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SYNTHESIS AND SPECTROSCOPIC STUDIES OF 1-(ARYLTHIOMETHYL) BENZOTRIAZOLES

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1-Chloromethylbenzotriazoles convert a variety of aromatic thiols into their respective 1-(arylthiomethyl) benzotriazoles which further react with aldehydes and ketones to form 1-(1-arylthio-2-hydroxyeth-1-yl) benzotriazole derivatives. The products structure is established by ^1H, ^{13}C NMR and elemental analysis.

Key words: Synthesis and spectroscopic studies, Aminomethylation, Benzotriazole.

Introduction

Aminomethylation (or Mannich reaction) of benzotriazole with aldehydes and amines [1-3] is a well known procedure for preparation of 1-(arylamino) benzotriazoles. Urea, thiourea and substituted thioureas gave Mannich bases with benzotriazole in the presence of cuprous chloride [4]. Recently benzotriazole has been developed in our laboratory as a highly efficient synthetic auxillary group for various chemical transformations [5-7].

Although the importance of N-substitute benzotriazoles as biological building blocks is supreme and many of the possible derivatives have been extensively investigated to have significant pharmacological biological activity [8-10]. There is surprisingly little work on the chemistry of N-substituted benzotriazoles [11,12]. In continuation to our studies on the synthetic uses of N-substituted benzotriazoles [12], the present work is mainly concerned with lithiation of thioethers 2 (Scheme 1) the subsequent electrophilic displacement of the lithium by aldehydes and ketones and identification of compounds 3 by ^1H, ^{13}C NMR, mass spectra and elemental analysis. Such sequence provide convenient and versatile methods for the synthesis of diverse 2- hydroxythioethers 3.

Materials and Methods

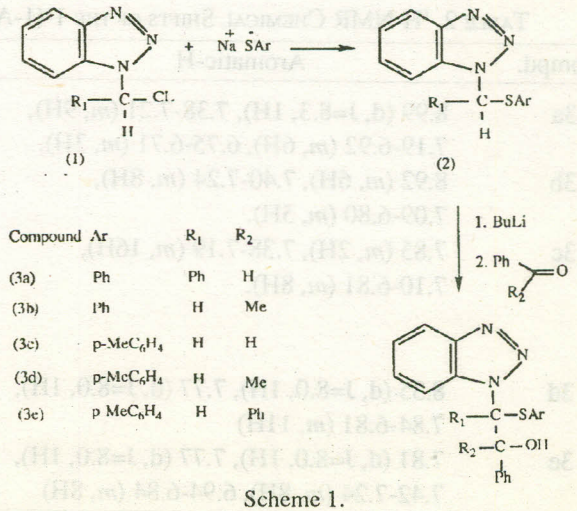
Melting points were measured with a hot-stage microscope or a capillary melting point apparatus and are uncorrected. I.R. spectra were recorded on a Perkin-Elmer Model 283D grating spectrometer for Nujol mulls, ^1H and ^{13}C NMR chemical shifts were measure on a Varian EM 360L (60Mz) spectrometer with Me_4Si as an internal standard and mass spectra on a AEJMS30 mass spectrophotometer. Tetrahydrofuran (THF) was distilled from sodium-benzophenone prior to use.

The following compounds were prepared by the literature methods quoted; 1-chloromethylbenzotriazole 1 (R_1=H), m.p. 136- 138° (lit. m.p. 136-138°) [12] and 1-(arylthiomethyl) benzotriazoles 2a-e [11-13].

General procedure for the preparation of 1-(Arylthio-2-hydroxy-2-phenyleth-1-yl) benzotriazoles 3a-e.-To 1- (arylthiomethyl) benzotriazoles 2 (0.01 mol.) in dry THF (50 ml) was added BuLi (1.5M, in hexane. 8.0ml, 0.012 mol.) at -78° under argon. The solution was stirred at -78° for 1.5hr and the required electrophile (0.01 mol.) in dry THF (20 ml) was added dropwise at -78°. The mixture was stirred at -78° (2 hrs) and at room temperature (12 hrs). Aqueous NH_4Cl solution (20%, 100ml) was added and extracted with CH_2Cl_2 (2x50ml). The organic layer, after drying over $MgSO_4$, was evaporated (30°/20mm) to give an oily residue which solidified upon trituration with light petroleum. The solid after filteration was recrystallized from the appropriate solvent (Table 1).

