DIHYDROCHALCONES AS SYNTHONS FOR 2-AMINO- AND 2-MERCAPTO-4-ARYL-5-ARYLMETHYLTHIAZOLES

Vinod Kumar Ahluwalia*, Krishan Kumar Arora, and Gurvinder Kaur
Department of Chemistry, University of Delhi, Delhi-110 007, India

Abstract - 2-Amino- and 2-mercapto-4-aryl-5-arylmethylthiazoles have been synthesised by the respective condensation of thiourea and ammonium dithiocarbamate with α-bromo-α,β-dihydrochalcones which in turn are obtained by the bromination of the corresponding dihydrochalcones.

Since nineteenth century a large number of thiazoles with different substituents have been synthesised which are known to be associated with diverse biological activities[1]. But survey of the literature reveals that no thiazole having 4-aryl 5-arylmethyl substituents has ever been synthesised. Retro-synthetic analysis shows that such thiazoles can be obtained from dihydrochalcones. Earlier attempts to prepare these thiazoles from dihydrochalcones via dibromodihydrochalcones have met with failure[2].

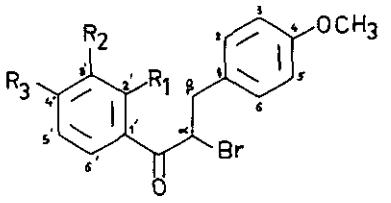
We carried out the condensation of α,β-dihydrochalcones with thiourea in presence of iodine (as per the normal procedure introduced by King et al.[3] for the synthesis of thiazoles) but only starting material was recovered. The difficulty was, however, overcome by carrying out the condensation with corresponding α-bromo-α,β-dihydrochalcones.

Thus, the bromination of α,β-dihydro-4-methoxy-4'-methylchalcone with bromine in carbon tetrachloride at 30-35°C gave a product which showed carbonyl absorption at 1680 cm^{-1} in its ir spectrum. Its nmr spectrum showed, besides other signals, a multiplet due to two protons (C_β-H) at δ 3.22-3.57 and a triplet due to one proton (C_α-H) at δ 5.28. Hence it was assigned the structure α-bromo-α,β-dihydro-4-methoxy-4'-methylchalcone (1).

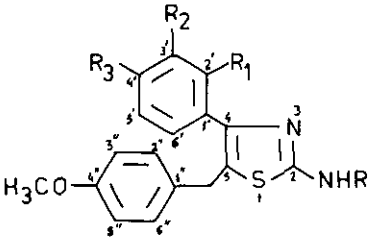
α-Bromodihydrochalcone (1) on condensation with thiourea in absolute ethanol afforded a product. Its ir spectrum showed absorptions at 3440 and 3280 cm^{-1} (NH_2 stretching). Its nmr spectrum showed a two proton singlet at δ 4.02 (CH_2

at C_5) and a broad singlet due to two protons (exchanged with D_2O) at δ 5.30 (NH_2 at C_2). On the basis of this and elemental analysis, it was assigned the structure, 2-amino-5-(4"-methoxyphenylmethyl)-4-(4'-methylphenyl)thiazole (2). The presence of an amino group in 2 was further confirmed by the preparation of its acetyl derivative (3).

α-Bromodihydrochalcone (1) on condensation with ammonium dithiocarbamate in absolute ethanol afforded a compound as colourless shining needles. Its nmr spectrum showed besides other signals, one proton singlet (D_2O exchanged) at δ 1.71 and two protons singlet at δ 3.87 (CH_2 at C_5). Its ir spectrum showed absorption at 2510 cm^{-1} (SH stretching). On this basis it was assigned the structure, 2-mercapto-5-(4"-methoxyphenylmethyl)-4-(4'-methylphenyl) thiazole (4). The presence of mercapto group in 4 was further confirmed by the synthesis of its S-methyl derivative (5).

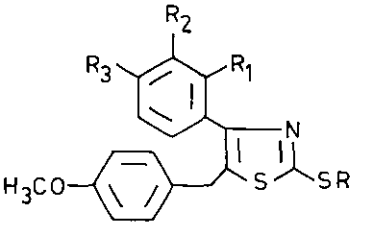


(1,6,11)



(2,7,12; R = H)

(3,8,13; R = $COCH_3$)



(4,9,14; R = H)

(5,10,15; R = CH_3)

	R_1	R_2	R_3
1-5	H	H	CH_3
6-10	OCH_3	H	OCH_3
11-15	OCH_3	CH_3	OCH_3

Similar results were obtained when reaction was extended to other dihydrochalcones. Thus, α-bromo-α,β-dihydro-2',4,4'-trimethoxychalcone(6) on condensation with thiourea and ammonium dithiocarbamate afforded 7 and 9 respectively.

