Pergamon

Tetrahedron, Vol. 53, No. 16, pp. 5847-5854, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00244-5

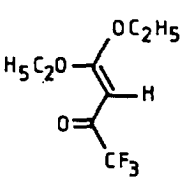
Fluoro Organics: Facile Syntheses of Novel 2- or 4-Trifluoromethyl-1H-Arylo-1,5-diazepines, Oxazepines, Thiazepines, 2 -(1,1,1-trifluoroacetonyl)Imidazoles, Oxazoles and Thiazoles[1]

A. Chandra Sheker Reddy, P. Shanthan Rao and R.V. Venkataratnam*

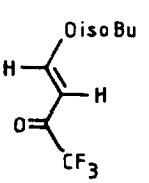
Organic Division-II, Indian Institute of Chemical Technology,
Hyderabad 500 007, India.

Abstract: Exclusive formation of either 2- or 4-trifluoromethyl(1H,5)arylodiazepines (**5,7**)/(**6,8**) was observed in the condensation of 1,1,1-trifluoro-3-(isobutoxymethylene)-2-propanones **2/3** with o-arylenediamines **4** under microwave irradiation conditions. Thermal reactions under the same temperature and time produced no products. Orthoaminophenols **9** and o-aminothiophenol **12** with **2** and **3** under the same conditions produced the respective oxazepines **10,11** and thiazepines **13,14**. The synthetic equvalent **1** gave similarly benzimidazoles **15**, benzoxazoles **16** and benzthiazoles **17**.

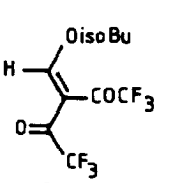
Arylodiazepines belong to an important class of compounds possessing a wide variety of medicinal properties[2]. Introduction of a trifluoromethyl group in the diazepine segment of the arylodiazepines is expected to enhance their anxiolytic activity and improve their pharmocological properties, as has been observed in the case of trifluoromethyl substitution in benzazepinone calcium antogonists.[3,4,5] In our earlier work[6], we have successfully employed trifluoroacetyl ketene diethyl acetal **1** to introduce a trifluoroacetonyl group in imidazoles, oxazoles, quinazolines and perimidines with a view to incorporate



1



2



3

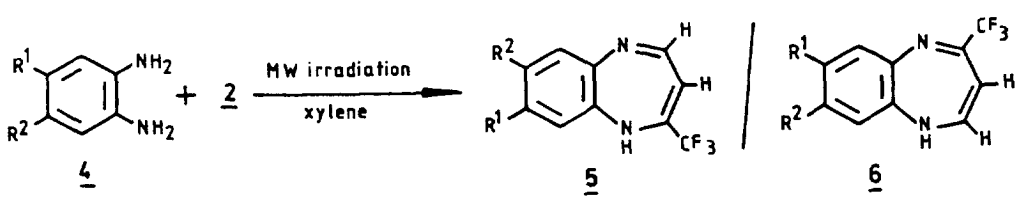
*Emeritus Scientist (CSIR),

IICT Communication No.3780

juvenile hormone - esterase inhibiting activity[7]. In the present work, we wanted to modify the synthon 1 in such a way that it is useful to introduce a trifluoromethyl group in the ring formation reaction. Accordingly, if one of the two leaving ethoxy groups in 1 is replaced by a hydrogen and the other by a more facile isobutoxy leaving group, we get synthon 2. We selected synthon 2 and its derivative 3 as being useful in introducing a trifluoromethyl group in the diazepine segment as desired or in any other seven membered ring system formed when they are condensed with o-arylenediamines 4 or other nucleophiles 9, 12. The synthons 2 and 3 were prepared by reported procedures.[8,9] Condensation of the synthons with o-arylenediamines 4 in refluxing xylene led to a complex mixture of products unsuitable for preparative work.

Following examples of organic synthesis under microwave irrdiation,[10,11] we examined the condensation of 4 with 2 and 3 in xylene under microwave irradiation in our preliminary communication.[1] We achieved a neat reaction producing a single product, 5 or 6 and 7 or 8 respectively from 2 and 3 (scheme 1 and 2). A similar study[12] on the synthesis of 1,5-arylodiazepine-2-ones under microwave irradiation reported on having obtained mixtures of two isomeric arylodiazepinones with dissymetrical o-arylenediamines. In our work, products **6a-d** and **8a-d**, 4-trifluoromethyl (1H,5)arylodiazepines were exclusively formed from o-arylenediamines **4a-d**. Products **5a, 5b, 7a** and **7b**, 2-trifluoromethyl(1H,5) a vlodiazepines were formed from o-arylenediamines **4e** and **4f**. The products **5,6,7** and **8** were found to exist as monohydrates.