Results and Discussion

1-(Arylthio-2-hydroxyeth-1-yl) benzotriazoles 3a-e were prepared as shown in Scheme 1. 1-Chloromethylbenzotriazole 1 [13] reacts readily with the sodium salt of thiols to give thioethers 2 [11,12] in almost quantitative yields. Lithiation of the thioethers 2 with BuLi at -78° followed by reaction with



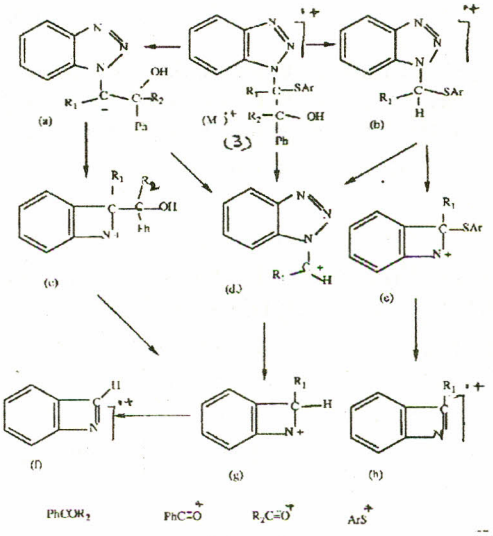
Compound	Ar	R_1	R_2
(3a)	Ph	Ph	H
(3b)	Ph	H	Me
(3c)	p-MeC_6H_4	H	H
(3d)	p-MeC_6H_4	H	Me
(3e)	p MeC_6H_4	H	Ph

Scheme 1.

aldehydes and ketones resulted in the 1-(arylthio-2-hydroxyeth-1-yl) benzotriazole derivatives 3a-e in good yields (Table 1). Compounds 3a-e were fully characterized by their ^1H, ^{13}C NMR., I.R. spectra and elemental analysis. The hydroxyl (OH) group is confirmed by the broad I.R. absorption band at 3300-3400 cm^{-1}. Chemical shifts and multiplicities of the ^1H NMR, signals of CH attached to benzotriazole and phenyl ring 3a-e are also very indicative of the product structure (Table 2). The singlet of the CH attached to benzotriazole around 6.42, 6.62 and 6.82 ppm in the ^1H NMR spectra (Table 2), 78.5, 78.6 and 81.9 ppm in the ^{13}C NMR spectra (Table 3) for compounds 3b-e are the most characteristic spectral data for their identification. The doublet of PhCH at 6.37 ppm in the ^1H NMR spectra for compound 3a is due to its coupling with the hydroxyl proton, which in turn also shows a doublet at 4.45 ppm. Compound 3c, which shows two sets of doublets at 6.16 and 6.63 ppm for CH attached to benzotriazole and a pair of doublets at 5.53 and 5.63 ppm for PhCH, due to mutual coupling, is found to be approximately a 1:1 mixture of diastereoisomers.

The mass spectra of 5 related compounds 3a-e are discussed in terms of a general fragmentation pattern (Scheme 2). Accurate mass measurements gave the elemental composition of ions but the structures drawn for fragment ions are intended to represent constitutions rather than molecular geometries. Peaks less than 10% of that of the base peak have been neglected.

The fragmentation pattern of compounds 3a-e (Scheme 2) are simple. They show molecular ion M^+ which apparently



Scheme 2.

TABLE 1. SYNTHESIS OF THE 1-(1-ARYLTHIO-2-HYDROXY-2-PHENYL ETH-1-YL) BENZOTRIAZOLES 3 a-e.

Compd.	Yield %	Solvent for recryst.	M.P. (°C)	Formula	Analysis (%) Required C	H	N	Found C	H	N
3a	50	MeOH	166-168	$C_{26}H_{21}N_3OS$	73.75	4.96	9.92	73.53	4.95	9.85
3b	54	MeOH	145-147	$C_{21}H_{19}N_3OS$	69.80	5.26	11.60	69.58	5.35	11.72
3c	58	EtOH-H_2O	138-140	$C_{21}H_{19}N_3OS$	69.80	5.26	11.60	69.88	5.26	11.68
3d	80	EtOH	201-203	$C_{22}H_{21}N_3OS$	70.40	5.60	11.11	70.16	5.59	11.12
3e	75	EtOH	143-145	$C_{27}H_{23}N_3OS$	74.14	5.26	9.61	74.05	5.27	9.60

TABLE 2. ^1H-NMR CHEMICAL SHIFTS OF THE 1-(1-ARYLTHIO-2-HYDROXY-2-PHENYL ETH-1-YL) BENZOTRIAZOLES 3a-e[a].

