BROMINATION OF 4,4-DISUBSTITUTED 1,4-DIHYDROPYRIDINES

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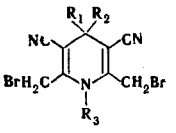
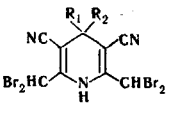
Little study has been devoted to the bromination of 1,4-dihydropyridines. The bromination of carboxylic acid esters of 1,4-dihydropyridines gives tetrabromo derivatives, the structure of which has not been proved [1, 2]. The oxidation of 1,4-dihydropyridines with bromine is indicated in [3].

The methyl groups in the 2 and 6 positions are selectively brominated in the bromination of 4,4-disubstituted 1,4-dihydropyridines. Dibromo derivatives Ia-d are obtained when the reaction is carried out under mild conditions (in chloroform at 30°C).



I a-d



II a-c

I a $R_1=R_2=CH_3$; $R_3=H$; b $R_1=R_2=C_2H_5$; $R_3=H$; c $R_1+R_2=-(CH_2)_5-$; $R_3=H$; d $R_1=R_2=R_3=CH_3$;
II a $R_1=R_2=CH_3$; b $R_1+R_2=-(CH_2)_5-$; c $R_1+R_2=-(CH_2)_4-$

The maxima at 340-360 nm characteristic for dihydropyridines are retained in the UV spectra of Ia-d and IIa-c, and maxima also appear at 245-270 nm. The absorption of nitrile groups at 2210-2200 cm^{-1}, of multiple bonds at 1600-1660 cm^{-1}, and of an NH bond (except for Id) at 3220-3280 cm^{-1} is observed in the IR spectra of Ia-d and IIa-c. Signals from the protons of 2,6-methyl groups are absent in the PMR spectra of Ia-d and IIa-c, but they do contain signals from protons of 2,6-methylene groups at δ 4.10-4.80 ppm (Ia-d) and signals of 2,6-methylidyne protons at δ 6.60-7.30 ppm (IIa-c).

2,6-Bis(bromomethyl)-3,5-dicyano-4,4-dimethyl-1,4-dihydropyridine (Ia). A 0.3-ml (5 mmole) sample of bromine was added to a solution of 0.5 g (2.5 mmole) of 3,5-dicyano-2,4,4,6-tetramethyl-1,4-dihydropyridine in 10 ml of chloroform, and the mixture was heated at 30° for 10 min. The solvent was then removed by vacuum distillation, and the residue was crystallized from ethanol–water (1:1) to give yellow crystals of Ia with mp 147-149°. Found: C 38.3; H 3.2; Br 47.0; N 12.2%. $C_{11}H_{11}Br_2N_3$. Calculated: C 38.4; H 3.2; Br 46.4; N 12.1%. Compounds Ib-d were similarly obtained.

2,6-Bis(dibromomethyl)-3,5-dicyano-4,4-dimethyl-1,4-dihydropyridine (IIa). A 0.6-ml (10 mmole) sample of bromine was added to a solution of 0.5 g (2.5 mmole) of 3,5-dicyano-2,4,4,6-tetramethyl-1,4-dihydropyridine in 10 ml of glacial acetic acid, and the mixture was refluxed for 2 h. It was then filtered, and the solid material was crystallized from ethanol–water (1:2) to give yellow crystals of IIa with mp 167-168°. Found: C 26.4; H 1.9; N 8.4%. $C_{11}H_9Br_4N_3$. Calculated: C 26.2; H 1.7; N 8.3%. Compounds IIb,c were similarly obtained.

LITERATURE CITED

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2. B. Benary, Ber., 51, 567 (1918).
3. O. Mumm and J. Diederischen, Ann., 538, 195 (1939).

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