Scheme - 1



4 5 6

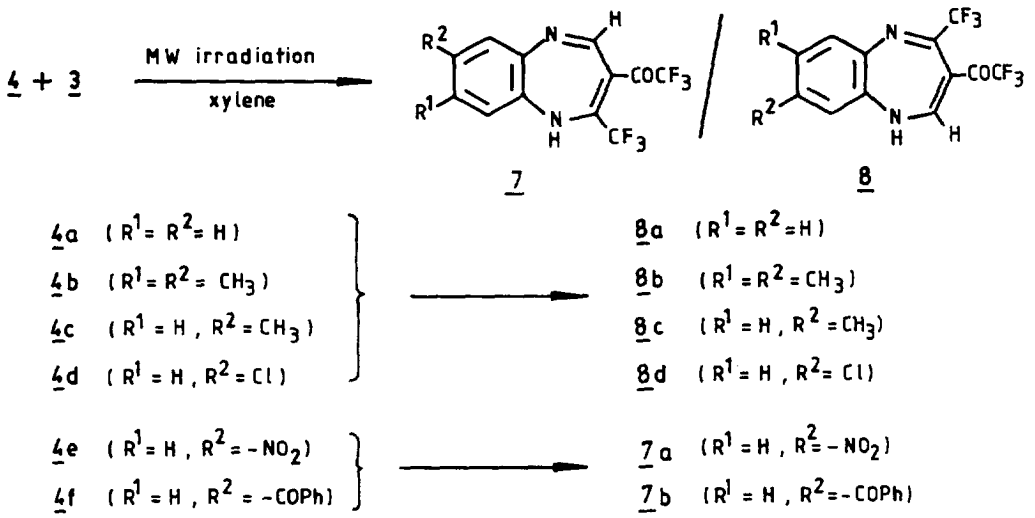
4a ($R^1 = R^2 = H$)
4b ($R^1 = R^2 = CH_3$)
4c ($R^1 = H, R^2 = CH_3$)
4d ($R^1 = H, R^2 = Cl$)

6a ($R^1 = R^2 = H$)
6b ($R^1 = R^2 = CH_3$)
6c ($R^1 = H, R^2 = CH_3$)
6d ($R^1 = H, R^2 = Cl$)

4e ($R^1 = H, R^2 = -NO_2$)
4f ($R^1 = H, R^2 = -COPh$)

5a ($R^1 = H, R^2 = -NO_2$)
5b ($R^1 = H, R^2 = -COPh$)

Scheme-2



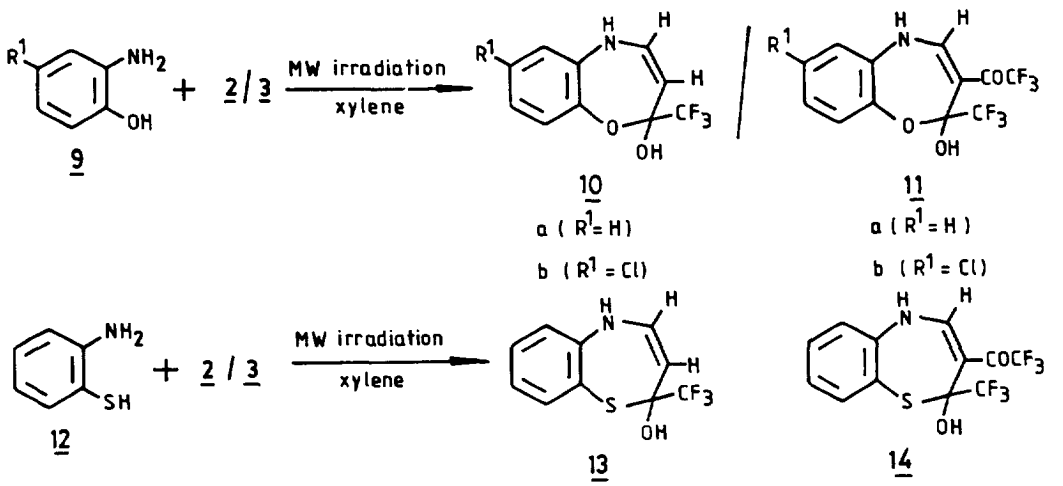
Structures **5/7** and **6/8** of the products were established on the basis of spectroscopic data and the mode of formation. Since only either one of them is formed exclusively, the diagnostic features of ^1H NMR spectra were used in differentiating between the two isomeric structures. The spectra of **6/8** show the following characteristics: For **6** a broad signal for NH (exchangeable in D_2O), a doublet of doublet for H-C(2) (reducing to a doublet with D_2O exchange) and a doublet for H-C(3); For **8** the signal for H-C(2) was a doublet changing into singlet on D_2O exchange. Similarly in the spectra of **5**, H-C(3) and H-C(4) appeared as two doublets unaffected by D_2O exchange and in **7**, H-C(4) gave rise to a singlet signal unaffected by D_2O exchange. Thus the relative positions of the protons and the trifluoromethyl groups were determined in the diazepine part of the molecule.