Similarly α-bromo-α,β-dihydro-3'-methyl-2',4,4'-trimethoxychalcone (11) afforded 12 and 14. All these products were assigned the structures on the basis of elemental analysis, ir and nmr spectral data. Acetylation of 7 and 12 gave 8 and 13 and methylation of 9 and 14 afforded 10 and 15, respectively. Table 1 summarises the yield, mp and spectral data ofall these compounds.

All the thiazole derivatives synthesised have shown 30-60% fungal inhibition against Aspergillus fumigatus and Aspergillus niger and marginal antibacterial activity against Staphylococcus aureus and Escherichia coli.

Table 1.

Compound[a]	Yield [%]	mp[b] [°C]	ir [ν_{max}^{KBr} cm^{-1}]	nmr ($CDCl_3$/TMS) [δ (ppm)]
1	95.4	oil	1680	2.35(3H,s, CH_3); 3.22-3.57(2H,m,C_β-H) 3.80(3H,s,OCH_3); 5.28(1H, t, J 7Hz, C_α-H); 6.81(2H,d,J 9Hz,C_3-H and C_5-H) 7.19 and 7.24(each 2H,each d, J 9Hz, C_2-H,C_6-H,$C_{3'}$-H and $C_{5'}$-H) and 7.86(2H,d,J 9Hz,$C_{2'}$-H and $C_{6'}$-H).
2	88.0	176-177	3440 and 3280	2.37(3H,s,CH_3); 3.78(3H,s,OCH_3);4.02 (2H,s,CH_2); 5.30(2H,br s,exchanged with D_2O,NH_2); 6.84(2H,d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.12 and 7.23(each 2H, each d, J 9Hz,$C_{3'}$-H, $C_{5'}$-H,$C_{2''}$-H and $C_{6''}$-H) and 7.44(2H,d,J 9Hz,$C_{2'}$-H and $C_{6'}$-H).
3	86.9	142-143	3180 and 1650	1.63(3H,s,$COCH_3$); 2.40(3H,s,CH_3);3.49 (1H,br s,exchanged with D_2O,NH);3.80 3H,s,OCH_3); 4.14(2H,s,CH_2);6.84(2H, d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.13 and 7.23(each 2H,each d,J 9Hz,$C_{3'}$-H,$C_{5'}$-H $C_{2''}$-H and $C_{6''}$-H) and 7.44(2H,d,J 9Hz, $C_{2'}$-H and $C_{6'}$-H).
4	85.7	184-185	2510	1.71(1H,br s,exchanged with D_2O);2.40 (3H,s,CH_3); 3.77(3H,s,OCH_3); 3.87(2H, s,CH_2); 6.85(2H,d,J 9Hz,$C_{3''}$-H and

				$C_{5''}$-H); 7.08(2H,d,J 9Hz, $C_{2''}$-H and $C_{6''}$-H) and 7.28(4H,s,$C_{2'}$-H,$C_{3'}$-H, $C_{5'}$-H and $C_{6'}$-H).
5	85.7	oil	-	2.35(3H,s,CH_3); 2.58(3H,s,SCH_3); 3.67 (3H,s,OCH_3); 4.02(2H,s,CH_2); 6.85(2H, d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.16 and 7.31(each 2H, each d,J 9Hz, $C_{3'}$-H, $C_{5'}$-H and $C_{2''}$-H, $C_{6''}$-H).
6	90.5	oil	1655	2.89-3.62(2H,m,C_β-H); 3.63,3.70 and 3.74(each 3H, each s, 3xOCH_3); 5.40 (1H,t,J 7Hz,C_α-H); 6.32(1H,d,J 2.5Hz $C_{3'}$-H); 6.43(1H,dd,J 9Hz and 2.5Hz, $C_{5'}$-H); 6.73(2H,d,J 9Hz,C_3-H and C_5-H); 7.12(2H,d,J 9Hz,C_2-H and C_6-H) and 7.70(1H, d, J 9Hz, $C_{6'}$-H).
7	79.8	174-175	3450 and 3280	3.73,3.75 and 3.77(each 3H,each s, 3xOCH_3); 3.81(2H,s,CH_2); 5.05(2H,br s, exchanged with D_2O, NH_2); 6.50(1H,d, J 2.5Hz,$C_{3'}$-H); 6.53(1H,dd,J 9Hz and 2.5Hz, $C_{5'}$-H); 6.78(2H,d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.10(2H,d,J 9Hz,$C_{2''}$-H and $C_{6''}$-H) and 7.25(1H,d,J 9Hz,$C_{6'}$-H).
8	90.9	170-171	3180 and 1655	1.65(3H,s,$COCH_3$); 3.72,3.78 and 3.84 (each 3H,each s, 3xOCH_3); 3.89(2H,s, CH_2); 6.53(2H,m,$C_{3'}$-H and $C_{5'}$-H); 6.79(2H,d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.07(2H,d,J 9Hz,$C_{2''}$-H and $C_{6''}$-H) and 7.26(1H,d,J 9Hz,$C_{6'}$-H).
9	89.8	169-170	2520	1.72(1H,s,exchanged with D_2O); 3.79 (6H,s,2xOCH_3);3.81(3H,s,OCH_3);3.83(2H, s,CH_2); 6.51(2H,m,$C_{3'}$-H and $C_{5'}$-H); 6.82(2H,d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.06(2H,d,J 9Hz,$C_{2''}$-H and $C_{6''}$-H) and

