Synthesis Of 2,4-Diaryl-2, 3-Dihydro-1, 5-Benzothiazepines

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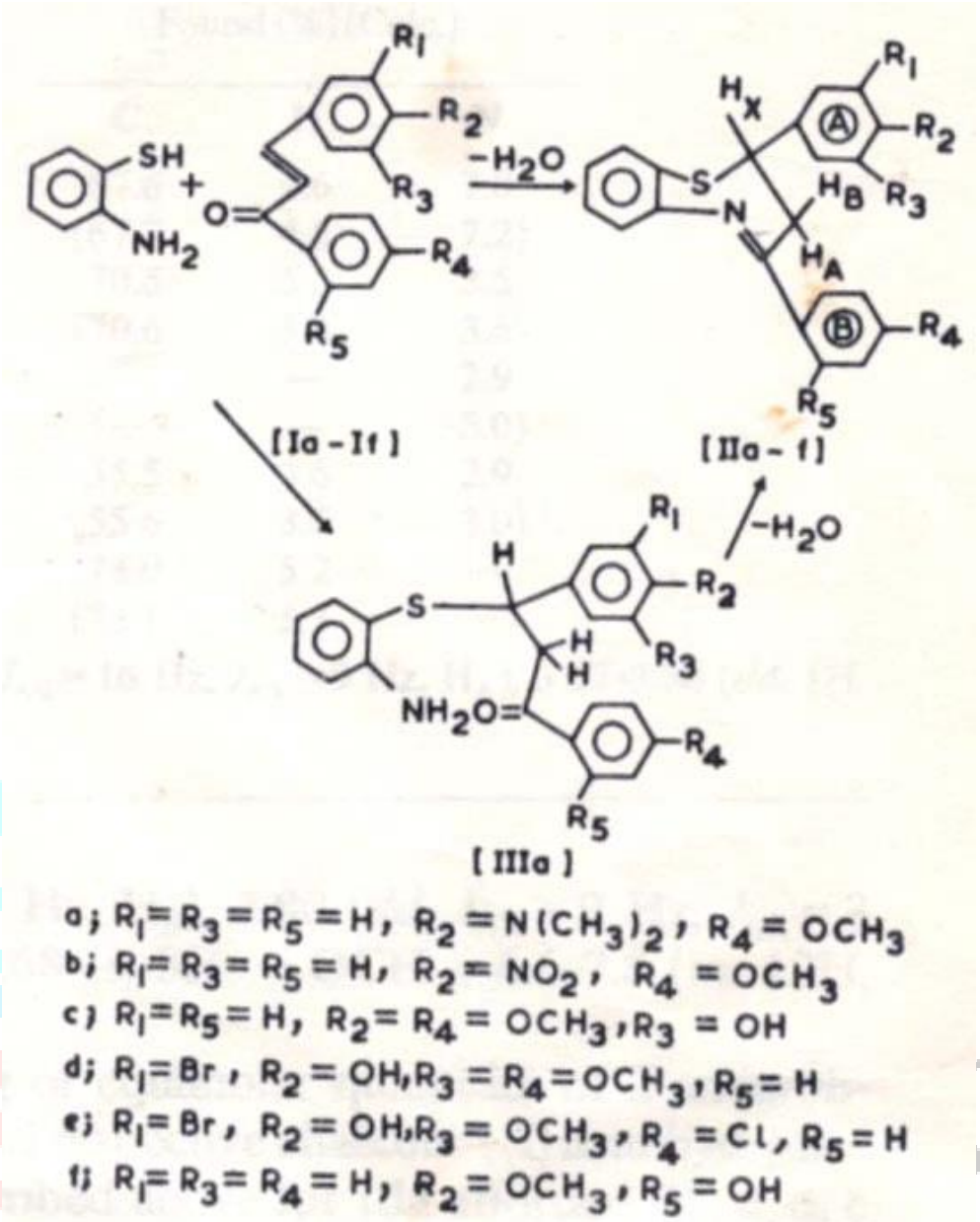
INTRODUCTION

Our work on the synthesis of 1, 5-0benzothiazepines, we report herein the synthesis of six new 2, 3-dihydro-1, 5-benzothiazepines[1-2] having a methoxyl group at various positions in the phenyl ring at position 2 or 4, alone or alongwith other groups.