The placement of substituents in the benzene segment was made on the basis of the mode of formation which may be formulated by counting upon the relative reactivities of the amino groups in that particular o-arylenediamine to intiate the reaction by displacing the isobutoxy group and to cyclise onto the carbonyl. Though the reaction course is same in all cases, the structure of the final stable product is determined by the influence of the trifluoromethyl as well as the nitro and benzoyl groups. Thus, the presence of the trifluoromethyl group at C(4) in the diazepine seems to stabilise structure **6/8** (as obtained from **4a-d**). Contrastingly, the effect of NO_2 or COPh is to stabilise structure **5/7**, despite interaction with the effect of the trifluoromethyl group. The remarkable feature about the products is that there is no prototropic shift from 1H to 5H.

The utility of synthons **2** and **3** in the facile formation of seven membered rings under microwave

irradiation has been demonstrated in the preparation of oxazepines 10,11 and thiazepines 13,14 from 9 and 12 respectively (**scheme 3**). Structures 10,11,13 and 14 were assigned on the diagnostic features of ^{1}H NMR spectra and other complementary spectroscopic data. In contrast to the diazepines, these products have an hydroxyl group attached to the carbon bearing the trifluoromethyl substituent and do not undergo facile dehydration.

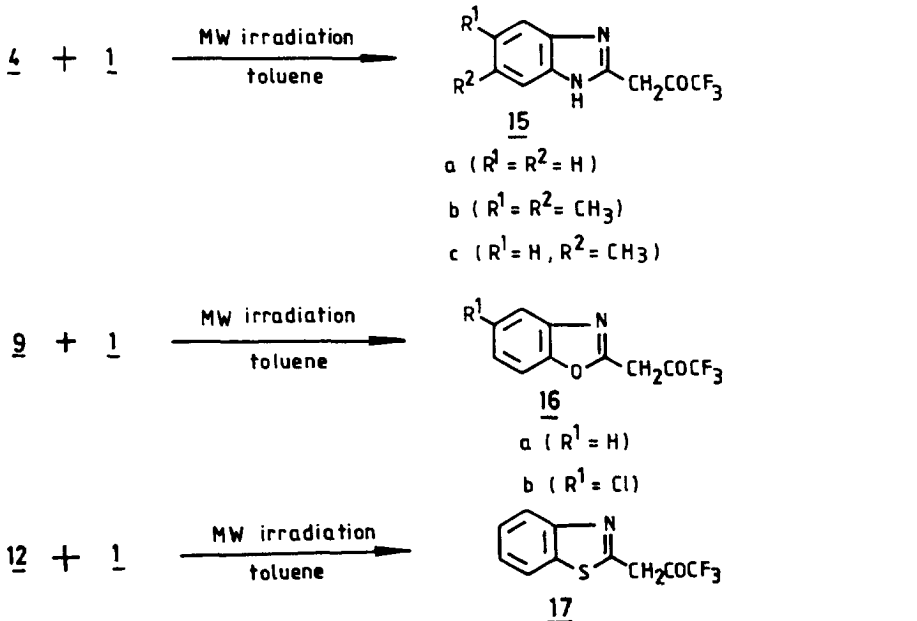
Scheme -3



9 10 11 12 13 14

a (R^1= H)
b (R^1 = Cl)

