New Compounds

Synthesis of an Allylic Alcohol and Chloride in the Nortriptyline Series

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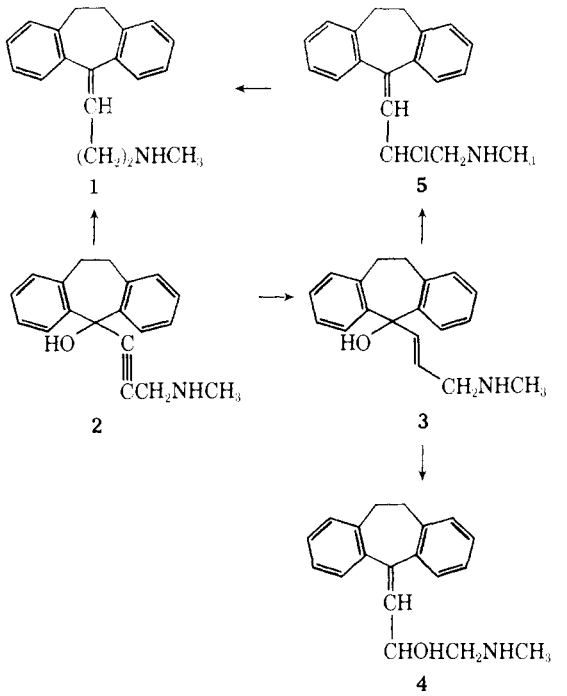
The conventional synthesis of nortriptyline (**1**) from the acetylenic carbinol **2** by catalytic reduction and dehydration has been described.[1] Partial hydrogenation of **2** yields the vinyl carbinol **3**.[1] I wish to report the rearrangement of **3** to the allylic alcohol **4** and to the chloride **5** and the hydrogenolysis of **5** to **1**.

The tertiary vinyl carbinol **3** undergoes a very facile rearrangement in the presence of acid. The product of this rearrangement with aq HCl is **4**, whereas with dry HCl in $CHCl_3$ the product is **5**. Catalytic hydrogenolysis of **5** affords **1** in good yield. Compound **4** and the corresponding ketone **6**, have been described as antidepressant and anxiolytic agents.[2]



Experimental Section

Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values. Melting points were taken in an open capillary and are uncorrected.

5-(2-Hydroxy-3-methylaminopropylidenyl)-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene (4).—A soln of 5-hydroxy-5-(3-methylaminopropenyl)-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene (**3**) (27.9 g, 100 mmoles) in 100 ml of 3 *N* HCl was prepared by warming the mixture gently. After 1 hr at room temp the mixture was made basic with 50% NaOH. The product was extracted into 1 l. of Et_2O, washed with H_2O, dried (Na_2SO_3), filtered, and evaporated *in vacuo*. Two recryst from C_6H_6–Skelly B (1:5) afforded **4** (20 g of yellow rosettes): mp 110–112°; uv max (95% EtOH) 242 mμ (ε 14,500). *Anal.* ($C_{19}H_{21}NO$) C, H, O.

An attempt to prepare **5** from **4** with HCl in $CHCl_3$ under the same conditions which gave **5** from **3** afforded only **4** as the HCl salt. Thus, a soln of **4** (2.8 g, 10 mmoles) in $CHCl_3$ (100 ml) was treated with anhyd HCl. The resultant ppt was collected by filtration, washed with Et_2O, dried (Na_2SO_3), and recrystd from EtOH–$(CH_3)_2CO$–Et_2O (1:1:10). The product was **4**·HCl (2.0 g), mp 166–167°. *Anal.* ($C_{19}H_{22}ClNO$) C, H, N.

5-(2-Chloro-3-methylaminopropylidenyl)-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene·HCl (5).—A soln of 5 g (18 mmoles) of **3** in 200 ml of warm (40°) $CHCl_3$ was satd with HCl gas. The reaction mixture was concd *in vacuo* to *ca.* 0.5 vol and was poured into 400 ml of dry Et_2O. Crude **5** was collected by filtration. Two recrystn from $CHCl_3$–Et_2O (1:5) gave **5** (5.2 g, 87%): mp 141–143° dec; uv max (95% EtOH) 243 mμ (ε 15,000). *Anal.* ($C_{19}H_{21}Cl_2N$) C, H, Cl.

Nortriptyline·HCl (1).—A 3.4-g (10 mmoles) sample of **5** was added to a prereduced mixture of NaOAc (3.3 g, 40 mmoles), PtO_2 (0.1 g), and glacial AcOH (200 ml). The reaction mixture was shaken with H_2 at 3.16 kg/cm² until 10 mmoles had been consumed. Pt was removed by filtration, and AcOH was distilled *in vacuo*. The residue was treated with 10 ml of 50% NaOH soln. The pptd 1 (free base) was extd into 500 ml of Et_2O, washed twice with 25-ml portions of H_2O, dried (Na_2SO_4), and filtered. The filtrate was treated with HCl gas until pptn of 1·HCl was complete. The product was collected by filtration and recrystd twice from EtOH–Et_2O (1:10) giving pure **1**·HCl, mp 206–208°, identical with an authentic sample of nortriptyline·HCl by mmp and by ir, uv, and nmr spectra. *Anal.* ($C_{19}H_{22}ClN$) C, H, Cl, N.

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(1) L. R. Peters and G. F. Hennion, *J. Med Chem.*, **7**, 390 (1964).

(2) Soc. Ind. pour la Fab. des Antibiotiques, Belgium Patent 730,094 (1969) (Derwent 39,820).

Acylthiazolidines

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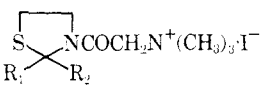
In a search for lipotropic agents based on the thiazolidine ring[1a,b] we have synthesized a series of new compounds of the general formulas in Tables I and II. The

TABLE I



No.	R_1	R_2	Mp, °C	Formula	—Analyses for I⁻— Calcd	Found
1	H	H	dec	$C_8H_{17}INOS$	40.38	39.45
2	H	C_6H_5	dec	$C_{14}H_{21}INOS$	33.54	32.98
3	H	$CH_3(CH_2)_6$	dec	$C_{15}H_{31}INOS$	31.69	31.10
4	H	4-ClC_6H_4	dec	$C_{14}H_{20}ClINOS$	30.74	30.15
5	H	4-$CH_3OC_6H_4$	dec	$C_{15}H_{23}INO_2S$	31.07	30.20

(1) (a) P. Maitre and A. Cier, *Sem. Hop.*, **39**, 2173 (1963). (b) D. A. Carneiro Filho and D. P. Brandao Egidio, *Hospital (Rio de Janeiro)*, **75**, 1187 (1969); *Chem. Abstr.*, **72**, 11312 (1970).