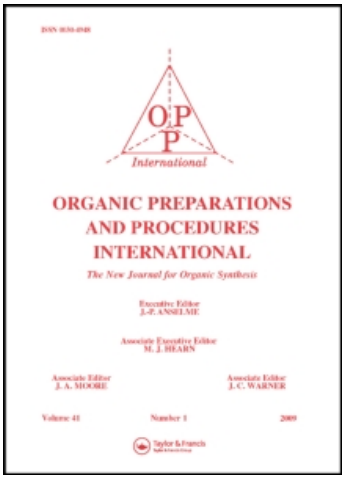

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1,5-BENZOD IAZEP IN-2(1H)-ONES

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1,5-BENZODIAZEPIN-2(1H)-ONES

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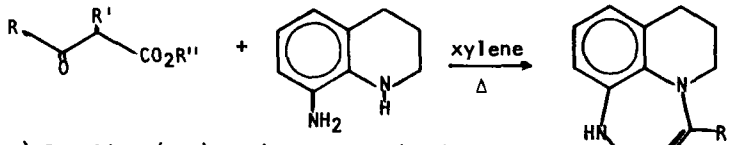
Aromatic 1,2-diamines condense with β-keto esters in xylene to give 1,4-diazepinones (I) and/or the isomeric imidazolidinones (II).[1-5] We now report the synthesis and characterization of five new 1,4-diazepines (equations 1 and 2).



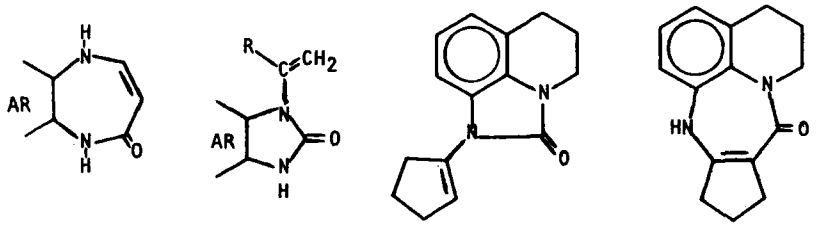
(1)

a) R = R' = $(CH_2)_3$; b) R = R' = $(CH_2)_4$

c) R = 1-adamantyl, R' = H

III

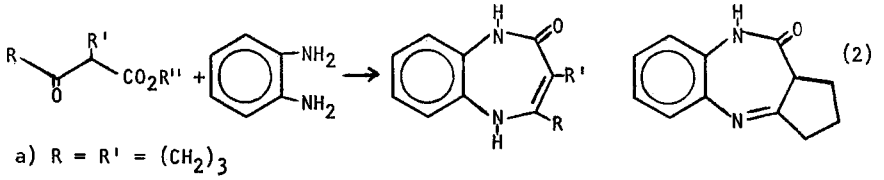
Compound IIIa was isolated in 75% yield directly upon cooling the reaction mixture of 8-amino-1,2,3,4-tetrahydroquinoline[6] and 2-carbalkoxycyclopentanone after 2 hrs. of reflux in xylene. The position of the carbonyl absorption of IIIa at 1632 cm^{-1} ruled out IV as an alternative



I II IV V

structure as imidazolidinones absorb[2-4] at 1701-1718 cm^{-1}, but was consistent with the values (1623-1661 cm^{-1}) reported for I.[1,4] Furthermore, the nmr spectrum of IIIa exhibits an amide peak at δ 7.30 and no vinylic protons. The isomeric diazepine structure V was rendered unlikely by the fact that the hydrogenation product of IIIa (VI) could not be acetylated by acetic anhydride at room temperature; the hydrogenation product of V would in contrast be expected to be readily acetylated under these conditions. This view was further supported by the nmr spectrum of VI, which exhibited an amide resonance at δ 8.03, whereas an amine NH resonance might have been expected further upfield (δ 5 to 3).[7]

Condensation of o-phenylenediamine with β-ketoesters gave the expected diazepines VII in reasonable yields; VIIa had been reported earlier[1] with the same mp. (uncorrected) and a slightly different infrared spectrum (CH_2Cl_2 solution vs. nujol mull). An nmr spectrum of VIIa was consistent with the tautomeric structure VIII in solution, a phenomenon previously observed in this class of compounds.[2]