				7.17(1H,d,J 9Hz, $C_{6'}$-H).
10	95.2	Oil	-	2.57(3H,s, CH_3); 3.75(6H,s,2xOCH_3); 3.82(3H,s,OCH_3); 3.91(2H,s,CH_2); 6.45 (2H,m,$C_{3'}$-H and $C_{5'}$-H); 6.76(2H,d, J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.08(2H,d, J 9Hz,$C_{2''}$-H and $C_{6''}$-H) and 7.22(1H, d,J 9Hz, $C_{6'}$-H).
11	89.6	Oil	1650	2.08(3H,s,CH_3); 2.98-3.69(2H,m,C_β-H); 3.34,3.72 and 3.84(each 3H,each s, 3xOCH_3); 5.58(1H,t,J 7Hz,C_α-H); 6.57 (1H,d,J 9Hz, $C_{5'}$-H); 6.71(2H,d,J 9Hz, C_3-H and C_{5-H}); 7.14(2H,d,J 9Hz,C_2-H and C_6-H) and 7.39(1H,d,J 9Hz,$C_{6'}$-H).
12	79.8	181-182	3435 and 3270	2.14(3H,s,CH_3); 3.50,3.73 and 3.80 (each 3H, each s, 3xOCH_3); 3.82(2H,s, CH_2); 4.94(2H, br s, exchanged with D_2O, NH_2); 6.61(1H,d,J 9Hz, $C_{5'}$-H); 6.75(2H,d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.05(2H,d,J 9Hz,$C_{2''}$-H and $C_{6''}$-H) and 7.27(1H,d,J 9Hz and $C_{6'}$-H).
13	90.9	140-141	3170 and 1650	1.64(3H,s,$COCH_3$); 2.18(3H,s,CH_3); 3.34,3.66 and 3.77(each 3H, each s, 3xOCH_3); 3.83(2H,s,CH_2); 6.65(1H,d, J 9Hz, $C_{5'}$-H); 6.75(2H,d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 7.06(2H,d,J 9Hz, $C_{2''}$-H and $C_{6''}$-H) and 7.26(1H,d,J 9Hz,$C_{6'}$-H).
14	92.8	185-186	2510	1.71(1H,s,exchanged with D_2O); 2.11 (3H,s,CH_3); 3.50,3.70 and 3.74(each 3H,each s,3xOCH_3); 3.77(2H,s,CH_2); 6.59(1H,d,J 9Hz,$C_{5'}$-H); 6.73(2H,d, J 9Hz,$C_{3''}$-H and $C_{5''}$-H); 6.96(2H,d, J 9Hz,$C_{2''}$-H and $C_{6''}$-H) and 7.05(1H, d,J 9Hz, $C_{6'}$-H).

15	85.0	Oil	-	2.13(3H,s,CH_3); 2.56(3H,s,SCH_3); 3.44, 3.63 and 3.76(each 3H,each s,3xOCH_3); 3.81(2H,s,CH_2); 6.54(1H,d,J 9Hz,$C_{5'}$-H); 6.61(2H,d,J 9Hz,$C_{3''}$-H and $C_{5''}$-H);6.93 (2H,d,J 9Hz,$C_{2''}$-H and $C_{6''}$-H) and 7.05 (1H,d,J 9Hz,$C_{6'}$-H).

a. Satisfactory microanalysis obtained for all the products.

b. Not corrected

ACKNOWLEDGEMENTS

We acknowledge the financial assistance provided by I.C.A.R., New Delhi, India.

REFERENCES

1. 'The Chemistry of Heterocyclic Compounds', ed by J.V. Metzger, vol.34, John Wiley and Sons, New York, 1979.
2. T.C. Sharma and M.M. Bokadia, Indian J. Chem., 1976, 14B, 65.
3. L.C. King and R.H. Dodson, J. Am. Chem. Soc., 1945, 67, 2242; 1946, 68,871.

Received, 17th May, 1985