Scheme -4



15
a ($R^1 = R^2 = H$)
b ($R^1 = R^2 = CH_3$)
c ($R^1 = H, R^2 = CH_3$)

16
a (R^1 = H)
b (R^1 = Cl)

17

Synthon 1, in contrast with synthons 2 and 3, induces the formation of only five-membered heterocycles on condensation with o-arylenediamines and other similar nucleophiles whether carried out

thermally in refluxing toluene[6] or by microwave irradiation as in the present work. Thus, the reaction of **1** with **4,9** and **12** gives respectively benzimidazoles **15**, benzoxazoles **16** and benzthiazoles **17** ; all are new products except **15a** and **16a** (scheme 4). Structures were assigned on the basis of spectroscopic data. Each of the ^{1}H NMR spectra of **15b,15c,16b** and **17** shows the presence of a vinylic proton and an enolic proton, thus indicating the presence of -CH=C(OH)-CF_3 functional group.

EXPERIMENTAL

General Aspects: Melting points were determined in open ended capillary tubes on a Mettler FP 51 melting point apparatus and are uncorrected. ^{1}H NMR spectra were taken on Varian Gemini (200 MHz) spectrometer by using $CDCl_3$/DMSO-d_6 as the solvent. Chemical shifts were expressed in ppm downfield from TMS as an internal standard. Mass spectra were recorded on VG Micromass 7070H instrument. Thin layer chromatography was carried out on Merck 5735 Kieselgel 60 F_{254} fluorescent plates. Flash chromatography was performed with silica gel (60-120 mesh) or neutral alumina. Elemental analyses were carried out on a Perkin-Elmer 240B apparatus. Microwave irradiation experiments were carried out on 980W multimode reactor.

General procedure for 2- or 4-trifluoromethyl-(1H,5)arylodiazepines (5,6,7,8), oxazepines (10,11) and thiazepines (13,14): An Erlenmeyer flask containing a mixture of **2/3** (15 mmoles), *o*-diamine / *o*-aminophenol / *o*-aminothiophenol (15 mmoles), and *o*-xylene (10 ml) was activated by microwave irradiation for a specified time. The mixture was cooled, concentrated partially removing the solvent by rotavapor. The residue was passed through a column of silica gel using hexane-chloroform mixtures as the eluant to give the corresponding crystalline compounds in good purity.

7-Nitro-2-trifluoromethyl-(1H,5)benzodiazepine (5a): Reaction time: 20 mins.; Yield, 73%; m.p.129^{0}C; IR (KBr): 1180, 1590, 3300 cm^{-1}; ^{1}H NMR (DMSO-d_6) : δ 5.70 (d,J=9.0 Hz,1H,H-C(3)), 6.60-7.80 (m,3H,ArH), 8.00 (d,J=9.0 Hz,1H,H-C(4)), 11.40 (d,br.,1H,NH); MS m/z: 275(M^+,60), 206(15), 164(100), 118(46); Anal. Calcd. for $C_{10}H_8F_3N_3O_3$: C, 43.64, H, 2.19, N, 15.27. Found: C, 43.58, H, 2.25, N, 15.43. **7-Benzoyl-2-trifluoromethyl-(1H,5)benzodiazepine (5b):** Reaction time: 20 mins.; Yield, 75%; m.p.118^{0}C; IR (KBr): 1200, 1680, 3310 cm^{-1}; ^{1}H NMR (DMSO-d_6): 5.71 (d,J=9.2 Hz,1H,H-C(3)), 6.80 (d,J=9.2 Hz,1H,H-C(4)), 7.31-7.80 (m,8H,ArH), 11.70 (d,br.,1H,NH); MS m/z: 334(M^+,63), 290(15), 223(88), 105(100); Anal. Calcd. for $C_{17}H_{13}F_3N_2O_2$: C, 61.08, H, 3.31, N, 8.38. Found: C, 61.13, H, 3.38, N, 8.41.

4-Trifluoromethyl-(1H,5)benzodiazepine (6a): Reaction time: 15 mins.; Yield, 85%; m.p.155^{0}C; IR (KBr): 1210, 3300 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.70 (d,J=6.5 Hz,1H,H-C(3)), 6.75-7.11 (m,4H,ArH), 7.61 (dd,J=6.5,6.5 Hz,1H,H-C(2)), 11.80 (s,br.,1H,NH); MS m/z: 230(M^+,28), 161(42), 119(100); Anal. Calcd. for $C_{10}H_9F_3N_2O$: C, 52.17, H, 3.06, N, 12.17. Found: C, 52.25, H, 3.12, N, 12.21.

