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

Mohammed N. Samimi, Udo Kraatz, and Friedhelm Korte*

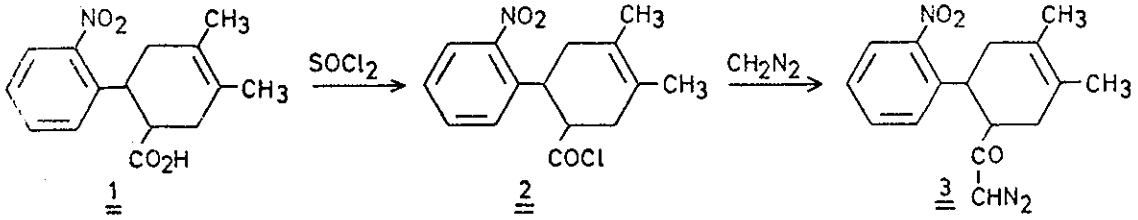
Institut für Chemie der TU-München und Institut für ökologische Chemie der Gesellschaft für Strahlen- und Umweltforschung mbH München, D-8050 Freising-Weihenstephan, Am Löwentor

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-dimethyl-butadiene, 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

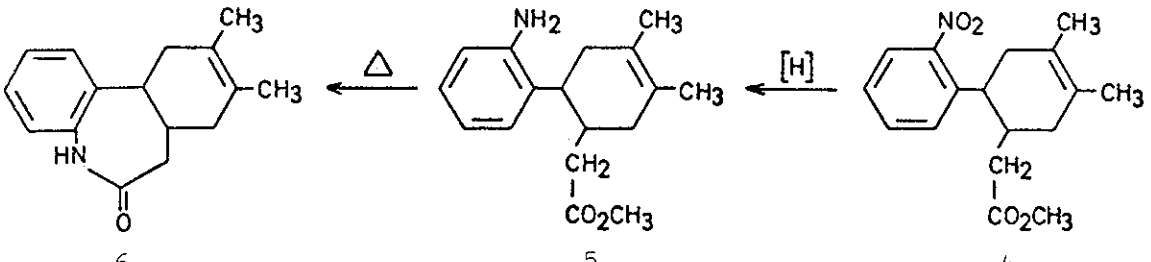
of the carboxylic acid 1 to the acid chloride 2, m. p. 75°(from ether), i. r. ($CHCl_3$) $\nu_{C=O}$ 1780 cm^{-1}, ν_{NO_2} 1520 and 1350 cm^{-1}, could easily be attained with thionyl chloride.



1 2 3

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 80%. 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.



6 5 4

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.

REFERENCES

1. G. R. Proctor, Chem. and Ind. 1960, 408.
2. W. C. Peaston and G. R. Proctor, J. Chem. Soc. (C), 1968, 2481.
3. H. Erdtman and L. Malmborg, Acta Chem. Scand., 1970, 24, 2252.
4. R. F. C. Brown and M. Butcher, Tetrahedron Letters 1971, 667.
5. Taken from the thesis M. N. Samimi, University Bonn, 1975.
6. E. C. Taylor and E. J. Stroiny, J. Amer. Chem. Soc., 1956, 78, 5104.
7. K. Alder, M. Schumacher and O. Wolff, Liebigs Ann. Chem., 1949, 564, 79.
8. J. G. Martin and R. K. Hill, Chem. Rev., 1961, 61, 537.

Received, 22nd June, 1976