Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 5383–5386

TETRAHEDRON

Synthesis of quaternary allylammonium salts via ring opening of 1-benzyl-2-(bromomethyl)aziridines

Matthias D'hooghe, Willem Van Brabandt and Norbert De Kimpe*

Department of Organic Chemistry, Faculty of Agricultural and Applied Biological Sciences, Ghent University, Coupure Links 653, B-9000 Ghent, Belgium

Received 26 September 2002; revised 21 November 2002; accepted 27 November 2002

Abstract—Treatment of 1-benzyl-2-(bromomethyl)aziridine, and some aryl substituted analogues, with an excess of iodomethane resulted in *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium salts, in good yields. These quaternary allylammonium salts are of importance in different fields, from organic synthesis and polymeric chemistry to agricultural use.

1. Introduction

At present, little is known about the chemistry of 2-(halomethyl)aziridines, a potential class of β-haloamines to serve as building blocks in synthetic organic chemistry. In former research, allylic amines were prepared via a radical-induced ring opening[1,2,3] or via sonochemical cleavage[4] of 2-(bromomethyl)aziridines. 2-(Bromomethyl)aziridines were also transformed into pyrrolizidines by cascade reactions of *N*-alkenylaziridinylmethyl radicals,[5] and 2-methyleneaziridines were synthesised by dehydrobromination.[6] The aim of the presented research was to evaluate the reactivity of 1-benzyl-2-(bromomethyl)aziridines with regard to iodoalkanes. Due to the absence of an electron withdrawing group at the nitrogen atom, the aziridine ring is less susceptible to direct ring opening, and the lone pair at nitrogen can react as a nucleophile in for example a substitution reaction with an alkyl halide. When 1-substituted 2-(bromomethyl)aziridines and iodomethane were used, *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium salts were formed in an exclusive way, via an unexpected ring opening. The importance of a general method for the preparation of *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium salts can be concluded from the various applications of these compounds. Like many other quaternary ammonium salts, *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium salts are useful in organic synthesis for phase transfer catalysis[7] and also as starting material or reagent,[8–11] for example for the synthesis of heterocyclic compounds by debenzylation of quaternary ammonium salts.[9] Due to their intrinsic properties, they are used for dyeing and printing cellulose textiles[12] and as emulsion stabilizers, for example in polymerisation processes.[13–16] Ammonium salts in general,[17–23] and *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium salts in particular,[24] are of significant importance in agriculture, because of their plant growth regulating activity. Related ammonium salts also exhibit antimicrobial activity, which makes them attractive as potential antibiotics.[25–27] As a final example of the applicability of the title compounds, improved antistatic properties of photographic material can be mentioned.[28] The majority of the contributions concerning allylammonium salts was found in the patent literature.

2. Results and discussion

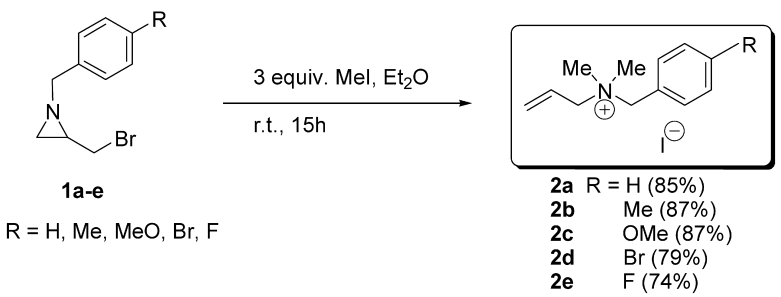
In the present report 1-benzyl-2-(bromomethyl)aziridines **1**, including benzyl substituted derivatives, were synthesized via a known procedure, starting from 4-substituted benzaldehydes.[4] Treatment of these benzaldehydes with allylamine yielded the corresponding aldimines, which were then treated with bromine, followed by a reduction step in order to form the aziridines **1** in high yields. The obtained 1-benzyl-2-(bromomethyl)aziridines **1** were treated with an excess of iodomethane in dry ether. After 15 hours at room temperature, *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium iodides **2** were isolated in good yields (Scheme 1).

These results were quite unexpected, based upon the reaction intermediates. The nucleophilic nitrogen atom of the aziridine attacked iodomethane in a S_N2 reaction, resulting in an intermediate aziridinium salt. Because of the presence of a fairly good nucleophilic counter ion, i.e. iodide, ring opening of this activated aziridinium salt via a S_N2 or S_N1 type reaction onto an aziridine carbon atom was expected. The obtained results indicate that in fact another

Keywords: allylation; ring opening; 2-(bromomethyl)aziridines; ammonium salts.

