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TETRAHYDROCARBAZOLE DERIVATIVES

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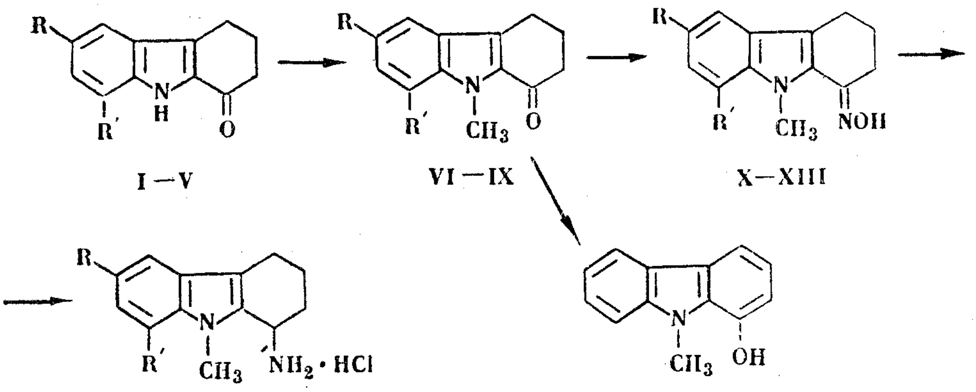
Fischer's method is used to synthesize a number of 1-keto-1, 2, 3, 4-tetrahydrocarbazole and 1-keto-1, 2, 3, 4-tetrahydro-9-methylcarbazole derivatives. The oximes of these ketocarbazoles are converted to the corresponding 1-amino-1, 2, 3, 4-tetrahydro-9-methylcarbazole hydrochlorides. 1-hydroxy-9-methylcarbazole is obtained by dehydrogenating a ketocarbazole derivative with palladium on barium sulfate.

A number of derivatives of 1-keto-1, 2, 3, 4-tetrahydrocarbazole (I-V) are prepared by cyclization, Fischer's method, from cyclohexane-1, 2-dione monoarylhydrazines [3]. The properties of the carbonyl group in these compounds are considerably repressed, obviously because of strong hydrogen bonding. 1-keto-1, 2, 3, 4-tetrahydrocarbazole does n not exhibit the usual reactions of carbonyl compounds, though the corresponding N-methyltetrahydrocarbazolones (VI-IX) readily give oximes (X-XIII) with hydroxylamine.

Reduction of the oximes with sodium in alcohol gives 1-aminotetrahydrocarbazole derivatives (XIV-XVI). Dehydrogenation of N-methyl-1-keto-1, 2, 3, 4-tetrahydrocarbazole (VI) over a palladium catalyst gives N-methyl-1-hydroxycarbazole (XVII).



XIV—XVI

XVII

I, VI, X, XIV: R=R'=H; II, VII, XI: R=CH_3, R'=H; III, VIII, XII, XV: R=OCH_3, R'=H; IV, IX, XIII, XVI: R=H, R'=CH_3; V: R=H, R'=OCH_3.

Experimental

1-Keto-1, 2, 3, 4-tetrahydrocarbazole (I). 1500 ml 2.5 N sulfuric acid were added to a well-dispersed suspension of 40 g (0.2 mole) cyclohexanone-1, 2-dione monophenylhydrazone in 500 ml alcohol.

This reaction mixture was refluxed for 1 hr 30 min, using good stirring, after which the whole was cooled with ice. The crystals separating were filtered off, and washed with a small amount of cold methanol. Yield of I, 25 g. Table I gives mp and IR spectrum absorption band position.

The other derivatives of 1-keto-1, 2, 3, 4-tetrahydrocarbazole were synthesized similarly (Table 1).

1-Keto-1, 2, 3, 4-tetrahydro-9-methylcarbazole (VI). A saturated aqueous solution of 30 g sodium hydroxide was added all in one lot to 30 g (0.16 mole) carbazole I dissolved in 180 ml acetone, followed by 30 ml dimethyl sulfate added gradually over 5 min, with good stirring. Then the reaction mixture was stirred 45 min at room temperature, cooled, and then water gradually added until the oily layer first separated out, crystallized. The crystals were separated and recrystallized from acetone, using a small amount of activated carbone. Yield of VI 22.8 g. Table 2 gives mp and IR spectrum fundamental absorption bands for VI and similar compounds VII-IX prepared.