Compd.	Aromatic-H	CH	OH	Me
3a	8.99 (d, J=8.3, 1H), 7.38-7.21 (*m*, 9H), 7.19-6.92 (*m*, 6H), 6.75-6.71 (*m*, 3H).	6.37 (d, J=4.3)	4.45 (d, J=4.3)	—
3b	8.92 (*m*, 6H), 7.40-7.24 (*m*, 8H), 7.09-6.80 (*m*, 5H).	6.42 (s) –	4.24 (br. s)	2.12 (s)
3c	7.85 (*m*, 2H), 7.38-7.19 (*m*, 16H), 7.10-6.81 (*m*, 8H).	6.26 (d, J=6.0), 6.16 (d, J=6.0), 5.63 (d, J=6.0), 5.53 (d, J=6.0)	4.09 (br. s)	2.18 (s), 2.16 (s)
3d	8.35 (d, J=8.0, 1H), 7.77 (d, J=8.0, 1H), 7.84-6.81 (*m*, 11H)	6.62 (s) –	6.23 (br. s)	2.23 (s), 2.15 (s)
3e	7.81 (d, J=8.0, 1H), 7.77 (d, J=8.0, 1H), 7.42-7.24 (*m*, 8H), 6.94-6.84 (*m*, 8H)	6.82 (s) –	5.29 (br. s)	2.10 (s)

a. In $CDCl_3$ with reference Me_4Si.

TABLE 3. ^{13}C-NMR CHEMICAL SHIFTS OF THE 1-(ARYLTHIO-2-HYDROXY-2-PHENYL ETH-1-YL) BENZOTRIAZOLES 3a-e[a].

Compd.	Benzotriazole-C-signals						Aromatic-C-signals	CR_1	CR_2	Me
	C-3a	C-4	C-5	C-6	C-7	C-7a				
3a	146.1	119.9	124.3	127.4	114.1	133.0	136.6, 136.2, 134.8, 130.0, 129.7, 129.0, 128.8, 128.6, 128.5, 128.1, 127.1, 126.8.	81.8	77.0	--
3b	144.9	119.5	124.4	127.3	114.2	133.2	135.5, 134.9, 130.2, 128.9, 128.8, 128.6, 128.5, 127.2	78.5	77.1	20.6
3c	145.8	119.7,	124.0	127.2	111.6	133.9	139.3, 134.0, 129.9, 129.8, 128.6 128.5, 128.4, 126.5.	75.5	73.5	21.1
3d	145.3	118.3	124.9	127.1	114.6	132.3	144.4, 137.5, 131.8, 129.4, 128.7, 126.4, 126.0, 123.2	78.6	77.1	28.4 20.5
3e	144.8	119.8	124.8	127.4	110.5	133.3	143.7, 143.3, 139.4, 134.7, 129.8, 128.5, 128.4, 128.0, 127.6, 127.1, 125.9, 123.9.	81.9	76.4	21.1

a. In $CDCl_3$ with reference Me_4Si.

TABLE 4. RELATIVE ABUNDANCE (%) OF THE PRINCIPAL IONS IN THE MASS SPECTRA OF THE 1-(1-ARYLTHIO-2-HYDROXY-2-PHENYL ETH-1-YL) BENZOTRIAZOLES 3a-e.

