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SYNTHESIS OF TETRAHYDRO-5H-DIBENZ[b,d]AZEPIN-6(7H)-ONE

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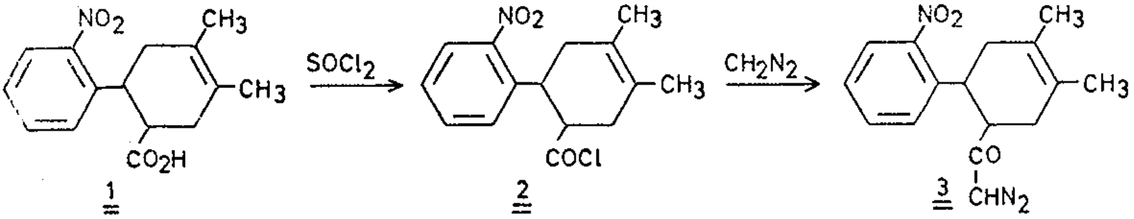
9,10-Dimethyl-7a,8,11,11a-tetrahydro-5H-dibenz[b,d]azepin-6(7H)-one is synthesized in six steps starting from o-nitrocinnamic acid.

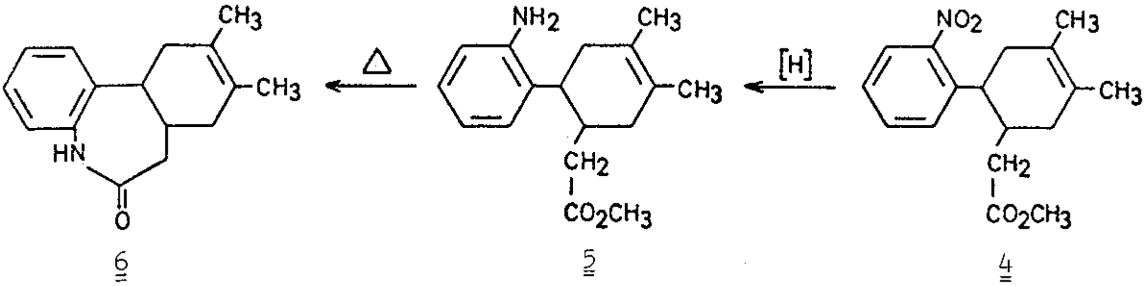
There are few examples of dibenz[b,d]azepines known$^{1-4)}$. Since we are interested in different derivatives of this heterocyclic system, we have tried to synthesize dibenz[b,d]azepin-6-ones 6 as follows$^{5)}$.

Beginning with trans-o-nitrocinnamic acid and 2,3-dimethylbutadiene, we could obtain 70% yield of phenylcyclohexenic acid 1, m. p. 176°, in a Diels-Alder addition. To our surprise, the reaction at 130° and for the time of 62 h takes place best in p-xylene as a solvent, whereas the yield decreases rapidly in o-xylene or in a mixture of o/p-xylenes. This observation shows how sensitive this reaction is to changes in reaction parameters. This fact had already been stated years before for the addition of butadiene to o-nitrocinnamic acid$^{6)}$. Although in previous experiments high yields of the Diels-Alder adduct of isoprene with o-nitrocinnamic acid could be obtained$^{6)}$, we were not able to repeat such a yield under comparable conditions. The conversion of the carboxylic acid 1 to the acid chloride 2, m. p. 75°(from ether), i. r. ($CHCl_3$) $\nu_{C=O}$ 1780 cm^{-1}, ν_{NO_2} 1520 and 1350 cm^{-1}, could easily be attained with thionyl chloride.



In order to achieve a chain lenghtening according to Arndt-Eistert reaction, the acid chloride 2 was reacted with a solution of diazomethane in ether and converted into the diazoketone 3, m. p. 137°, with a yield of 60%. In i. r. spectra ($CHCl_3$) of 3, rather intense bands could be observed at 2105 (ν_{N_2}), 1630 ($\nu_{C=O}$), 1520 and 1360 cm^{-1} (ν_{NO_2}); n. m. r. ($CDCl_3$) δ 4.8 (1H, s, $-CHN_2$).

The following Wolff rearrangement of the diazoketone 3 was carried out in methanol with silver benzoate, dissolved in triethylamine. Methyl ester 4 could thus be obtained with a yield of 65%, m. p. 81°; i. r. ($CHCl_3$) $\nu_{C=O}$ 1725 cm^{-1}, ν_{NO_2} 1520 and 1350 cm^{-1}; n. m. r. ($CDCl_3$) δ 3.6 (3H, s, $-CO_2CH_3$), 2.3 (2H, m, $-\underline{CH_2}-CO_2CH_3$). In the next step, this methyl ester 4 was reduced in ethanolic solution with Raney nickel and hydrazine to the amino acid ester 5, m. p. 75° (from ethanol), without effecting the C=C-double bond; n. m. r. ($CDCl_3$) δ 3.45(5H, s, $-CO_2CH_3$ and $-NH_2$), 2.5 (2H, m, $-\underline{CH_2}-CO_2CH_3$); i. r. ($CHCl_3$) ν_{NH_2} 3450 and 3350 cm^{-1}, $\nu_{C=O}$1720 cm^{-1}. During this reaction, a hydrazinolysis of the ester group in 4 did not yet take place.



In opposition to the usual easy intramolecular cyclization of amino acid esters, this ester 5 does not show such a distinct tendency. Only after 3 h of heating at a temperature of 180° did the expected cyclization to give dibenz[b,d]azepin-6-one 6, m. p. 219° (from ethanol/water), take place. In the n. m. r. spectra ($CDCl_3$) of 6 the methylene protons next to the carbonyl group appear as multiplet at δ 2.5. As expected, we found the amide proton (-NH-CO-) at δ 8.1; i. r. ($CHCl_3$) ν_{NH} 3370 and $\nu_{C=O}$ 1655 cm^{-1}. The two olefinic methyl groups of 6 as well as of the compounds 1 - 5 are the cause of the sharp singlet at δ 1.65 which is superimposed on the broad multiplet of the alicyclic protons.

Analogously to similar reactions, the Diels-Alder addition should proceed stereospecificly[7,8] to 1 and the cyclohexene ring should be connected trans with the azepine system in 6, provided that the configuration has not been changed during the reaction sequence.

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