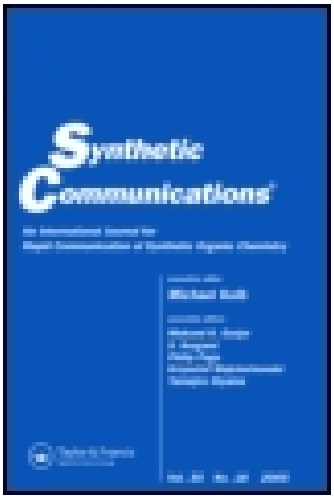


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Novel One-Pot Synthesis of Aziridines Containing Sydnone Moiety

N. Satheesha Rai [a], Balakrishna Kalluraya [a] & B. Lingappa [a]
[a] Department of Studies in Chemistry, Mangalore University, Mangalagangothri, Karnataka, India
Published online: 03 Jul 2007.

To cite this article: N. Satheesha Rai, Balakrishna Kalluraya & B. Lingappa (2007) Novel One-Pot Synthesis of Aziridines Containing Sydnone Moiety, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 37:13, 2267-2273, DOI: 10.1080/00397910701397227

To link to this article: http://dx.doi.org/10.1080/00397910701397227

Synthetic Communications®, 37: 2267–2273, 2007

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910701397227

Novel One-Pot Synthesis of Aziridines Containing Sydnone Moiety

N. Satheesha Rai, Balakrishna Kalluraya, and B. Lingappa
Department of Studies in Chemistry, Mangalore University,
Mangalagangothri, Karnataka, India

Abstract: A novel series of 1,1a-dihydro-1-aryl-2-(3-aryl-sydnone-4-yl)-azirino[1,2-a] quinoxalines were prepared in a one-pot reaction of 2,3-dibromo-1-(3-arylsydnone-4-yl-)-3-arylpropan-1-one with o-phenylenediamine employing triethylamine in ethanol. The new compounds were well characterized by IR, ^{1}H NMR, mass spectra, and C,H,N analysis.

Keywords: aziridines, dibromochalcones, quinoxalines, sydnone derivatives

INTRODUCTION

The aziridine moiety represents one of the most valuable three-membered ring systems in organic chemistry because of its versatile building-block nature for the synthesis of many nitrogen-containing biologically active molecules.[1–4] The aziridine moiety is present in a wide variety of natural biologically active compounds, such as antitumor and antibiotic agents.[5] Synthetic aziridines exhibit multiple biological properties such as enzyme inhibitors and DNA alkylation agents.[6]

Sydnones are a novel class of mesoionic aromatic heterocycles that serve as versatile synthetic intermediates with a masked azomethine imine unit.[7,8] Because of their mesoionic character, they have been the subject of continual study since their discovery. Interest in sydnone derivatives has been

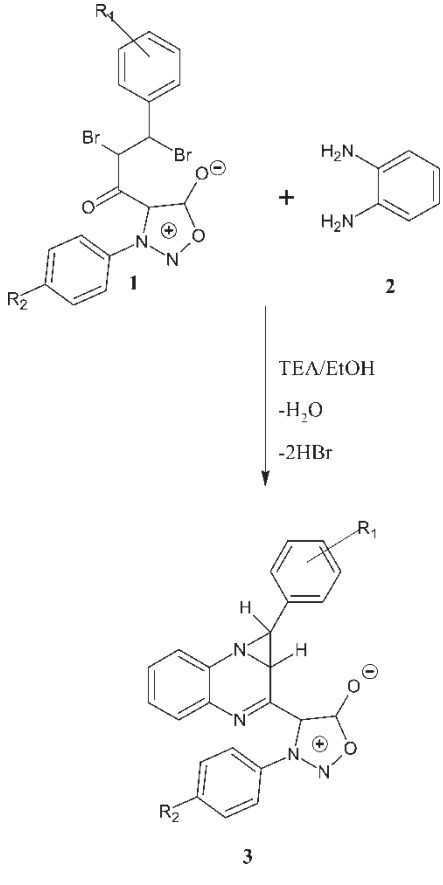
Received December 1, 2006
Address correspondence to Balakrishna Kalluraya, Department of Studies in Chemistry, Mangalore University, Mangalagangothri 574 199, Karnataka, India. E-mail: bkalluraya_2001@yahoo.com

encouraged by the discovery that they exhibit various pharmacological activities.[9,10]

Prompted by the these observations and in continuation of our research in sydnone chemistry,[11–13] a project was undertaken to synthesize a novel series of aziridines containing the sydnone moiety.