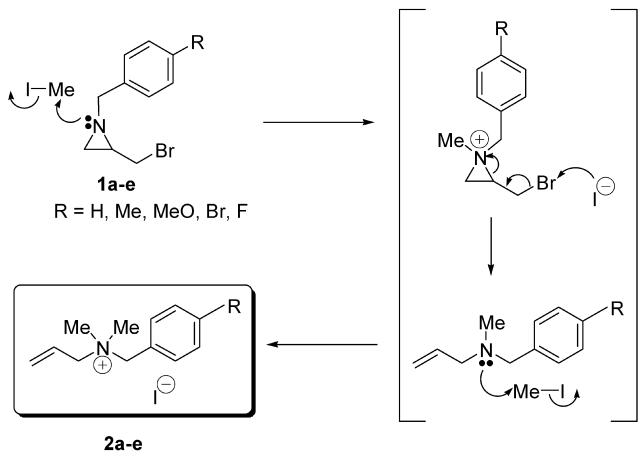
* Corresponding author. Tel.: +0032(9)-2645951; fax: +0032(9)-2646243; e-mail: norbert.dekimpe@UGent.be

0040–4020/03/$ - see front matter
doi:10.1016/S0040-4020(03)00771-3



Scheme 1.

mechanism is occurring. Apparently the iodide anion attacked the bromo atom (halophilic reaction), resulting in bromoiodide and the corresponding allylic amine. This tertiary allylic amine reacted then further with the excess of iodomethane, yielding the quaternary allylammonium salts **2** (Scheme 2).



Scheme 2.

When 1-benzyl-2-(bromomethyl)aziridines **1** were treated with iodomethane in dry dichloromethane at room temperature, no reaction was observed, and the starting aziridines were recovered completely. Extension of the conversion of aziridines **1** to allylammonium salts **2** using other electrophiles was also evaluated. After treatment of 1-benzyl-2-(bromomethyl)aziridine **1a** with an excess of iodoethane, 1-iodopropane or 1-iodobutane in ether at room temperature, no selective reaction occurred and complex reaction mixtures were isolated, pointing to the peculiar role of the reactive iodomethane and the etheral solvent in this reaction.

3. Experimental

3.1. General

^{1}H NMR spectra were recorded at 270 MHz (JEOL JNM-EX 270) with $CDCl_3$ as solvent and tetramethylsilane as internal standard. ^{13}C NMR spectra were recorded at 68 MHz (JEOL JNM-EX 270) with $CDCl_3$ as solvent. IR spectra were measured with a Perkin Elmer Spectrum One FT-IR. Mass spectra were recorded with an Agilent 1100, series: MS, detector: VL, 70 eV, ES 4000 V. Diethyl ether was dried by distillation over sodium benzophenone ketyl; ethanol was used as received from the supplier.

1-Benzyl-2-(bromomethyl)aziridines **1** were synthesized via a known procedure.[4]

3.1.1. 2-(Bromomethyl)-1-(4-fluorobenzyl)aziridine 1e (96%). Spectral data of 2-(bromomethyl)aziridines **1a–d** have been reported elsewhere.[1,6]

^{1}H NMR (270 MHz, $CDCl_3$): δ=1.61 (d, $J_{H,H}$=6.27 Hz, 1H, N(H_{cis}CH)CH), 1.79 (d, $J_{H,H}$=3.30 Hz, 1H, N(HCH_{trans})CH), 1.88–1.96 (m, 1H, NCH), 3.26 and 3.30 (2×d×d, $J_{H,H}$=10.48, 5.45, 7.26 Hz, 2H, CH_2Br), 3.36 and 3.49 (2×d, $J_{H,H}$=13.37 Hz, 2H, NCH_2C$_6$H$_4$), 6.97–7.08 and 7.31–7.33 (m, 4H, C$_6$H$_4$). ^{13}C NMR (68 MHz, $CDCl_3$): δ=35.27 (CH_2Br), 35.54 (NCH_2CH), 40.14 (NCH), 63.27 (NCH_2C$_6$H$_4$), 114.88 and 115.18, 129.63 and 129.74 (2×FHC$_{ortho}$ and 2×FHC$_{meta}$), 134.43 and 134.46 (NCH$_2$C), 160.11 and 163.70 (FC). IR (NaCl): ν=3048 cm^{-1}, 2985, 2900, 2835, 1605, 1510. MS (70 eV): m/z (%): 244/6(M$^+$+1, 87), 109(100).

