SYNTHESIS OF 1,3-DIHYDRO-5-ALKYL-2H-1,4-BENZODIAZEPIN-2-ONES

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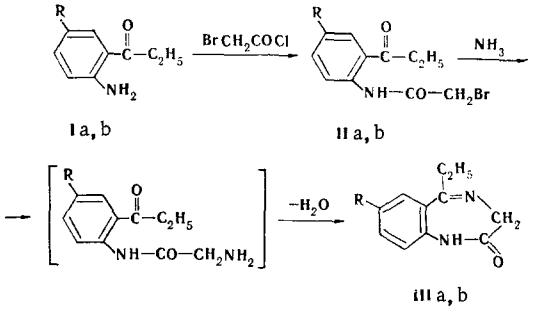
Almost all of the 1,4-benzodiazepin-2-ones described in the literature contain phenyl groups in the 5-position [1]. There is only one paper [2] in which mention is made of the synthesis of 5-alkyl-1,4-benzodiazepin-2-ones.

We have been able to show that 2-aminoacylbenzenes (Ia, b) that contain an aliphatic acyl group (see [3-5] for their preparation) can be readily converted to 1,3-dihydro-5-ethyl-1,4-benzodiazepin-2-ones (III).



I-III a R=H; b R=Cl

For example, bromoacetanilides (IIa, b) are obtained by the action of bromoacetyl chloride on 2-aminoacylbenzenes (Ia, b). The bromine atom in IIa, b is readily replaced by an amino group by treatment with ammonia, and the resulting amino derivatives immediately cyclize to give 1,4-benzodiazepin-2-ones (IIIa, b).*

EXPERIMENTAL

The PMR spectra of CCl_4 solutions were recorded with a JNM H-60 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra of mineral-oil suspensions and CCl_4 solutions were recorded with an IKS-22 spectrometer.

2-(N-Bromoacetyl)aminopropiophenone (IIa). A 6.3-g (0.04 mole) sample of bromoacetyl chloride and 13 ml of 3 N sodium hydroxide solution were added simultaneously at 10° to a solution of 4.5 g (0.03 mole) of amino ketone Ia [3] in 120 ml of dioxane, after which the mixture was stirred at 10° for 1 h and poured into ice water. The aqueous mixture was extracted with methylene chloride, and the extract was washed with water, dried with magnesium sulfate, and concentrated in vacuo to give 6.4 g (80%) of 2-(N-bromoacetyl)aminopropiophenone (IIa) with mp 56-57° [from benzene–petroleum ether (1:3)]. PMR spectrum, δ, ppm:† 1.63 t (3H), 3.34 q (2H), 4.31 s (2H), 7.30-8.30 m (4H). Found: C 49.0; H 4.6%. $C_{11}H_{12}BrNO_2$. Calculated: C 48.9; H 4.5%.

*While this material was being prepared for publication, a German patent appeared in which the same scheme for the synthesis of 1,4-benzodiazepinones was proposed, but for other examples see [6].

†The abbreviations used here and elsewhere are: s is singlet, d is doublet, t is triplet, q is quartet, m is multiplet, and dd is doublet of doublets.

M. V. Lomonosov Moscow State University. N. P. Pirogov Moscow State Medical Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 572-573, April, 1974. Original article submitted November 20, 1973.

4-Chloro-2-(N-bromoacetyl)aminopropiophenone (IIb). This compound (mp 103°) was obtained in 80% yield from amino ketone Ib [4] as described above. PMR spectrum, δ, ppm: 1.59 t (3H), 3.31 q (2H), 4.27 s (2H), 7.83 dd H_4 (J_o = 9 Hz, J_m = 2.4 Hz), 8.12 d H_6 (J_m = 2.4 Hz), 8.98 d H_3 (J_o = 9 Hz). Found: C 43.3; H 3.6%. $C_{11}H_{11}ClBrNO_2$. Calculated: C 43.4; H 3.6%.

5-Ethyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (IIIa). An ether solution of 2.7 g (0.01 mole) of 2-(N-bromoacetyl)aminopropiophenone (IIa) was added at −10 to 0° to 150 ml of a 15% solution of ammonia in methanol, and the mixture was then allowed to stand at room temperature for 24 h. The solvent was then evaporated, and the residue was chromatographed with a column containing activity II aluminum oxide (elution by ethyl acetate) to give 1.2 g (80%) of 1,4-benzodiazepin-2-one IIIa with mp 123-124° (from ethyl acetate). PMR spectrum, δ, ppm: 1.43 t (3H), 3.07 q (2H), 4.32 s (2H), 7.30-7.90 m (4H). IR spectrum: 1692 (C = O), 1610 (C = N), 3215 (N−H) cm^{-1}. Found: C 69.9; H 6.5%. $C_{11}H_{12}N_2O$. Calculated: C 70.2; H 6.4%.

7-Chloro-5-ethyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (IIIb). This compound [1.5 g (75%)] with mp 134° [2] was obtained as described above from 3.1 g (0.01 mole) of 4-chloro-2-(N-bromoacetyl)aminopropiophenone (IIb). The results of analysis for C and H were in agreement with the calculated values.

LITERATURE CITED

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