RESULTS AND DISCUSSION

The reaction between 2,3-dibromo-1-(3-arylsydnone-4-yl-)-3-arylpropan-1-one **1a–f** and o-phenylenediamine **2** in the presence of triethyl amine in ethyl alcohol resulted in the formation of 1,1a-dihydro-1-aryl-2-(3-aryl-sydnone-4-yl)-azirino[1,2-a] quinoxalines **3a–i** Scheme 1. The generality of this method with respect to various precursors is summarized in Table 1.



Scheme 1.

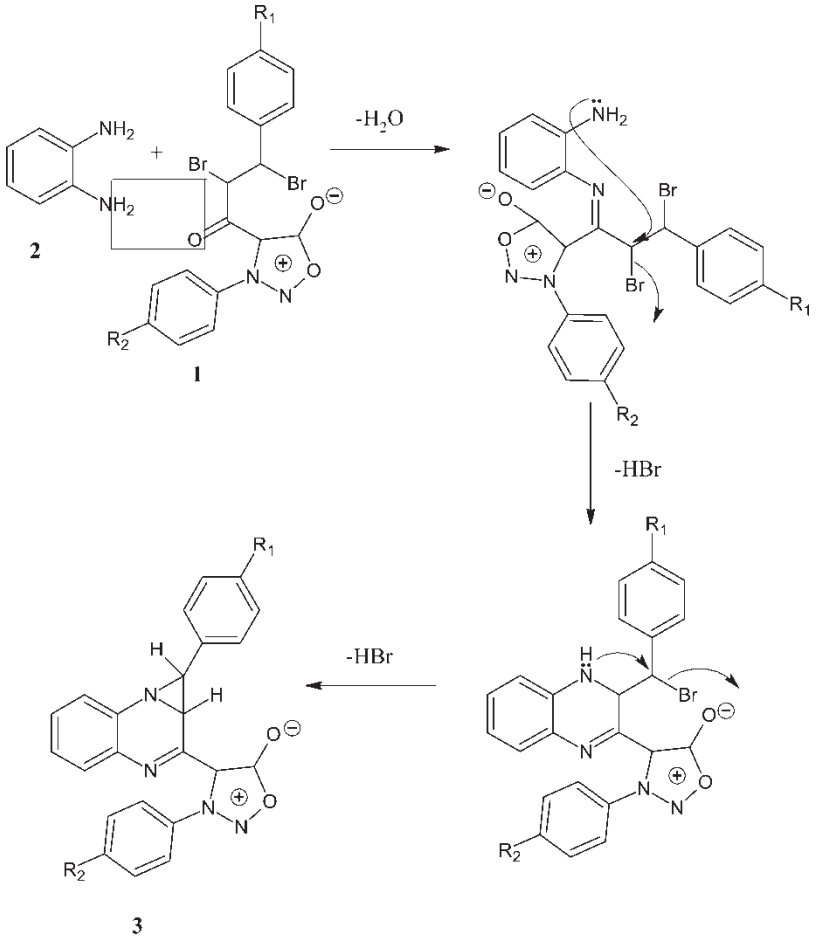
Table 1. Characterization data of 1,1a-dihydro-1-aryl-2-(3-aryl-sydnone-4-yl)-azirino[1,2-a] quinoxalines **3a–i**

