SYNTHESIS OF 6,7-DIHYDRO-5H-DIBENZ[*c,e*]AZEPINE

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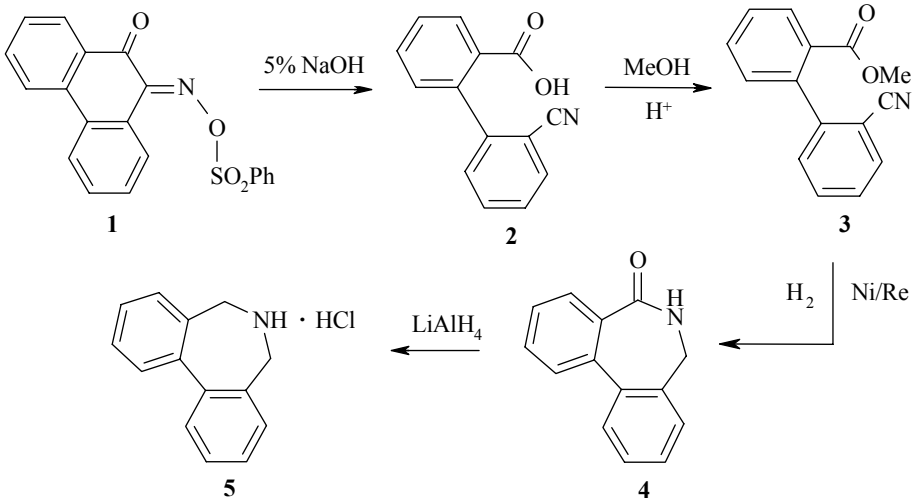
Continuing our investigation of hetero- and benzazepines [1-3] we encountered an undeveloped synthon 6,7-dihydro-5H-dibenz[*c,e*]azepine (**5**). This was first obtained in low yield from *o,o*'-dibromoethyldiphenyl and ammonia [4] or by a photochemical route [5] from N-benzyl-N-(2-iodobenzyl)amine but the yield did not exceed 20%. However, thanks to this effort a pharmacological examination of azepine **5** and its derivatives has shown that derivatives with substituents in position 6 (especially 6-allyl) (azapetine) show sympatholytic activity [4]. Later, a selective α-adrenoblocking action was shown for azapetine and its derivatives [6, 7].

This served as an stimulus in searching for a convenient route to azepine **5** and its derivatives. By analogy with the methods we have previously developed for the preparation of azepine structures [1-3] a reductive cyclization of methyl 2-(2-cyanophenyl)benzoate **3** with hydrogen over Raney nickel gave a 60% yield of 6,7-dihydro-5H-dibenz[*c,e*]azepin-7-one (**4**). The lactam **4** was readily soluble in ether and was reduced by a general method using lithium aluminium hydride in ether to give a good yield of the base **5**.

As shown in the scheme we have been able to separate in the initial stages the O-benzenesulfonate monooxime of 9,10-phenanthrenequinone (**1**) and to carry out its fission to 2-(2-cyanophenyl)benzoic acid (**2**) and then to its methyl ester **3**.



1 **2** **3** **4** **5**

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The ^{1}H NMR spectrum was recorded on a Perkin-Elmer (90 MHz) spectrometer using DMSO-d_6 and with HMDS as internal standard. UV Spectra were taken on a Specord UV-vis spectrophotometer using 95% ethanol. Monitoring of the reaction course and purity of the compounds obtained was carried out by TLC on Alufol plates with iodine vapor to reveal the spots.

O-Benzenesulfonate monooxime of 9,10-phenanthrenequinone (1) was prepared by our previously reported method [8] and had mp 140-141°C.

2-(2-Cyanophenyl)benzoic acid (2) was prepared by method [9] and had mp 171°C.

Methyl 2-(2-cyanophenyl)benzoate (3) was obtained by method [10] and had mp 78°C.

6,7-Dihydro-5H-dibenz[*c,e*]azepin-7-one (4). The catalyst (skeletal nickel prepared from nickel aluminium alloy (10 g)) was placed in a round bottomed flask adapted for catalytic hydrogen reduction and a solution of compound **3** (11.85 g, 50 mmol) in methanol (100 ml) was added rapidly. The reaction flask was sealed with a tube for delivery of gases and hydrogen was passed through several times. After shaking for 3.5-4 h approximately 2.3 l of hydrogen had been absorbed. The solution was decanted and the catalyst was washed with methanol (2 × 20 ml). The combined alcohol solution was filtered, methanol was distilled off, and the residue was recrystallized from ethanol to give the product (6.5 g, 60%) with mp 190-191°C and R_f 0.76 (benzene–ethanol, 6: 1). Found, %: C 80.16; H 5.03; N 6.45. $C_{14}H_{11}NO$. Calculated, %: C 80.38; H 5.26; N 6.69. UV spectrum, λ_{max}, nm (log ε): 246 (4.17), 287 (3.49).

6,7-Dihydro-5H-dibenz[*c,e*]azepine hydrochloride (5). A solution of compound **4** (6.27 g, 30 mmol) in dry 1,4-dioxane was added to a solution of lithium aluminium hydride (1.3 g) in dry ether (300 ml) and refluxed for 5 h. It was then carefully decomposed with ethyl acetate and water, basified strongly with concentrated aqueous NaOH solution, the ether layer was separated, and the aqueous layer was extracted several times with ether. The ether extracts were combined and dried over sodium sulfate. Anhydrous hydrogen chloride was passed through the ether solution to give compound **5** as the hydrochloride (3.5-3.7 g, 50-54%) with mp 283-285°C (mp 285-286°C [4]). ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.4-7.7 (8H, m, arom.); 3.75 (4H, s, 2 CH_2); 3.25 (1H, s, NH). Found, %: C 72.29; H 5.32; Cl 15.11; N 5.81. $C_{14}H_{13}N.HCl$. Calculated, %: C 72.57; H 5.61; Cl 15.33; N 6.04.

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