3.2. General procedure for the synthesis of *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium salts 2

The synthesis of *N*-allyl-*N*-benzyl-*N*,*N*-dimethylammonium iodide **2a** from 1-benzyl-2-(bromomethyl)aziridine **1a** is representative for all other preparations.

To a solution of 1-benzyl-2-(bromomethyl)aziridine **1a** (0.23 g, 1.0 mmol),[4] in dry diethyl ether (2 mL), iodomethane (0.43 g, 3.0 mmol) was added dropwise at room temperature. The reaction mixture was then stirred for 15 hours at room temperature. The solvent was decanted and the precipitated salt was washed with dry ether (3×5 mL). After removal of the residual solvent in vacuo, a viscous brown ammonium salt was obtained. The salt was purified by recrystallisation from ethanol. Due to the hygroscopic nature of these salts no accurate melting points could be measured, and IR spectra had to be recorded in $CDCl_3$.

3.2.1. *N*-Allyl-*N*-benzyl-*N*,*N*-dimethylammonium iodide 2a (85%). ^{1}H NMR (270 MHz, $CDCl_3$): δ=3.15 (s, 6H, $(CH_3)_2N^+$), 4.20 (d, $J_{H,H}$=7.25 Hz, 2H, CHCH_2N^+), 4.73 (s, 2H, PhCH_2N^+), 5.85–5.94 (m, 2H, CH=CH_2), 6.05–6.18 (m, 1H, CH=CH$_2$), 7.29–7.65 (m, 5H, C$_6$H$_5$). ^{13}C NMR (68 MHz, $CDCl_3$): δ=49.99 ($(CH_3)_2N^+$), 67.01 and

68.36 (2×CH_2N^+), 123.92 (*C*H=CH_2), 126.16 ($C_{arom,quat}$), 129.76 and 133.30 (C_{ortho} and C_{meta}), 131.37 and 131.46 (CH=*C*H_2 and C_{para}). IR (NaCl, $CDCl_3$): ν=3028 cm^{-1}, 2976, 2953, 1602, 1585, 1474, 1454.

3.2.2. *N*-Allyl-*N*-(4-methylbenzyl)-*N*,*N*-dimethylammonium iodide 2b (87%). ^1H NMR (270 MHz, $CDCl_3$): δ=2.40 (s, 3H, CH_3C), 3.13 (s, 6H, $(CH_3)_2N^+$), 4.17 (d, $J_{H,H}$=6.93 Hz, 2H, CHC*H*$_2N^+$), 4.66 (s, 2H, PhC*H*$_2N^+$), 5.84–5.94 (m, 2H, CH=C*H*$_2$), 6.04–6.17 (m, 1H, C*H*=CH_2), 7.30–7.33 and 7.48–7.51 (2×m, 4H, 2×Me*H*C_{ortho} and 2×Me*H*C_{meta}). ^{13}C NMR (68 MHz, $CDCl_3$): δ=21.56 (*C*H_3C), 49.90 ($(CH_3)_2N^+$), 66.88 (CH*C*H_2N^+), 68.48 (Ph*C*H_2N^+), 123.14 ($CH_2C_{arom,quat}$), 123.95 (*C*H=CH_2), 130.42 and 133.21 (2×MeHC_{ortho} and 2×MeHC_{meta}), 131.36 (CH=*C*H_2), and 141.67 (Me*C*). IR (NaCl, $CDCl_3$): ν=3014 cm^{-1}, 2973, 1614, 1515, 811.

3.2.3. *N*-Allyl-*N*-(4-methoxybenzyl)-*N*,*N*-dimethylammonium iodide 2c (87%). ^1H NMR (270 MHz, $CDCl_3$): δ=3.09 (s, 6H, $(CH_3)_2N^+$), 3.86 (s, 3H, OCH_3), 4.08 (d, $J_{H,H}$=6.93 Hz, 2H, CHC*H*$_2N^+$), 4.62 (s, 2H, PhC*H*$_2N^+$), 5.86–5.93 (m, 2H, CH=C*H*$_2$), 6.06–6.21 (m, 1H, C*H*=CH_2), 7.02–7.05 (m, 2H, 2×MeO*H*C_{ortho}), 7.52–7.56 (m, 2H, 2×MeO*H*C_{meta}). ^{13}C NMR (68 MHz, $CDCl_3$): δ=49.81 ($(CH_3)_2N^+$), 56.06 (OCH_3), 66.72 and 68.36 (2×CH_2N^+), 115.16 (2×MeOHC_{ortho}), 117.75 and 123.93 (*C*H=CH_2 and $CH_2C_{arom,quat}$), 131.32 (CH=*C*H_2), 134.82 (2×MeOHC_{meta}), 161.51 (MeO*C*). IR (NaCl, $CDCl_3$): ν=2961 cm^{-1}, 2836, 1611, 1514, 1472, 1257.