The required chalk ones (1a=f) were prepared by literature method[2-7] and reacted with 2-aminothiophenol in anhyd toluene to obtain 2, 4-diaryl-2, 3-dihydro-1, 5-benzothiazepines (Iia-f) invariably in one-step in satisfactory yields. However, in the reaction of 4-(N, N-dimethylamino)-4'-methoxybenzalacetophenone (Ia) with 2-aminothiophenol; IIIa (m.p. 158º, yield 37%) was also obtained besides IIa in a major amount (yield 48%; m.p. 142º). IIIa showed IR absorptions at 3450 (N-H, asym), 3360 (N-H, sym) and 1680 cm-1 (C=0). Absence of absorption in the region 2650-2550 cm^{-1} indicated the absence of thiol group. It appears that the reaction is initiated by nucleophilic attack of sulphydryl electrons rather than by lone pair of electrons of amino group at β-carbon of the chalkone, and therefore, IIIa was characterised as an intermediate compound. Its dehydrative cyclization in methanol containing gl. acetic acid afforded IIa, identical with the product obtained above in major amount (yield 48%).

Compounds IIb-f were obtained in one-step from the reactions of respective chalkones with 2-aminothiophenol without isolation of any other product as intermediate.

The non-equivalence of methylene protons in the seven membered non-planar ring with δHa, 2.68-2.82 and δH_B, 3.32-3.38 with the uniform coupling constant of J_{AB}=16 Hz, J_{AX} = 9 Hz and J_{BX} = 8 Hz and all the three protons H_A, H_B and H_x appearing as double doubles (table 1) might be due to the presence of a chiral centre in the molecule. IN the mass spectra of IIa, b, c and f the highest ion peak appeared at *m/z* 388, 390, 391 and 361 respectively corresponding to their molecular weights. IId showed M^+ peak at *m/z* 469 followed by (M^+ +2) peak of almost equal intensity at *m/z* 471 due to the presence of one bromine atom. IIe exhibition isotopic cluster of peaks at m/z 473 (M^+), 475 (M^+ +2) and 477 (M^+ +4) due to the presence of one chlorine and one bromine atoms. The characterization data of IIb = f are given in Table -1.



M.ps are uncorrected. IR spectra were taken in KBr pellets on a Perkin-Elmer infracord-577 spectrometer, PMR spectra in $CDCI_3$ on Perkin-Elmertrometer using TMS as internal standard and mass spectra on a varian Match-7 instrument. TLC was run on silica gel G plates using benzene-ethanolammonia (7:2:1) as irrigant.3-(2-Aminophenylmercapto)-3-(p-N, N-dimethyl-aminophenyl)-p-methoxypropiophenone(IIIa).

A mixure of 2-aminothiophenol (1.25g 0.01 mol) and p-(N, N-dimethylamino)-4'-methoxybenzalacetophenone (Ia, 2.81 g, 0.01 mol) in anhyd. toluene (20ml) was refluxed for 3 hr till the colour changed from light yellow to orange. Removal of toluene under reduced pressure gave a residue which on crystallisation from methanol gave two products, IIa (yield 48%, m.p. 142º) and IIIa. IIIa was obtained in orange crystals, m.p. 158º, yield 1.5g (37%) (Found: C, 71.4; H, 6.0; N, 6.6.$C_{24}H_{26}N_2O2_S$ requires C, 70.9; H, 6.4; N, 6.9%); IR: 3450 (N-H, sym), 1680 (C=0): PMR; δ 2.26 (s, 6H - N $(CH_3)_2$], 4.68 (t, 1H, = CH), 3.34 (q, 2H, $-CH_2-$), 3.68 (s, 3H, $-OCH_3$), 4.20 (s, 2H, $-NH_2$) and 6.40-8.20 (m, 12H, Ar-H).

