SYNTHESIS OF SOME 5,5-DISUBSTITUTED 2-THIOHYDANTOIN DERIVATIVES

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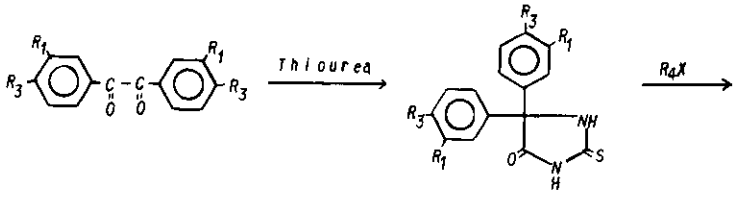
Abstract -- Treatment of 5,5-diphenyl-2-thiohydantoin (2a) with allyl bromide in basic alcohol solution gave 5,5-diphenyl-2-allylthiohydantoin (3a) in 78.5% yield, whose derivatives (3b), (3f), (4a-c), and (6) were also prepared in a similar fashion.

A series of N-and S-alkyl derivatives of 5,5-diphenyl-2-thiohydantoin were prepared as possible anticonvulsants. The 5,5-disubstituted 2-thiohydantoins[1] (2a-b) required as starting materials were prepared by reaction of 4,4'-disubstituted benzil (1a-b) with thiourea, followed by acidification of the solution with hydrochloric acid. The reaction of (2a) (1.0g) with allyl bromide under reflux in ethanol in the presence of sodium hydroxide gave 5,5-diphenyl-2-allylthiohydantoin[2,3] (3a) (mp 165-166°C; 78.5% yield). Likewise the derivatives (3b) (mp 155-160°C; 75% yield), (3c) (mp 204-205°C; 85.2% yield), (3d) (mp 176-178°C; 91.3% yield), (3e) (mp 215-220°C; 94.5% yield), and (3f) (mp 165-168°C; 51.4% yield) were obtained from (2a) and (2b). The compounds (3c), (3d), and (3e) were allowed to react with appropriate alkyl halide to give (4a) (mp 108-110°C; 76.6% yield), (4b) (mp 124-125°C; 85.9% yield), and (4c) (mp 120-122°C; 84.3% yield) respectively. Bromination of 4,4-dimethoxybenzil (1c)[4], followed by reaction of 5 with thiourea afforded 5,5-bis-(p-methoxyl-3-bromophenyl)-2-thiohydantoin (6) (mp 293-295°C; 78.4% yield).



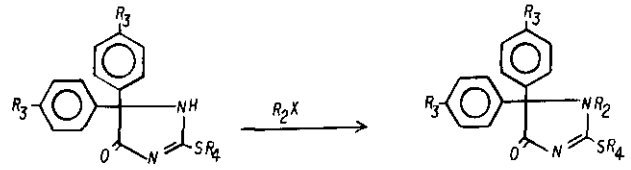
1a (R_1 = H, R_3 = H); 1b (R_1 = H, R_3 = Me)

1c (R_1 = H, R_3 = OMe); 5 (R_1 = Br, R_3 = OMe)

2a (R_1 = H, R_3 = H)

2b (R_1 = H, R_3 = Me)

6 (R_1 = Br, R_3 = OMe)



3a (R_3 = H, R_4 = allyl); 3b (R_3 = H, R_4 = isoamly)

3c (R_3 = H, R_4 = Me); 3d (R_3 = H, R_4 = Et)

3e (R_3 = Me, R_4 = Me); 3f (R_3 = Me, R_4 = Et)

4a (R_2 = Et, R_3 = H, R_4 = Me)

4b (R_2 = Me, R_3 = H, R_4 = Et)

4c (R_2 = R_3 = R_4 = Me)

Table 1. Physical data of new heterocyclic compounds[5]

Compound	m/e (M^+)	^{1}HNMR (δ)
3a	308	(DMSO - d_6) 3.9 (2H, d, J=6.9 Hz), 5.3 (2H, t, J=13.8 Hz) 5.9 (1H, m), 7.4 (10H, m).
3b	338	($CDCl_3$) 0.9 (6H, d, J=7.5 Hz), 1.7 (3H, m), 3.3 (2H, t, J=7.5 Hz).
3f	324	($CDCl_3$) 1.4 (3H, t, J=7.3 Hz), 2.3 (6H, s), 3.3 (2H, q, J=7.3 Hz), 7.1-7.4 (8H, dd, J=8.0 Hz, J=8.0 Hz).
4a	310	(DMSO-d_6) 1.2 (3H, t, J=7.1 Hz), 2.7 (3H, s), 3.5 (2H, q, J=7.1 Hz), 7.3-7.4 (10H, m).
4b	310	($CDCl_3$) 1.4 (3H, t, J=7.3 Hz), 3.1 (3H, s), 3.2 (2H, q, J=7.3 Hz), 7.4 (10H, m).
4c	324	($CDCl_3$) 2.4 (6H, s), 2.8 (3H, s), 3.3 (3H, s), 7.3-7.7 (8H, dd, J=8.0, J-8.0 Hz).
6	484	(DMSO-d_6) 3.8 (6H, s), 7.2-7.5 (6H, m), 11.2 (1H, s), 12.2 (1H, s).

REFERENCES

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(5) All new compounds gave satisfactory high resolution mass spectral data.

Received, 22nd September, 1981