Oxime of 1-keto-1, 2, 3, 4-tetrahydro-9-methylcarbazole (X). 5.2 g (0.26 mole) VI and 3.63 g (0.052 mole) hydroxylamine hydrochloride were added to a cooled solution of 4.18 g (0.10 mole) sodium hydroxide in 60 ml ethanol, the whole refluxed for 30 min, cooled to room temperature, and poured onto ice. The colorless crystals which separated

TABLE 1

1-Keto-1, 2, 3, 4-Tetrahydrocarbazole Derivatives (I-V)

Compound no.	Compound	mp, °C	IR spectrum (in vaseline) cm^{-1}	Formula	Found%			Calculated %			% Yield
					C	H	N	C	H	N	
I	1-keto-1, 2, 3, 4-tetrahydro-6-methylcarbazole	170–171 [2]	3300 (NH) 1645 (CO) 1545 (NH)	$C_{12}H_{11}NO$	—	—	—	—	—	—	68
II	1-keto-1, 2, 3, 4-tetrahydro-6-methylcarbazole	194–195 [3]	3290 (NH) 1645 (CO) 1545 (NH)	$C_{13}H_{13}NO$	—	—	—	—	—	—	76.2
III	1-keto-1, 2, 3, 4-tetrahydro-6-methoxycarbazole	215—216	3280 (NH) 1645 (CO) 1540 (NH)	$C_{13}H_{13}NO_2$	72.5 72.29	6.16 6.07	—	72.53	6.08	—	42
IV	1-keto-1, 2, 3, 4-tetrahydro-8-methylcarbazole	165–166 [4]	—	$C_{13}H_{13}NO$	—	—	—	—	—	—	65
V	1-keto-1, 2, 3, 4-tetrahydro-8-methoxycarbazole	120—121	3310 (NH) 1660 (CO) 1550 (NH)	$C_{13}H_{13}NO_2$	73.13 73.34	6.07 5.92	6,9 7,18	72.54	6.09	6.51	37

TABLE 2

9-Methylcarbazole Derivatives (VI-IX)

Compound no.	Compound	IR spectrum (in vaseline) cm^{-1}	mp, °C	Formula	Found %			Calculated %			% Yield
					C	H	N	C	H	N	
VI	1-keto-1, 2, 3, 4-tetrahydro-9-methylcarbazole	1650 (CO) 1530 (C=C)	104 [5]	$C_{13}H_{13}NO$	—	—	—	—	—	—	70
VII	1-keto-1, 2, 3, 4-tetrahydro-6, 9-dimethylcarbazole	1650 (CO) 1535 (C=C)	112—113	$C_{14}H_{15}NO$	78.81 78.39	6.65 6.93	— —	78.84	7.10	—	Quantitative
VIII	1-keto-1, 2, 3, 4-tetrahydro-6-methoxy-9-methylcarbazole	1655 (CO) 1520 (C=C)	85.5—86.5	$C_{14}H_{15}NO_2$	73.20 73.20	6.34 6.71	— —	73. 36	6.55	—	Quantitative
IX	1-keto-1, 2, 3, 4-tetrahydro-8, 9-dimethylcarbazole	1650 (CO) 1535 (C=C)	140.5—141	$C_{14}H_{15}NO$	78.70 79.05	6.91 7.09	6.49 6.34	78.84	7.10	6.59	97

TABLE 3

Substituted 9-Methylcarbazole Oximes

Compound No.	Oxime	IR spectrum (in vaseline) cm^{-1}	mp, °C	Formula	Found %			Calculated %			% Yield
					C	H	N	C	H	N	
X	1-keto-1, 2, 3, 4-tetrahydro-9-methylcarbazole	3280 (=N—OH) 1605 (C=N)	185—186	$C_{13}H_{14}N_2O$	72.79 72.98	6.47 6.57	13.12 13.21	72.86	6.54	13.05	98.2
XI	1-keto-1, 2, 3, 4-tetrahydro-6 9-dimethylcarbazole	3310—3290 (=N—OH) 1610 (C=N)	175—176	$C_{14}H_{16}N_2O$	74.05 74.15	6.65 7.47	— —	73.64	7.06	—	86.3
XII	1-keto-1, 2, 3, 4-tetrahydro-6-methoxy-9-methylcarbazole	3430 (=N—OH) 1620 (C=N)	173—174	$C_{14}H_{16}N_2O_2$	69.30 69.78	6.76 6.67	11.41 11.58	68.85	6.55	11.47	93.6
XIII	1-keto-1, 2, 3, 4-tetrahydro-8, 9-dimethylcarbazole	3300—3280 (=N—OH) 1625 (C=N)	178—179	$C_{14}H_{16}N_2O$	73.59 73.78	7.07 7.00	12.09 11.98	73.64	7.06	12.27	99

