cl}_2, \text{RT, 2h; } \text{ k}) \text{ NaOH/H}_0/\text{MeOH, RT, 3h; } \text{ l} \text{ tBuOK, PhCH}_3, \\ \text{80°C, 3h30; m} \text{ lithium dicyclohexylamide, 6 eq; n} \text{ MoO}_5, \text{HMPA, Pyr, 3 eq, THF, -78°C, 3 min,} \\ \text{aq. sodium sulfite; o} \text{ LiBH(C}_2\text{H}_5)_3, \text{ THF, reflux, 4h; p} \text{ Pb(OAc)}_4, \text{ PhCH}_3, \text{ reflux, 0.5h.} \\ \end{array}$

Treatment of the α -sulphonyl carbanion <u>11</u> in THF (generated from lithium dicyclohexylamide (6 eq.)) with molybdenum peroxide (MoO₅, HMPA, Pyr) in THF at -78°C, for 3 mins, followed by quenching of the reaction mixture with saturated aqueous sodium sulfite yielded the ketone <u>2</u>, identical in every respect with the ketone obtained from <u>1</u> by oxidative decyanation (35% overall). Finally in the third approach to prepare <u>2</u>, we now turned our attention to intermediate <u>15</u>. The synthesis of <u>15</u> again started from 1 (Scheme).

The transformation of $\underline{15}$ to $\underline{2}$ was satisfactorily accomplished (87%) on reflux of $\underline{15}$ in toluene solution with 2 eq. of lead tetraacetate over 0.5 hrs.⁵

In summary, the preparation of cyclopentanoids carrying functional groups has been demonstrated to be feasible in a few steps from readily available tartaric acid.

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- All new compounds described in this work have been fully characterized by means of high-resolution mass spectra, 200 or 400 MHz⁻¹ H NMR, IR-spectra, [α]_D and combustion analysis.

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