Compounds	R_1	R_2	Mol. formula	Mol. wt.	Yield (%)	Mp (°C)	Nature of the solid	Analysis (%) found (calculated)		
								C	H	N
3a	p-Br	Me	$C_{24}H_{17}N_4O_2Br$	472/474	74	159–161	Orange crystals	60.86 (60.88)	3.52 (3.59)	11.81 (11.83)
3b	p-Br	OMe	$C_{24}H_{17}N_4O_3Br$	488/490	68	144–146	Orange	58.84 (58.89)	3.42 (3.47)	11.51 (11.45)
3c	p-Br	H	$C_{23}H_{15}N_4O_2Br$	458/460	65	153–155	Reddish orange	60.10 (60.13)	3.25 (3.26)	12.19 (12.20)
3d	H	Me	$C_{24}H_{18}N_4O_2$	394	69	138–140	Light orange	73.10 (73.09)	4.54 (4.56)	14.20 (14.21)
3e	2,6-dichloro	H	$C_{23}H_{14}N_4O_2Cl_2$	448/450/452	70	162–164	Brownish orange crystals	61.45 (61.48)	3.10 (3.11)	12.45 (12.47)
3f	3,4-methylene dioxy	OMe	$C_{25}H_{18}N_4O_5$	454	58	237–239	Light orange	66.10 (66.07)	3.94 (3.96)	12.32 (12.33)
3g	p-OMe	H	$C_{24}H_{18}N_4O_3$	410	55	203–205	Brownish, shining	70.21 (70.24)	4.38 (4.39)	13.64 (13.65)
3h	p-OMe	OMe	$C_{25}H_{20}N_4O_4$	440	58	184–186	Light yellowish	68.17 (68.18)	4.53 (4.54)	12.71 (12.72)
3i	p-Cl	Me	$C_{24}H_{17}N_4O_2Cl$	428/430	69	147–149	Orange crystals	67.19 (67.21)	3.95 (3.96)	13.06 (13.07)

Note: Solvent for recrystallization was EtOH.

The starting material 2,3-dibromo-1-(3-arylsydnone-4-yl-)-3-arylpropan-1-one **1a–f** was prepared by the direct bromination of 1-(3-arylsydnone-4-yl)-3-aryl-2-propene-1-one. These propenones were in turn obtained by the condensation of an appropriate aldehyde with 3-substituted-4-acetyl sydnones.[14] 3-Substituted-4-acetylsydnone was prepared according to the procedures reported in literature.[15] A probable mechanistic pathway for the formation of aziridine quinoxaline **3** is shown in Scheme 2.

In conclusion, we studied the reaction of sydnone dibromides with o-phenylene diamine to get aziridines **3a–i** in a one-pot reaction, and the yields ranged from 55 to 74%.



Scheme 2. Probable mechanistic pathway.

EXPERIMENTAL

General

Melting points were determined by the open capillary method and are uncorrected. All compounds were analyzed satisfactorily for C, H, and N. IR spectra (KBr disc) were recorded on a Jasco FT IR 430 spectrophotometer. ^{1}H NMR spectra were recorded on Bruker AC 300F (300 MHz or 400 MHz) NMR spectrometer using DMSO-d_6 as solvent and TMS as internal standard. The chemical shifts are expressed in δ scale downfield from TMS, and proton signals are indicated as s, singlet; d, doublet; and m, multiplet. Mass spectra were recorded either on a Jeol JMS-D 300 mass spectrometer or API 3000 LCMS instrument operating at 70eV.

General Procedure

Preparation of 2,3-Dibromo-1-(3-arylsydnone-4-yl-)-3-arylpropan-1-one **1a–f**

1-(3-Arylsydnone-4-yl)-3-aryl-2-propene-1-one (0.1 mol) was dissolved in glacial acetic acid (25–30 ml) by gentle warming. A solution of bromine in glacial acetic acid (30% w/v) was added to it with constant stirring till the yellow color of bromine persisted. The reaction mixture was stirred at room temperature for 1–2 h. The separated solid was filtered, washed with petroleum ether, and dried. Further purification was done by recrystallization from ethanol.

Preparation of 1,1a-Dihydro-1-aryl-2-(3-aryl-sydnone-4-yl)-azirino[1,2-a] Quinoxalines **3a–i**

A mixture of 2,3-dibromo-1-(3-arylsydnone-4-yl-)3-arylpropan-1-one (0.01 mol), o-phenylene diamine (0.01 mol), and triethylamine (0.05 mol) was dissolved in 15 ml ethanol by heating. The clear solution was allowed to stand at room temperature for 24 h. The solid obtained was collected by filtration. It was recrystallized from ethanol to afford **3a–i** in 55–74% yield.

The characterization data of the compounds **3a–i** are given in Table 1.