7,8-Dimethyl-4-trifluoromethyl-(1H,5)benzodiazepine (6b): Reaction time: 20 mins.; Yield, 93%; m.p.148^{0}C; IR (KBr): 1200, 1580, 3280 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.20 (s,6H,2CH_3), 5.60 (d,J=6.6

Hz,1H,H-C(3)), 6.60 (s,1H,ArH), 6.80 (s,1H,ArH), 7.60 (dd,J=6.6,6.6 Hz,1H,H-C(2)), 11.80 (s,br.,1H,NH); MS m/z: 258(M^+,69), 147(100); Anal. Calcd. for $C_{12}H_{13}F_3N_2O$: C, 55.81, H, 4.29, N, 10.89. Found: C, 55.87, H, 4.35, N, 10.94.

8-Methyl-4-trifluoromethyl-(1H,5)benzodiazepine (6c): Reaction time: 20 mins.; Yield, 86%; m.p.165^{0}C; IR (KBr): 1200, 3310 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.30 (s,3H,CH_3), 5.65 (d,J=6.5 Hz,1H,H-C(3), 6.51-7.00 (m,3H,ArH), 7.52 (dd,J=6.5,6.5 Hz,1H,H-C(2)), 11.78 (s,br.,1H,NH); MS m/z: 244(M^+,40), 175(12), 133(100); Anal. Calcd. for $C_{11}H_{11}F_3N_2O$: C, 54.09, H, 3.71, N, 11.47. Found: C, 54.15, H, 3.78, N, 11.56.

8-Chloro-4-trifluoromethyl-(1H,5)benzodiazepine (6d): Reaction time: 20 mins.; Yield, 80%; m.p.158^{0}C; IR (KBr): 1200, 1560, 3320 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.68 (d,J=6.6 Hz,1H,H-C(3)), 6.75-7.10 (m,3H,ArH), 7.50 (dd,J=6.6,6.6 Hz,1H,H-C(2)), 11.65 (s,br.,1H,NH); MS m/z: 264(M^+,76), 195(20), 153(100); Anal. Calcd. for $C_{10}H_8ClF_3N_2O$: C, 45.38, H, 2.28, N, 10.58. Found: C, 45.46, H, 2.32, N, 10.64.

7-Nitro-3-trifluoroacetyl-2-trifluoromethyl-(1H,5)benzodiazepine (7a): Reaction time: 25 mins.; Yield, 78%; m.p.116^{0}C; IR (KBr): 1200, 1680, 3300 cm^{-1}; ^{1}H NMR (DMSO-d_6): 7.00-7.80 (m,3H,ArH), 8.40 (s,1H,H-C(4)), 11.10 (d,br.,1H,NH); MS m/z: 371(M^+,10), 164(100), 69(20); Anal. Calcd. for $C_{12}H_7F_6N_3O_4$: C, 38.82, H, 1.35, N, 11.32. Found: C, 38.88, H, 1.42, N, 11.39.

7-Benzoyl-3-trifluoroacetyl-2-trifluoromethyl-(1H,5)benzodiazepine (7b): Reaction time: 22 mins.; Yield, 80%; m.p.108^{0}C; IR (KBr): 1210, 1690, 3320 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.41-7.91 (m,8H,ArH), 8.31 (s,1H,H-C(4)), 11.65 (d,br.,1H,NH); MS m/z: 430(M^+,15), 334(10), 223(100), 105(80), 77(70); Anal. Calcd. for $C_{19}H_{12}F_6N_2O_3$: C, 53.03, H, 2.34, N, 6.51. Found: C, 53.09, H, 2.40, N, 6.62.

3-Trifluoroacetyl-4-trifluoromethyl-(1H,5)benzodiazepine (8a): Reaction time: 10 mins.; Yield, 76%, m.p.133^{0}C; IR (KBr): 1180, 1680, 3300 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.80-7.18 (m,4H,ArH), 8.33 (d,J=12.4 Hz,1H,H-C(2)), 12.30 (s,br.,1H,NH); MS m/z: 326(M^+,16), 257(11), 119(100); Anal. Calcd. for $C_{12}H_8F_6N_2O_2$: C, 44.18, H, 1.85, N, 8.58. Found: C, 44.27, H, 1.95, N, 8.63.