were filtered off, washed with water, dried in a vacuum desiccator and recrystallized from alcohol. Table 3 gives mp, elementary analysis data and positions of the main IR absorption spectrum bands for X and similarly synthesized oximes XI-XIII.

1-amino-1, 2, 3, 4-tetrahydro-9-methylcarbazole hydrochloride (XIV). A 3-necked flask is fitted with an effective stirrer and a Dimroth reflux condenser, and a solution of 7.14 g (0.033 mole) oxime X in 340 ml absolute alcohol put in it. Then 34 g (1.48 g-atom) sodium, cut in large pieces, were added over 5-10 min, the reaction mixture stirred and heated for 15-25 min until the sodium completely dissolved, an equal volume of water added, the alcohol vacuum-distilled off, and the alkaline residue extracted with ether. Dilute hydrochloric acid (1:1) was used to extract the amine from the ether solution. Crystals of the hydrochloride formed in the aqueous layer, and were filtered off and dried. Yield XIV 4.9 g (62.8%) mp 256-258° (from methanol). Found: C 65.81, 66.11, H 7.06, 7.03; N 11.86; 11.60%. Calculated for $C_{13}H_{16}N_2 \cdot HCl$: C 65.96; H 7.19; N 11.84%. IR spectrum (vaseline) : 3040, 1600 cm^{-1} (NH_3^+).

1-amino-1, 2, 3, 4-tetrahydro-6-methoxy-9-methylcarbazole hydrochloride (XV). 4.35 g (0.018 mole) oxime XII, 200 ml absolute alcohol, 20 g (0.87 g-atom) sodium were used in the experiment, which was run using the same conditions as when reducing the oxime X. Aqueous acetic acid was issued to extract the amine from the ether extract, and the aqueous solution was then made alkaline with a concentrated potassium hydroxide solution to liberate the amine, which was then extracted with ether. The ether extract was dried with potassium hydroxide, then to it was added gradually, with ice cooling, an ether solution of hydrogen chloride, precipitating the hydrochloride, XV, which was removed and dried. (The amine resinified if excess ethereal hydrogen chloride was added.) Yield 2.7 g (58.7%), mp 229-231°(from methanol). Found: C 62.68, 62.40; H 7.29, 7.21; N 10.45; 10.40%. Calculated for $C_{14}H_{18}N_2O \cdot HCl$: C 63.03; H 7.18; N 10.50%.

1-Amino-1, 2, 3, 4-tetrahydro-8, 9-dimethylcarbazole hydrochloride (XVI). The experiment used 6.5 g (0.029 mole) oxime XIII, 300 ml absolute alcohol, 30 g (1.30 g atom) sodium, and was carried out as described immediately above. Yield of XVI 5.8 g (78.4%), mp 242-243°(from methanol). Found: N 11.30; 11.43%. Calculated for $C_{14}H_{18}N_2 \cdot \cdot HCl$: N 11.17%.

1-Hydroxy-9-methylcarbazole (XVII). 7 g (0.03 mole) tetrahydrocarbazole derivative VI and 2.6 g 5% $Pd/BaSO_4$ were placed in an rb flask, fitted with a Bunsen valve, and heated at 300-310° for 3 hr 30 min. After cooling the reaction mixture was dissolved in ether, the catalyst separated off, and the ether distilled off. The residue was dissolved in 100 ml methanol, the solution filtered, and the filtrate refluxed with active carbon to remove resinous impurities. Dilution with water then precipitated crystals, which were separated off and dried in a vacuum desiccator. Yield of XVII 3.5 g (50.7%), mp 106-107° (from benzene-petroleum ether). Found: C 79.31, 79.59; H 5.61; 5.81; N 7.31, 7.41%. Calculated for $C_{13}H_{11}NO$: C 79.16; H 5.62; N 7.10%. IR spectrum (vaseline): 3500 cm^{-1} (OH).

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