Spectral Data for Compounds 3a–i

3a: IR (KBr, cm^{-1})γ 1772 cm^{-1} (Sydnone C═O), 1617 cm^{-1}(C═N). ^{1}H NMR ($CDCL_3$, 400 MHz) δ 2.49 (s, 3H, CH_3); δ 2.91 (d, 1H, Aziridne C_2-H); 3.67 (d, 1H, Aziridne C_3-H); 6.73 (d,d,1H, Quinoxaline C_4-H); 7.23 (d,d,1H, Quinoxaline C_7-H); δ 7.02–7.11 (m, 2H, Quinoxaline C_5-H and

C_6-H); 7.24 (d, 2H, ortho protons of p-tolyl); 7.34 (d, meta protons of p-tolyl); 7.45 (d, meta protons of p-bromophenyl); 7.49 (d, ortho protons of p-bromomphenyl). MS, m/z, 472/474 for $C_{24}H_{17}N_4O_2Br$.

3b: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.11 (d, 1H, Aziridine C_2-H); 3.41 (d, 1H, Aziridne C_3-H); 3.79 (s, 3H, OCH_3); 6.81 (d, d, 1H, Quinoxaline C_4-H); 7.01 (d, 2H, ortho protons of p-anisyl); 7.52 (d, 2H, meta protons of p-bromophenyl); 7.68 (d, 2H, ortho protons of p- bromophenyl); 7.03–7.16 (m, 5H, Quinoxaline C_5-H,C_6-H,C_7-H and meta protons of p-anisyl. MS, m/z, 488/490 for $C_{24}H_{17}N_4O_3Br$.

3c: IR (KBr, cm^{-1}) γ 1749 cm^{-1} (Sydnone C═O), 1599 cm^{-1}(C═N); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.17 (d, 1H, Aziridine C_2-H); 3.57 (d, 1H, Aziridne C_3-H); 6.54 (d, d, 1H, Quinoxaline C_4-H); 7.16 (d, d, 1H, Quinoxaline C_7-H); 7.01–7.12 (m, 2H, Quinoxaline C_5-H and C_6-H); 7.22 (d, 2H, meta protons of p-bromophenyl); 7.55–7.64 (m, 5H, ArH); 7.76 (d, 2H, ortho protons of p-bromophenyl). MS, m/z, 458/460 for $C_{23}H_{15}N_4O_2Br$.

3d: IR (KBr, cm^{-1}) γ 1747 cm^{-1} (Sydnone C═O), 1611 cm^{-1}(C═N); ^{1}H NMR ($CDCL_3$, 300 MHz) δ 2.33 (s, 3H, CH_3); 3.07 (d, 1H, Aziridine C_2-H); 3.48 (d, 1H, Aziridne C_3-H), 6.70 (d, d, 1H, Quinoxaline C_4-H); 7.06–7.21 (m, 3H, quinaoxaline C_5-H, C_6-H and C_7-H); 7.20 (d, 2H, ortho protons of p-tolyl); 7.30–7.36 (m, 5H, Ar-H), 7.62 (d, 2H, meta protons of p-tolyl). MS, m/z, 395 ($M^+ + 1$) for $C_{24}H_{18}N_4O_2$.

3e: ^{1}H NMR ($CDCL_3$, 400 MHz) δ 3.03 (d, 1H, Aziridne C_2-H); 3.51 (d, 1H, Aziridne C_3-H); 6.78 (d, d, 1H, Quinoxaline C_4-H); 7.19 (d, d, 1H, Quinoxaline C_7-H); 7.96–7.16 (m, 2H, Quinoxaline C_5-H and C_6-H); 7.24–7.48 (m, 8H, Ar-H). MS, m/z, 448/450/452 for $C_{23}H_{14}N_4O_2Cl_2$.

3f: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.86 (d, 1H, Aziridine C_2-H); 3.61 (d, 1H, Aziridne C_3-H), 3.74 (s, 3H, p-OCH_3), 5.41 (s, 2H, O-CH_2-O); 6.73 (d, d, 1H, Quinoxaline C_4-H); 7.21 (d, d, 1H, Quinoxaline C_7-H); 6.89–7.14 (m, 2H, Quinoxaline C_5-H and C_6-H); 7.16 (d, 1H, C_5-H of 3,4-methylenedioxyphenyl); 7.27 (d, 1H, C_2-H of 3,4-methylenedioxyphenyl); 7.31 (d, 1H, C_6-H of methylenedioxyphenyl); 7.24 (d, 2H, ortho protons of p-anisyl), 7.48 (d, 2H, meta protons of p-anisyl). MS, m/z, 455 ($M^+ + 1$) for $C_{25}H_{18}N_4O_5$.