3.2.4. *N*-Allyl-*N*-(4-bromobenzyl)-*N*,*N*-dimethylammonium iodide 2d (79%). ^1H NMR (270 MHz, $CDCl_3$): δ=3.16 (s, 6H, $(CH_3)_2N^+$), 4.17 (d, $J_{H,H}$=7.26 Hz, 2H, CHC*H*$_2N^+$), 4.71 (s, 2H, PhC*H*$_2N^+$), 5.88–5.97 (m, 2H, CH=C*H*$_2$), 6.02–6.20 (m, 1H, C*H*=CH_2), 7.53–7.56 (m, 2H, 2×BrHC_{meta}), 7.68–7.71 (m, 2H, 2×BrHC_{ortho}). ^{13}C NMR (68 MHz, $CDCl_3$): δ=50.01 ($(CH_3)_2N^+$), 67.35 (CH*C*H_2N^+), 68.05 (Ph*C*H_2N^+), 123.29 (*C*H=CH_2), 124.85 and 131.64 (BrC and $CH_2C_{arom,quat}$), 131.98 (CH=*C*H_2), 133.17 and 134.86 (2×BrHC_{ortho} and 2×BrHC_{meta}). IR (NaCl, $CDCl_3$): ν=2983 cm^{-1}, 1593, 1476, 1406, 1264.

3.2.5. *N*-Allyl-*N*-(4-fluorobenzyl)-*N*,*N*-dimethylammonium iodide 2e (74%). ^1H NMR (270 MHz, $CDCl_3$): 3.18 (s, 6H, $(CH_3)_2N^+$), 4.24 (d, $J_{H,H}$=7.26 Hz, 2H, CHC*H*$_2N^+$), 4.84 (s, 2H, PhC*H*$_2N^+$), 5.83–5.94 (m, 2H, CH=C*H*$_2$), 6.02–6.19 (m, 1H, C*H*=CH_2), 6.99–7.74 (m, 4H, C_6H_4). ^{13}C NMR (68 MHz, $CDCl_3$): δ=49.70 ($(CH_3)_2N^+$), 66.83 and 67.28 (2×CH_2N^+), 116.66 and 116.98; 124.63 and 124.67 (2×FHC_{ortho} and 2×FHC_{meta}); 126.07 (*C*H=CH_2); 129.50 (CH=*C*H_2); 136.26 and 136.39 ($CH_2C_{arom,quat}$); 162.73 and 166.39 (FC). IR (NaCl, $CDCl_3$): ν=3011 cm^{-1}, 2971, 2954, 1606, 1511.

Acknowledgements

The authors are indebted to the Fund for Scientific Research-Flanders (FWO-Vlaanderen) and to Ghent University for financial support.