Compd.	Ar.	R_1	R_2	M^+	a	b	c	d	e	f	g	h	$PhCOR_1$	PhC=O	R_2C=O	ArS	C_6H_5	C_4H_3
3a	Ph	Ph	H	35	25	39	20	100	80	30	80	30	40	45	–	20	77	33
3b	Ph	H	Me	20	25	30	20	80	70	25	70	20	30	40	100	30	25	20
3c	*p*-MeC_6H_4	H	H	50	100	50	40	60	45	25	40	25	30	30	–	20	40	30
3d	*p*-MeC_6H_4	H	Me	40	20	32	20	60	30	20	30	20	70	50	100	40	35	25
3e	*p*-MeCH	H	Ph	30	20	75	30	40	30	22	25	20	40	100	100	25	40	30

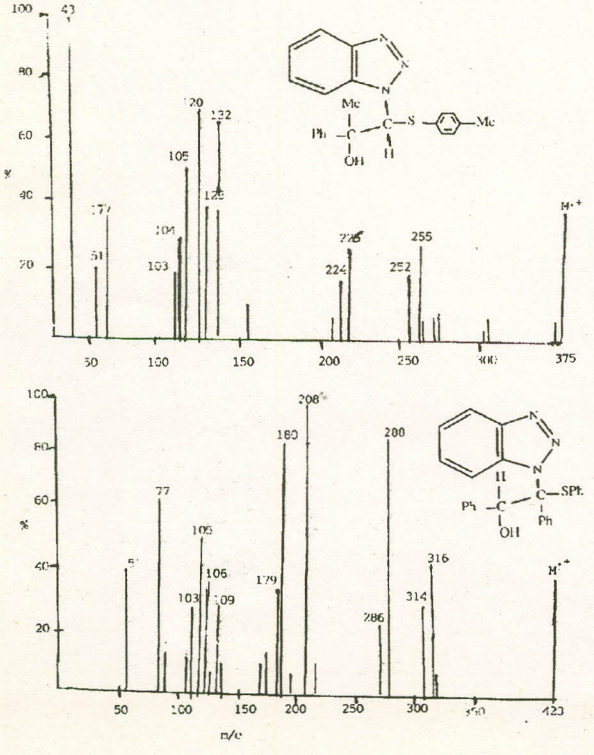


Fig. 1.

fragment by two major pathways. In the first pathway the molecular ion M^+ gives fragment ions a (M^+ -Ars^+), c and d, which undergo the usual further fragmentation supplying ions f and g. The second pathway is associated with the loss of PhCOR fragment providing ion b, which on further fragmentation give daughter ions e and h. The fragmentation pattern of compounds 3a-e also provide the fragment ions $PhCOR_2^+$, $PhCO^+$, R_2CO^+ and ArS^+.

The mass spectra of the 5 related compounds 3a-e are recorded (Table 4) of which that of 1-(2-hydroxy-1,2-diphenyl-1- phenylthioeth-1-yl) benzotriazole 3a and 1-(2-hydroxy-2-phenyl- 1,4'-tolylthioprop-1-yl) benzotriazole 3d are typical (Fig. 1).

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References

1. A.R. Katritzky, S. Rachwal and B. Rachwal, J. Chem. Soc. Perkin **I**, 799, (1987).

2. A.R. Katritzky, L. Uregdi and A. Mayence, Synthesis, 323 (1989).
3. A.R. Katritzky, M. Sutharchanadevl and L. Uregdi, J. Chem. Soc. Perkin **I**, 1847 (1990).
4. V. Mozolis and S. Jokubaityte, Liet. TSR Mekslu Akad. Darb. Ser. B. 129, (1970); Chem. Abstr., **75**, 77152r (1982).
5. A.R. Katritzky, S. Rachwal and B. Rachwal, J. Chem. Soc. Perkin **I**, 805 (1987).
6. A.R. Katritzky and M. Drewnisk, Tetrahedro Lett., **29**, 1755 (1988).
7. A.R. Katritzky and M. Drewnisk, J. Chem. Soc. Perkin **I**, 2339 (1988).
8. G. Rieveschl Jr., U.S. Patent 2527574 (1950); Chem. Abstr., **45**, 2022 (1951).
9. L.H. Goodson and R.B. Moffett, J. Am. Chem. Soc., **71**, 3219 (1949).
10. W.V. Drake and S.M. Mcelvain, J. Am. Chem. Soc., **56**, 697 (1934).
11. A.R. Katritzky, S. Rachwal, K.C. Caster, Fatma Mehni, Kum Wah Law and O. Rubio, J. Chem. Soc. Perkin **I**, 781 (1987).
12. A.R. katritzky, A.S. Afridi and W. Kuzmierkiewicz, J. Am. Chem. Soc. (Submitted for publication).
13. J.H. Burckhalter, V.C. Stephen and L.A.R. Hall, J. Am. Chem. Soc., **74**, 3868 (1952).