(2)

a) R = R' = $(CH_2)_3$

b) R = 1-adamantyl, R' = H

VII VIII

EXPERIMENTAL

Melting points were taken on a Unimelt apparatus and are corrected. Infrared spectra were taken as nujol mulls on a Perkin-Elmer 247 spectrophotometer. Ultraviolet spectra were taken on a Cary 15 spectrophotometer. Proton magnetic resonance spectra were obtained in deuterochloroform in part on a Varian A60-A and in part on a Varian T-60 spectrometer, with

tetramethylsilane as internal standard. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

3,4,8,9-Tetrahydro-5H,7H-cyclopenta[c]pyrido[1,2,3-ef]-1,5-benzodiazepin-2(1H)-one (IIIa).—A solution of 8-amino-1,2,3,4-tetrahydroquinoline (255 mg., 1.72 mM) and 2-oxocyclopentanecarboxylic ester[8] (255 mg., 1.72 mM) in 10 ml. of xylene was heated at reflux 2 hrs. After overnight refrigeration of the clear solution, the crystals which had precipitated were collected and washed with xylene-petroleum ether (1:1) to yield 310 mg. (75%) of IIIa, mp. 214-216°.

2a,3,4,5a,8,9-Hexahydro-5H,7H-cyclopenta[c]pyrido[1,2,3-ef]-1,5-benzodiazepin-2(1H)-one (VI).—A solution of 500 mg. of IIIa in 100 ml. of 95% EtOH was shaken in a Parr hydrogenator with 100 mg. of 10% Pd on $CaCO_3$ at 50 psi for 2 hrs. The crude solid was recrystallized from acetone to give 336 mg. of VI, mp. 216-218°. The analytical sample, mp. 217-218°, when mixed with IIIa melted at 85-87°; nmr δ 8.03 (s) 1H, 6.93 (m) 3H, 3.8 (m) 1H, 3.16 (m) 1H, 2.83 (m) 3H, 2.44 (m) 1H, 1.3-2.3 (m) 8H; ir 3175 (NH), 1655 (C=O), 1580, 1200, 819, 776, 741 cm^{-1}.

TABLE I. SPECTRAL DATA OF 1,5-BENZODIAZEPIN-2(1H)-ONES

Compd.	λ_{max}^{MeOH} nm (ε)	ir, cm^{-1}	nmr, δ
IIIa	257 (7660) 273 (7020) 283 (6090)	3180 (NH), 1632 (C=O), 1580, 1248, 1152, 720	7.30 (s) 1H, 6.83 (m) 3H, 3.5 (m) 2H, 2.67 (t) 6H, 1.8-2.0 (m) 4H
IIIb		3200, 3120, 3080, 3050 (NH), 1664 (C=O), 1584, 1285, 1262, 1242, 1144, 844, 740	
IIIc	285 (6170)	3290 (w, NH), 1668 (C=O), 1626, 1274, 741	7.2-7.4 (m, arom.) 4H, 3.8 (m, vinylic) 3H, 2.0 (m, methylene) 4H
VIIa	280 (3400)	3180 (NH), 1660 (C=O), 1640, 770	
VIIb	293 (4610)	3200-3000 (NH), 1620 (C=O), 1032, 760	

TABLE II. PREPARATION OF 1,5-BENZODIAZEPIN-2(1H)-ONES[a,b]

Compd.	mp. (°C)	Yield (%)	Reflux time (hrs)	Elemental Analyses C	H (found)	N
IIIa	214-216	75	2	74.97 (75.26)	6.71 (6.69)	11.66 (11.67)
IIIb	216-218[c]	24	3	75.56 (75.66)	7.13 (7.22)	11.02 (10.90)
IIIc	163-164[e]	52[d]	1	79.00 (78.81(	7.84 (7.82)	8.38 (8.35)
VIIa[f]	189-190[c]	44	1	71.97 (72.09)	6.04 (6.11)	13.99 (13.91)
VIIb	251-252[h]	54[g]	1	77.51 (77.64)	7.53 (7.62)	9.52 ((9.40)

a) The condensations were carried out by heating at reflux solutions of 4 mM each of the diamine and the β-keto ester in 20 ml. of xylene for the time indicated. b) IIIa crystallized upon cooling overnight while crude VIIb was precipitated upon dilution with petroleum ether. All other products were isolated by chromatography on 48 g. of Al_2O_3 and elution by the solvents indicated. c) Crude product eluted from column by benzene and by anh. ether. e) Recrystallized from acetone-water. f) Our uncorrected mp. 182-183° (lit[1] 182-184°). g) A second crop of crude product representing 9% was obtained. h) Recrystallized from acetone.

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