7,8-Dimethyl-3-trifluoroacetyl-4-trifluoromethyl-(1H,5)benzodiazepine (8b): Reaction time: 15 mins.; Yield, 84%; m.p.122^{0}C; IR (KBr): 1200, 1690, 3330 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.20 (s,6H,2CH_3), 6.70 (s,1H,ArH), 6.90 (s,1H,ArH), 8.35 (d,J=12.9 Hz,1H,H-C(2)), 12.30 (s,br.,1H,NH); MS m/z: 354(M^+,25), 285(37), 147(100); Anal. Calcd. for $C_{14}H_{12}F_6N_2O_2$: C, 47.46, H, 2.84, N, 7.90. Found: C,47.54, H, 2.93, N, 7.98.

8-Methyl-3-trifluoroacetyl-4-trifluoromethyl-(1H,5)benzodiazepine (8c): Reaction time: 16 mins.; Yield, 74%; m.p.161^{0}C; IR (KBr): 1200, 1670, 3340 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.21 (s,3H,CH_3), 8.28 (d,J=12.5 Hz,1H,H-C(2)), 7.10-7.52 (m,3H,ArH), 11.70 (s,br.,1H,NH); MS m/z: 340(M^+,28), 271(58), 174(100); Anal. Calcd. for $C_{13}H_{10}F_6N_2O_2$: C, 45.89, H, 2.36, N, 8.23. Found: C, 45.97, H, 2.41, N, 8.29.

8-Chloro-3-trifluoroacetyl-4-trifluoromethyl-(1H,5)benzodiazepine (8d): Reaction time: 18 mins.; Yield, 83%; m.p.143^{0}C; IR (KBr): 1190, 1680, 3300 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.91 (m,3H,ArH), 8.22 (d,J=12.6 Hz,1H,H-C(2)), 11.81 (s,br.,1H,NH); MS m/z: 360(M^+,16), 291(100), 192(33); Anal. Calcd. for

$C_{12}H_7ClF_6N_2O_2$: C, 39.96, H, 1.39, N, 7.76. Found: C, 40.06, H, 1.48, N, 7.86.

2-Hydroxy-2-trifluoromethyl-(1,5H)benzoxazepine (10a): Reaction time: 12 mins.; Yield, 82%; m.p.185°C; IR (KBr): 1200, 1580, 2870, 3320 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.71 (d,J=6.3 Hz,1H,H-C(3)), 6.93-7.18 (m,4H,ArH), 7.78 (dd,J=6.3,6.3 Hz,1H,H-C(4)), 10.41 (s,br.,1H,OH), 12.28 (s,br.,1H,NH); MS m/z: 231(M^+,56), 162(100), 120(30); Anal. Calcd. for $C_{10}H_8F_3NO_2$: C, 51.93, H, 3.48, N, 6.06. Found: C, 51.98, H, 3.57, N, 6.12.

7-Chloro-2-hydroxy-2-trifluoromethyl-(1,5H)benzoxazepine (10b): Reaction time: 15 mins.; Yield, 85%; m.p.208°C; IR (KBr): 1210, 1590, 2850, 3320 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 5.75 (d,J=6.5 Hz,1H,H-C(3)), 6.82-7.08 (m,2H,ArH), 7.20 (s,1H,ArH), 7.70 (dd,J=6.5,6.5 Hz,1H,H-C(4)), 10.23 (s,br.,1H,OH), 12.18 (s,br.,1H,NH); MS m/z: 265(M^+,42), 196(83), 154(100); Anal. Calcd. for $C_{10}H_7ClF_3NO_2$: C, 45.19, H, 2.65, N,5.27. Found: C, 45.28, H,2.73, N,5.36.

2-Hydroxy-3-trifluoroacetyl-2-trifluoromethyl-(1,5H)benzoxazepine (11a): Reaction time: 14 mins.; Yield, 89%; m.p.181°C; IR (KBr): 1190, 1630, 1690, 3420 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.84-7.21 (m,4H,ArH), 8.53 (d,J=12.1 Hz,1H,H-C(4)), 10.23 (s,br.,1H,OH), 12.60 (s,br.,1H,NH); MS m/z: 327(M^+,81), 258(72), 188(100); Anal. Calcd. for $C_{12}H_7F_6NO_3$: C, 44.05, H, 2.16, N, 4.28. Found: C, 44.12, H, 2.22, N, 4.36.