3g: ^{1}H NMR ($CDCL_3$, 400 MHz) δ 2.87 (d, 1H, Aziridne C_2-H); 3.57 (d, 1H, Aziridne C_3-H); 3.91 (s, 3H, p-OCH_3), 6.68 (d, d, 1H, Quinoxaline C_4-H); 7.16 (d, d, 1H, Quinoxaline C_7-H); 6.79–7.08 (m, 2H, Quinoxaline C_5-H and C_6-H); 7.32 (d, 2H, ortho protons of p-anisyl); 7.51 (d, 2H, meta protons of p-anisyl); 7.04–7.29 (m, 5H, Ar-H). MS, m/z, 411 ($M^+ + 1$) for $C_{24}H_{18}N_4O_3$.

3h: MS, m/z; 441 ($M^+ + 1$) for $C_{25}H_{20}N_4O_4$.

3i: ^{1}H NMR ($CDCL_3$, 400 MHz) δ 2.48 (s, 3H, p-CH_3); 2.92 (d, 1H, Aziridne C_2-H); 3.68 (d, 1H, Aziridne C_3-H); 6.72 (d, d, 1H, Quinoxaline C_4-H); 7.22 (d, d, 1H, Quinoxaline C_7-H); 6.98–7.14 (m, 2H, Quinoxaline C_5-H and C_6-H); 7.27–7.46 (m, 8H, ArH of p-chlorophenyl and p-tolyl). MS, m/z, 428/430 for $C_{24}H_{17}N_4O_2Cl$.

ACKNOWLEDGMENTS

The authors thank the head of Regional Sophisticated Instrumentation Centre (RSIC), Chandigarh, and Central Drug Research Institute (CDRI) Lucknow for spectral and analytical data. The authors are also thankful to University Grants Commission (UGC), New Delhi, for the financial assistance in the form of a major research project.

REFERENCES

1. Lindstrom, U. M.; Somfai, P. *Synthesis* **1998**, 109.
2. Zwanenburg, B.; Ten Holte, P. *Top. Curr. Chem.* **2001**, 94.
3. Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247.
4. Hu, X. E. *Tetrahedron* **2004**, *60*, 2701.
5. (a) Gerhart, F.; Higgins, W.; Tardif, C.; Ducep, J. *J. Med. Chem.* **1990**, *33*, 2157; (b) Kasai, M.; Kono, M. *Synlett* **1992**, 778; (c) Tanner, M. E.; Miao, S. *Tetrahedron Lett.* **1994**, *35*, 4073; (d) Hodgkinson, T. J.; Shipman, M. *Tetrahedron* **2001**, *57*, 4467.
6. (a) Toda, A.; Aoyama, H.; Mimura, N.; Ohno, H.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1998**, *63*, 7053; (b) Hwang, G. I.; Chung, J. H.; Lee, W. K. *J. Org. Chem.* **1996**, *61*, 6183; (c) Park, C. S.; Choi, H. G.; Lee, H.; Lee, W. K.; Ha, H. J. *Tetrahedron: Asymmetry* **2000**, *11*, 3283.
7. Hegde, J. C.; Rai, G.; Puranic, V. G.; Kalluraya, B. *Synth. Commun.* **2006**, *36*, 1285–1290.
8. (a) Padwa, A.; Burgess, E. M.; Gingirich, H. L.; Roush, D. M. *J. Org. Chem.* **1982**, *47* (5), 788; (b) Totoe, H.; McGowin, A. E.; Turnbull, K. *J. Supercrit. Fluids* **2000**, *18*, 131.
9. Dunkeley, C. S.; Thoman, C. J. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2899.
10. Shin, M. H.; Ke, F. Y. *Bioorg. Med. Cem.* **2004**, *12*, 4633.
11. Kalluraya, B.; Rahiman, A. M.; Banji, D. *Arch. Pharm. Med. Chem.* **2001**, *334*, 263.
12. Kalluraya, B.; Rai, G. *Synth. Commun.* **2003**, *33* (20), 3589–3595.
13. Kalluraya, B.; Rahiman, A. M. *Polish J. Chem.* **1997**, *71*, 1049.
14. Rahiman, A. M. Mangalore University, *PhD Thesis*, 2002.
15. Greco, C. Y.; Tobias, J.; Kier, L. B. *J. Heterocycl. Chem.* **1967**, *4*, 160.