Table 1—Characterization Data of 2, 4-Diaryl-2, 3-dihydro-1, 5-benzothiazepines (II)

Compd*	m.p. °C	Yield (%)	R_f	Mol. formula (M^+)	Found (%) (Calc.)		
					C	H	N
IIb	193	59	0.69	$C_{22}H_{18}N_2O_3S$ (390)	67.6 (67.7	4.6 4.6	7.0 7.2)
IIc	164	76	0.72	$C_{23}H_{21}NO_3S$ (391)	70.5 (70.6	5.3 5.4	3.5 3.6)
IId	175	58	0.74	$C_{23}H_{20}NO_3SBr$ (471)	— (—	— —	2.9 3.0)
IIe	170	57	0.70	$C_{22}H_{17}NO_2SClBr$ (473)	55.5 (55.6	3.6 3.6	2.9 3.0)
IIf	162	73	0.74	$C_{22}H_{19}NO_2S$ (361)	73.0 (73.1	5.2 5.3	— —)

*IR: 1602-1610 cm^{-1}; PMR: δ 3.79-3.85 (*s*, 3H, $-OCH_3$), 2.78-2.82 (*dd*, 1H, J_{AB} = 16 Hz, J_{AX} = 9 Hz, H_A), 3.32-3.38 (*dd*, 1H, J_{AB} = 16 Hz, J_{BX} = 8 Hz, H_B), 4.85-5.04 (*dd*, 1H, J_{AX} = 9 Hz, J_{BX} = 8 Hz, H_X).

4- Anisyl- 2, 3- dihydro- 2- (p- N, N-dimethylamino-phenyl)-1, 5-benzothiazepine (IIa)

Compound IIIa (2.01 g, 0.005 mol) in dry methanol (10 ml) and gl. acetic acid (0.5 ml) was refluxed for 1 hr and the reaction mixture kept overnight. The orange solid thus obtained was filtered and crystallised from methanol to give orange crystals, m.p. 142°, yield 1.42 g (71%), R_f 0.68 (Found: C, 73.8; H, 6.1: N, 7.1. $C_{24}H_{24}N_2OS$ requires C, 74.2; H, 6.2; N, 7.2%); IR: 3060 (arom C-H), 2900, 2835 (saturated C-H), 1612 (C=N), 1600, 1575 (arom. C=C); PMR: 2.50 [s,6H, $-N(CH_3)_2$]. 2.68 (dd, J_{AB} = 16 Hz, J_{AX} = 9 Hz, H_A), 3.32 (dd, J_{AB} = 16 Hz, J_{BX} = 8 Hz, H_B), 3.80 (dd, J_{AX} = 9 Hz, J_{BX} = 8 Hz, H_X), 3.68 (s, 3H, $-OCH_3$), 6.6-7.8 (m, 12H, Ar-H).

Refluxing of equimolar quantities of 2-aminothiophenol and respective chalkones (I) in anhyd. toluene as described above for IIIa afforded IIb, c, d, e and f in one step. The characterization data of these products are given in Table 1.

REFERENCES

1. Jung D.I, Choi T.W., Kim Y.Y. et al., Synthetic Communications. 2a (1999) no. 11, 1941 – 1951
2. Sivamurugan V., Deepa K., Palanichamy M., Murugesan V., Synthetic Communications. 34 (2004) no. 21, 3833 – 3846
3. Nageli H & Tamber J, Helv Chim Acta, 7 (1924) 333; Chem Abstr, 19 (1924) 2005.
4. Kaufmann H P, Ber dt chem Ges, 54(B) (1921) 795.
5. Bradsher K Charles, J Am chem Soc, 71 (1949) 3570.
6. Raiford L C & Stoesser W C, J Am chem Soc, 49 (1927) 1077.
7. Raiford L C & Gundy V G, J org Chem, 3 (1938) 265.
8. Dhar Durganath, J Indian chem Soc, 37 (1960) 799.