7-Chloro-2-hydroxy-3-trifluoroacetyl-2-trifluoromethyl-(1,5H)benzoxazepine (11b): Reaction time: 8mins.; Yield, 76%; m.p.182°C; IR (KBr): 1210, 1620, 1685, 3410 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.84-7.00 (m,2H,ArH), 7.18 (s,1H,ArH), 8.50 (d,J=12.3 Hz,1H,H-C(4)), 10.48 (s,br.,1H,OH), 12.42 (s,br.,1H,NH); MS m/z: 361(M^+,44), 292(32), 196(22), 154(100); Anal. Calcd. for $C_{12}H_6ClF_6NO_3$: C, 39.86, H, 1.67, N, 3.87. Found: C, 39.92, H, 1.75, N, 3.95.

2-Hydroxy-2-trifluoromethyl-(1,5H)benzthiazepine (13): Reaction time: 12 mins.; Yield, 71%; m.p.146°C; IR (KBr): 1210, 1640, 3420 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.63 (d,J=6.7 Hz,1H,H-C(3)), 7.12-7.48 (m,4H,ArH), 8.12 (dd,J=6.7,6.7 Hz,1H,H-C(4)), 9.00 (s,br.,1H,OH), 11.32 (s,br.,1H,NH); MS m/z: 247(M^+,34), 178(100), 136(25); Anal. Calcd. for $C_{10}H_8F_3NOS$: C, 48.56, H, 3.26, N, 5.66. Found: C, 48.62, H,3.30, N,5.63.

2-Hydroxy-3-trifluoroacetyl-2-trifluoromethyl-(1,5H)benzthiazepine (14): Reaction time: 8 mins.; Yield, 78%; m.p.135°C; IR (KBr): 1220, 1685, 3380 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.82-7.18 (m,4H,ArH), 7.61 (d,J=12.6 Hz,1H,H-C(4)), 9.60 (s,br.,1H,OH), 11.32 (s,br.,1H,NH); MS m/z: 343(M^+,46), 274(100), 242(25); Anal. Calcd. for $C_{12}H_7F_6NO_2S$: C,41.99, H, 2.05, N, 4.08. Found: C, 41.92, H, 2.12, N, 4.19.

General procedure for 5- or 5,6-disubstituted-2-trifluoroacetonyl benzimidazoles (15), benzoxazoles (16) and benzthiazoles (17): Equimolar quantities of *o*-diamine / *o*-aminophenol / *o*-aminothiophenol (15 mmoles) and **1** (15 mmoles) were taken in toluene (15 ml) in an Erlenmeyer flask and activated by microwave irradiation for a specified time. After completion of reaction the solvent was partially evaporated and the residue was passed through a column of silica gel using suitable eluant to give the corresponding compounds in good purity.

5,6-Dimethyl-2-(1,1,1-trifluoroacetonyl)-benzimidazole (15b): Reaction time: 9 mins.; Yield, 86%; m.p. 248^{0}C; IR (KBr): 1630, 3240 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.30 (s,6H,2CH_3), 5.42 (s,1H,-CH=), 7.11 (s,2H,ArH), 7.51 (s,br.,1H,OH), 9.31 (s,br.,1H,NH); MS m/z: 256 (M^+,48), 167 (100), 159 (23); Anal. Calcd. for $C_{12}H_{11}F_3N_2O$: C, 56.25, H, 4.32, N, 10.93. Found: C, 56.31, H, 4.24, N, 10.98.

6-Methyl-2-(1,1,1-trifluoroacetonyl)-benzimidazole (15c): Reaction time: 11 mins.; Yield, 92%; m.p. 239^{0}C; IR (KBr): 1620, 1640, 3280 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.43 (s,3H,CH_3), 5.40 (s,1H,-CH=), 6.95-7.20 (m,3H,ArH), 7.72 (s,br.,1H,OH), 9.63 (s,br.,1H,NH); MS m/z: 242 (M^+,24), 173 (100), 145 (37); Anal. Calcd. for $C_{11}H_9F_3N_2O$: C, 54.55, H, 3.74, N, 11.56. Found: C, 54.60, H, 3.76, N, 11.61.

