BROMINATION OF 1-SUBSTITUTED-3,5-DICARBALKOXY-2,6-DIMETHYL-1,4-DIHYDROPYRIDINES

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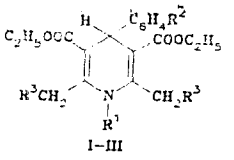
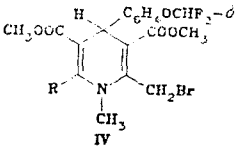
3,5-Dicarbalkoxy-2,6-dimethyl-1,4-dihydropyridines are brominated in the 2-methyl group by treatment with pyridine bromide perbromide or NBS. Subsequent heating causes cyclization to 1,4,5,7-tetrahydrofuro[3,4-b]pyridines [1, 2]. Under mild conditions the 2-bromomethyl derivatives could not always be isolated [3].

In contrast to the previously investigated 1-unsubstituted compounds we have found that the 1-alkyl (aryl, aralkyl) substituted series react with NBS to form the stable 2,6-bis(bromomethyl)-1,4-dihydropyridines I and IVa. These do not cyclize to furopyridines even with prolonged heating. The bromo derivative IVb,c are also obtained with the appropriate reagent ratios.



I–III



IV

I R^3=Br, II R^3=morpholino, III R^3=SCN; I—III a R^1=$CH_2C_6H_5$, b R^2=3-NO_2; b R^1=C_6H_5, R^2=4-Br; c R^1=$C_6H_4OCH_3$-4, R^2=H; IV a R=CH_2Br, b R=CH_3, c R=$CHBr_2$

The UV spectra of I and IV retained maxima characteristic of 1,4-dihydropyridines in the region 337-353 nm. The IR spectra show carbonyl group absorptions in the range 1680-1712 cm^{-1} and the PMR spectra show the 2,6-methylene group signals as quadruplets.

The 2,6-bis(bromomethyl) derivatives react under mild conditions in a nucleophilic substitution reaction with exchange of the bromine atom to form the amino and thiocyano derivatives II and III, their UV, IR, and PMR spectra corresponding to the structures indicated.

The 1-substituted 4-aryl-2,6-bis(bromomethyl)-3,5-dicarbalkoxy-1,4-dihydropyridines I and IVa are obtained by adding NBS (2 mmole) to a solution of the corresponding 2,6-dimethyldihydropyridine (1 mmole), stirring for 1 h at room temperature and standing for 24 h at 0°C. IVb is obtained when 1 mmole and IVc when 3 mmole of NBS are used. The dihydropyridines I and IV are yellowish crystals (from methanol).

Compound, yield (%), mp (°C), and PMR data (in DMSO-d_6 for the CH_2Br groups in δ units (ppm) with J = 11 Hz) are as follows:

Ia, 86, 149-151, 4.71 and 5.26

Ib, 80, 136-138, 3.93 and 4.68

Ic, 81, 124-126, 3.95 and 4.73

IVa, 48, 111-113, 4.76 and 4.91

IVb, 22, 120-122, 4.76 (1H, d) and 4.91 (1H, d)

IVc, 19, 115-117, 4.60 (1H, d) and 5.01 (1H, d), 8.54 (1H, s, $CHBr_2$).

Elemental analytical data for the dihydropyridines agreed with that calculated.

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0009-3122/89/2510-1193$12.50

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SYNTHESIS OF S,S-DIMETHYLSULFILIMINOAZINES

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Nitroso heterocycles are a little known class of compound. One of the few easy (and in this case the only) methods of synthesis is the oxidation of S,S-dimethylsulfilimines [1, 2].

We propose a practical and convenient synthesis of sulfiliminoazines II from the corresponding amino heterocycles I in DMSO using phosphoric anhydride.

$$\underset{\text{Ia-c}}{\text{Het-NH}_2} \xrightarrow{\text{DMSO, } P_2O_5} \underset{\text{IIa-c}}{\text{Het-N=S(CH}_3)_2}$$

I, II a Het = 3,5-dichloro-2-pyridyl; b Het = 3-chloro-2-quinoxalinyl; c Het = 3-chloro-2-pyrazinyl

Phosphoric anhydride (1 mmole) was added over 30 min at 20-25°C to DMSO (2.5 mole) and stirred for a further 30 min. The amine I was then added at such a rate that the temperature did not exceed 25°C and the product held at this temperature for a further 3 h. The product was poured into water (400 ml), neutralized with NaOH (20%), and extracted with dichloromethane. After evaporation of the extract the residue was precipitated from toluene using hexane to give Ia [78%, mp 94-95°C, PMR spectrum in $CDCl_3$: 2.79 (s, $2CH_3$), 7.42 (d, J = 2.3 Hz, H_4), 7.91 ppm (d, J = 2.3 Hz, 6-H)] or Ib (68%) or Ic (76%). The physicochemical data for Ib and Ic agreed with [2]. The S,S-dimethylsulfilimines Ia-c were readily converted to the corresponding nitroso heterocycles by oxidation with meta-chloroperbenzoic acid.

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