SYNTHESIS OF 4-(N-ALKYL/ARYL-N-NITROSOAMIDO)-2,3-DIHYDRO-1,4-BENZOTHIAZINES

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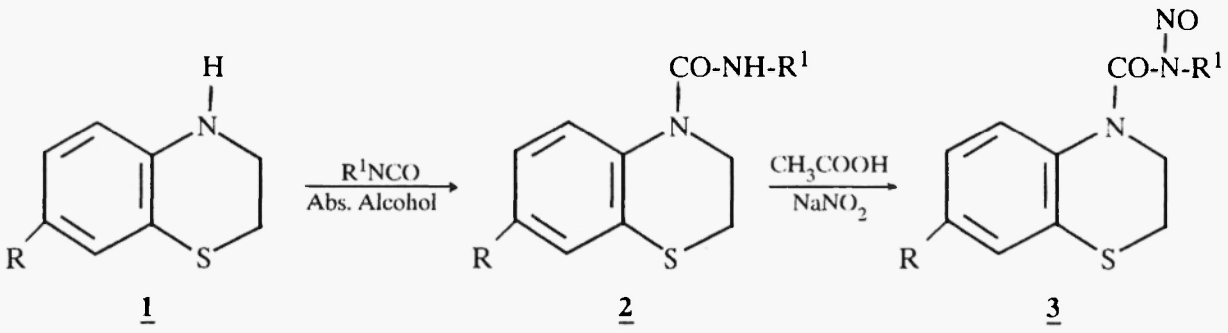
Abstract : Synthesis of title compounds in which heterocyclic nitrogen of 1,4-benzothiazines involves in constituting urea linkage is reported first time. Synthesis involves the reactions of 1,4-benzothiazines with alkyl/aryl isocyanates and subsequent nitrosation.

In continuation to our research programmes to develop synthesis for bioactive heterocycles (1-3) in search of better medicinal agents, it has been considered worthwhile to develop synthetic methodology for the title compounds. In these compounds amido linkage is attached to heterocyclic nitrogen and as such heterocyclic nitrogen is involved in forming urea linkage and constitute an interesting class of antineoplastic agents (4,5).

2,3-Dihydro-1,4-benzothiazines 1 have been prepared by the method reported elsewhere (6). 2,3-Dihydro-1,4-benzothiazine and its 7-chloro derivatives have been converted into 4-(N-alkyl/arylamido) derivatives 2 by their reaction with alkyl/aryl isocyanates. Amides were converted into nitrosoamides 3 by nitrosation with sodium nitrite in acetic acid (Scheme 1).



1 2 3

3a : R = H; R^1 = $CH_2CH_2CH_3$
3b : R = H; R^1 = C_6H_5Cl (m)
3c : R = H; R^1 = C_6H_5Cl (p)
3d : R = Cl; R^1 = $CH_2CH_2CH_3$
3e : R = Cl; R^1 = C_6H_5Cl (m)
3f : R = Cl; R^1 = C_6H_5Cl (p)

Scheme-1

The purity of all the synthesized compounds was checked by thin layer chromatography and structures have been characterized on the basis of elemental analysis and spectral studies NMR, IR and Mass (7).

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References

(1) R.R. Gupta, (Ed.) "Phenothiazines and 1,4-Benzothiazines – Chemical and Biomedical Aspects". Elsevier, Amsterdam, 1988 and references therein.

(2) V. Gupta, A. Gupta, R.S. Rathore and R.R. Gupta, Org. Pre. Int., 26, 7 (1994).

(3) R.R. Gupta, V. Saraswat, A. Gupta, M. Jain and V. Gupta, J. Heterocycl. Chem. 29, 1703 (1992).

(4) A.W. Prestayko, S.T. Crooke, L.H. Baker, S.K. Carter and P.S. Schein, (Eds.) "Nitrosourea : Current Status and New Developments." Academic Press, New York, 1981 and references cited in.

(5) D.E.V. Wilman, (Ed.) "The Chemistry of Antitumor Agents". Blackie and Sons, Glasgow 1990.

(6) C.M. Rajoria, Ph. D. Thesis, Univ. of Rajasthan, Jaipur 1994.

(7) All synthesized compounds give satisfactory elemental analyses. Spectral data for compounds are :

3a ^{1}H-NMR (DMSO-d_6) δ : 7.76-7.32 (4H, m, Ph), 4.24-4.02 (2H, t, CH_2), 3.61-3.32 (2H, t CH_2), 3.07-2.78 (2H,t,-CH_2), 1.96-1.52 (2H, m, CH_2 at C_2'), 1.26-1.01 (3H, t, CH_3 at C_3'); IR 1592 cm^{-1}; MS m/z, 265 (M^+).

3b ^{1}H-NMR (DMSO-d_6) δ : 7.92-7.47 (8H, m, Ph), 4.43-4.18 (2H, t, CH_2 at C_3), 3.74-3.48 (2H, t, CH_2 at C_2); IR 1586 & 753 cm^{-1}; MS m/z, 333 (M^+).

3c ^{1}H-NMR (DMSO-d_6) δ : 8.40-7.29 (8H, m, Ph), 4.43-4.27 (2H, t, CH_2 at C_3), 3.26-3.01 (2H, t, CH_2 at C_2); IR 1594 & 757 cm^{-1}; MS m/z, 333 (M^+).

3d ^{1}H-NMR ($CDCl_3$) δ : 7.41-6.97 (3H, m, Ph), 4.12-3.80 (2H, t, CH_2 at C_3), 3.36-3.23 (2H, t, CH_2 at C_2), 3.20-2.91 (2H, t, CH_2 at C_1')1.71-1.29 (2H,m, CH_2) at C_2', 1.10-0.69 (3H, t, CH_3 at C_3') ; IR 1650 & 649 cm^{-1}; MS m/z, 299 (M^+).

3e ^{1}H-NMR ($CDCl_3$) δ : 8.36-6.94 (7H, m, Ph), 4.87-4.64 (2H, t, CH_2 at C_3) ; IR 1593 & 756 cm^{-1}; MS m/z, 368 (M^+).

3f ^{1}H-NMR ($CDCl_3$) δ : 7.51-6.56 (7H, m, Ph), 3.74-3.51 (2H, t, CH_2 at C_3), 3.13-2.94 (2H, t, CH_2 at C_2); IR 1579 & 766 cm^{-1}; MS m/z, 333 (M^+).