5-Chloro-2-(1,1,1-trifluoroacetonyl)-benzoxazole (16b): Reaction time: 11 mins.; Yield, 96%; m.p. 170^{0}C; IR (KBr): 1620, 1640 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.12 (s,1H,-CH=), 7.31-7.50 (m,3H,ArH), 7.65 (s,br.,1H,OH); MS m/z: 263 (M^+,34), 194 (100), 166 (63); Anal. Calcd. for $C_{10}H_5ClF_3NO_2$: C, 45.54, H, 1.91, N, 5.77. Found: C, 45.59, H, 2.02, N, 5.89.

2-(1,1,1-Trifluoroacetonyl)-benzthiazole (17): Reaction time: 8 mins.; Yield, 93%; m.p. 229^{0}C; IR (KBr): 1630, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.21 (s,1H,-CH=), 7.35-7.70 (m,4H,ArH), 12.85 (s,br.,1H,OH); MS m/z: 245(M^+,26), 176(100), 148(83); Anal. Calcd. for $C_{10}H_6F_3NOS$: C, 48.96, H, 2.46, N, 5.71. Found: C, 48.89, H, 2.54, N, 5.82.

Acknowledgement: The authors are grateful to Dr.K.V.Raghavan, Director, IICT for his constant encouragement and to Council of Scientific and Industrial Research, New Delhi, India for the grant No. 21(280) / 93 /EMR-II. ACS Reddy thanks CSIR for the award of Senior Research Fellowship.

REFERENCES

1. A part of work has been published as a preliminary communication. Chandra Sheker Reddy, A.; Shanthan Rao, P.; Venkataratnam, R.V. *Tetrahedron Lett.* **1996**, 37, 2845.
2. Watthey, J.W.H.; Stanton, J.; Peet, N.P. in Azepines, Part 2, edited by Rosowsky, A. (John Wiley & sons) **1984**.
3. Floyd, D.M.; Kimball, S.D.; Kraocho, J.; Das, J.; Turj, C.F.; Moquin, R.V.; Lago, M.W.; Duff, D.J.; Lee, V.G.; White, R.E.; Ridgewell, R.E.; Moreland, S.; Brittain, R.J.; Normandin, D.E.; Hedberg, S.A.; Cucinotta, G.G. *J. Med. Chem.* **1992**, 35, 756.
4. Das, J.; Floyd, D.M.; Kimball, S.D.; Duff, K.J.; Vu, J.C.; Lago, M.W.; Moquin, R.V.; Lee, V.G.; Gongoutas, J.Z.; Malley, M.F.; Moreland, S.; Brittain, R.J.; Hedberg, S.A.; Cucinotta, G.G. *J. Med. Chem.* **1992**, 35, 773.
5. Kimball, S.D.; Floyd, D.M.; Das, J.; Hunt, J.T.; Krapcho, J.; Rovnyak, G.; Duff, K.J.; Lee, V.G.; Moquin, R.V.; Turk, C.F.; Hedberg, S.A.; Moreland, S.; Brittain, R.J.; McMullen, D.M.; Normandin, D.E.; Cucinotta, G.G. *J. Med. Chem.* **1992**, 35, 780.
6. Narsaiah, B.; Sivaprasad, A.; Venkataratnam, R.V. *J. Fluorine Chem.* **1994**, 66, 47.
7. Hammock, B.D.; Yehiai, A.I.; Badel, A.; Mullin, C.A.; Hazlikard, T.N.; Roe, R.M. *Pestic. Biochem. Physiol.* **1984**, 22, 209.
8. Hojo, M.; Masuda, R.; Kokuryo, Y.; Shioda, H.; Matsuo, S. *Chem. Lett.* **1976**, 499.
9. Hojo, M.; Masuda, R.; Okada, E. *Synthesis* **1990**, 347.
10. Gedye, R.; Smith, F.; Westaway, K.; Baldisera, L.; Rousel, J. *Tetrahedron Lett.* **1986**, 27, 279.
11. Giguere, R.J.; Bray, T.L.; Duncan, S.M.; Majetich, G. *Tetrahedron Lett.* **1986**, 27, 4945.
12. Bougrin, K.; Bennani, A.K.; Tetouani, S.F.; Soufiaoui, M. *Tetrahedron Lett.* **1994**, 35, 8373.

(*Received in UK* 20 *January* 1997; *revised* 5 *March* 1997; *accepted* 6 *March* 1997)