References

1. Abbaspour Tehrani, K.; Nguyen Van, T.; Karikomi, M.; Rottiers, M.; De Kimpe, N. *Tetrahedron* **2002**, *58*, 7145–7152.
2. De Kimpe, N.; De Smaele, D.; Bogaert, P. *Synlett* **1994**, *4*, 287–288.
3. Pak, C. S.; Kim, T. H.; Ha, S. J. *J. Org. Chem.* **1998**, *63*, 10006–10010.
4. De Kimpe, N.; Jolie, R.; De Smaele, D. *J. Chem. Soc., Chem. Commun.* **1994**, 1221–1222.
5. De Smaele, D.; Bogaert, P.; De Kimpe, N. *Tetrahedron Lett.* **1998**, *39*, 9797–9800.
6. De Kimpe, N.; De Smaele, D.; Sakonyi, Z. *J. Org. Chem.* **1997**, *62*, 2448–2452.
7. Paravyan, S. L.; Torosyan, G. O.; Babayan, A. T. *Arm. Khim. Zh.* **1979**, *32*, 708–711, *Chem. Abstr.* **1980**, *92*, 198051.
8. Wrobel, J. T.; Bien, A. S. *Rocz. Chem.* **1970**, *44*, 385–391, *Chem. Abstr.* **1970**, *72*, 131710.
9. Kametani, T.; Kigasawa, K.; Hiiragi, M.; Wagatsuma, N.; Wakisaka, K.; Kusama, O. *J. Med. Chem.* **1969**, *12*, 694–696.
10. Kametani, T.; Kigasawa, K.; Hiiragi, M.; Wagatsuma, N.; Wakisaka, K. *Tetrahedron Lett.* **1969**, *8*, 635–638.
11. Masuda, T.; Yamazaki, F. Jpn. Kokai Tokkyo Koho, 1987, JP 62000447 A2, 06/01/1987; *Chem. Abstr.* **1987**, *106*, 195874.
12. Dvorsky, D.; Cerovsky, K.; Socha, J. Czech. 1983, CS 211275 B, 15/08/1983; *Chem. Abstr.* **1984**, *101*, 92733.
13. Samour, C. M. Ger. Offen., 1970, DE 1952356, 23/04/1970; *Chem. Abstr.* **1970**, *73*, 15510.
14. Samour, C. M. US, 1975, US, 3925442, 09/12/1975; *Chem. Abstr.* **1976**, *84*, 60217.
15. Samour, C. M. US, 1976, US, 3983166, 28/09/1976; *Chem. Abstr.* **1977**, *86*, 17653.
16. Samour, C. M. US, 1977, US 4029658, 14/06/1977; *Chem. Abstr.* **1977**, *87*, 85833.
17. Matsuda, H.; Katori, T.; Okawa, K.; Ikegawa, T. Jpn. Kokai Tokkyo Koho, 1987, JP 62294603 A2, 22/12/1987, *Chem. Abstr.* **1988**, *108*, 217790.
18. Suzuki, A.; Gen, J.; Kajita, T.; Furushima, M.; Yoshinaka, S.; Suzuki, T.; Oda, A.; Tanaka, A. Jpn. Kokai Tokkyo Koho, 1988, JP 63135304 A2, 07/06/1988, *Chem. Abstr.* **1989**, *110*, 2902.
19. Yanai, A.; Sasagawa, T. Jpn. Kokai Tokkyo Koho, 1989, JP 01106848 A2, 24/04/1989; *Chem. Abstr.* **1989**, *111*, 232072.
20. Kamuro, Y.; Kakiuchi, T.; Takahashi, N.; Sakurai, S.; Kmiya, Y.; Takai, M.; Sato, K. Jpn. Kokai Tokkyo Koho, 1990, JP 02169554 A2, 29/06/1990, *Chem. Abstr.* **1991**, *114*, 121454.
21. Schott, E. P.; Rademacher, W. Eur. Pat. Appl., 1992, EP 472091 A1, 26/02/1992; *Chem. Abstr.* **1992**, *116*, 209716.
22. Merkys, A.; Miliuvene, L.; Noovickienne, L.; Saltyte, Z. *Biologija* **1993**, *4*, 45–53, *Chem. Abstr.* **1994**, *121*, 151217.
23. Kober, R.; Schneider, K.-H.; Stadler, R.; Ziegler, H.; Hofmeister, P.; Rademacher, W.; Goettsche, R.; Finch, C. W.; Kibler, E.; Callan, M. PCT Int. Appl., 1999, WO 9920106 A1, 29/04/1999; *Chem. Abstr.* **1999**, *130*, 292826.
24. Karsai, J.; Sebestyen, E.; Gaal, S.; Gardi, I.; Siki, K.; Kiss, G. PCT Int. Appl., 1986, WO 8607237 A1, 18/12/1986, *Chem. Abstr.* **1987**, *106*, 151620.
25. Demers, J. P.; Johnson, S.; Weidner-Wells, M. A.; Kanojia, R. M.; Fraga, S. A.; Klaubert, D. US 1999, US 5874436 A, 23/02/1999; *Chem. Abstr.* **1999**, *130*, 196658.
26. Demers, J. P.; Johnson, S.; Weidner-Wells, M. A.; Kanojia,

R. M.; Fraga, S. A.; Klaubert, D. PCT Int. Appl., 1997, WO 9748676 A1, 24/12/1997; *Chem. Abstr.* **1998**, *128*, 88670.
27. Nohr, R. S.; MacDonald, J. G. *J. Biomater. Sci., Polym. Ed.* **1994**, *5*, 607–619.
28. Tachibana, N.; Morita, S.; Shibue, T.; Saito, Y. Jpn. Kokai Tokkyo Koho, 1995, JP 07028193 A2, 31/01/1995; *Chem. Abstr.* **1995**, *123*, 44273.