Sonochemical Cleavage of 2-(Bromomethyl)aziridines by a Zinc–Copper Couple

Norbert De Kimpe,* Rob Jolie and Dirk De Smaele

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

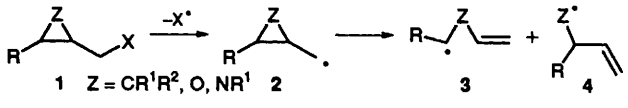
1-Alkyl- and 1-arylmethyl-2-(bromomethyl)aziridines are readily cleaved by the sonochemical zinc–copper couple in aqueous methanol at room temp. to afford allylamines.

Ring opening of small rings by radical rearrangement has received much attention (Scheme 1).[1] The cyclopropylmethyl radical **2** (Z = CR^1, R^2) has been shown to have a synthetic potential. The oxygen analogues, *i.e.* 2-oxiranylmethyl radicals **2** (Z = O), have witnessed a major interest in recent years.[2] Depending on the substitution pattern, they may undergo either carbon–oxygen or carbon–carbon bond cleavage (see **3**, **4**).[2] The epoxide ring opening by an adjacent carbon centred radical constitutes a useful strategy for the synthesis of heterocycles, *e.g.* tetrahydrofurans,[3] tandem cyclization to bicyclic products with bridged oxygen,[4,5] ring expansion,[6] *etc.* In principle, the nitrogen analogues, 2-aziridinylmethyl radicals **2** (Z = NR^1), have the same synthetic potential, which has not been developed or exploited yet. There has been a lack of general procedures for the synthesis of aziridines which are substituted on the carbon α to the ring with a group suitable for radical formation.[7]

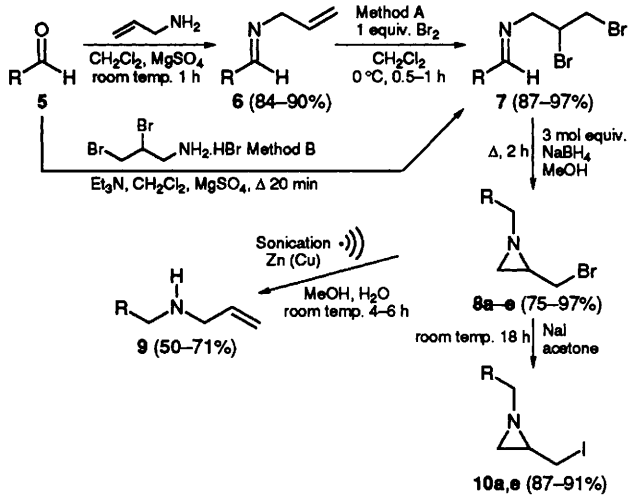
Only very recently, progress has been made in this area, showing that radical-induced cleavage of aziridines to allylamines[7,8] occurs and can be utilized for a pyrrolidine synthesis with appropriately olefin-substituted aziridines.[7] A drawback of the latter elegant approach is certainly that this process is limited to less common derivatives, *e.g.* *N*-phthalimido aziridines.[7] So far, the requisite α-aziridinylalkyl radicals were generated from thiocarbonylimidazoles, phenylselenides, and to a minor extent xanthates or sulfides.[8] Due to the marked lability of the 2-aziridinylmethyl xanthates and selenides, it is desirable to have access to stable precursors of 2-aziridinylalkyl radicals.

Here we report a facile entry into a stable class of such precursors, *i.e.* 2-(bromomethyl)aziridines **8**, and their conversion into allylamines by sonication in the presence of a zinc-copper couple (Scheme 2; Table 1). Imination of aromatic aldehydes **5a–c** with allylamine afforded *N*-allylimines **6a–c**, which were subsequently brominated by bromine in dichloromethane to give *N*-(arylidene)-2,3-dibromopropylamines **7a–c**. The synthesis of aliphatic derivatives **7d,e** required a different strategy, *i.e.* condensation of the aldehydes **5d,e** with 2,3-dibromopropylamine hydrobromide. The reaction of these functionalized imines **7** with sodium borohydride in methanol under reflux for 2 h afforded 1-alkyl- and 1-arylmethyl-2-(bromomethyl)aziridines **8a–e** in 75–97% yield. Most 2-(bromomethyl)aziridines **8** are stable liquids which can be distilled under vacuo, except 2-(bromomethyl)-1-(4-chlorophenyl)methylaziridine **8c** (R = 4-ClC_6H_4), which decomposed upon high-vacuum distillation. The latter compound **8c** was used as a crude compound with sufficient purity (>97%). All these new imines **7** and 2-(bromomethyl)aziridines **8** were fully characterized by spectroscopic methods (IR, ^1H and ^{13}C NMR, MS) and elementary analysis. This synthesis of 2-(bromomethyl)aziridines **8** is much better than the only reported entry involving a five step synthesis starting from acrylates *via* aziridine-2-carboxylic esters.[9] The latter report gives access to compounds **8** (two examples) in moderate yields, while only the bulky *N*-*tert*-butyl compound is obtained in 81% yield.[9]

In order to verify if 2-(bromomethyl)aziridines **8** are suitable substrates for analogous ring-opening reactions as



Scheme 1



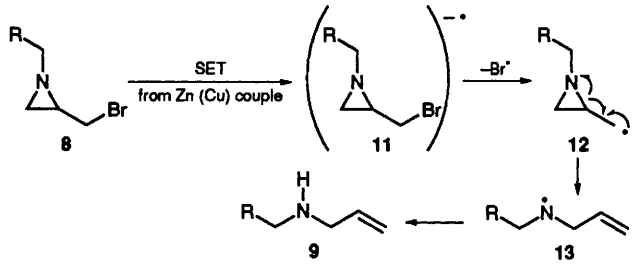
Scheme 2

Table 1 Synthesis of dibromoimines **7**, 2-(bromomethyl)aziridines **8** and allylamines **9**

R	Method[a]	Yield of **7**[b] (%)	Yield of **8** (%)	Bp **8** (°C/mmHg)	Yield of **9**[d] (%) (reaction time/h)
Ph	A	92	75	72–75/0.05[e]	53 (4)
Ph	B	87			
4-MeC_6H_4	A	93	85	80–82/0.08	71 (6)
4-MeC_6H_4	B	92			
4-ClC_6H_4	A	97	97	*c*	50 (6)
4-ClC_6H_4	B	91			
$CHEt_2$	B	95	84	42–49/0.03	57 (3)
$CHMe_2$	B	96	87	78–82/17	—

[a] Method A: bromination of *N*-allylimine **6** with bromine in CH_2Cl_2. Method B: reaction of aldehydes **5** with 2,3-dibromopropylamine. Both methods produce dibromoimines **7** in sufficient purity for further elaboration (>95%). [b] Compounds **7a–c** are thermolabile compounds and cannot be distilled. Compounds **7d,e** can be distilled: bp **7d**, 65–67 °C/0.09 mmHg; bp **7e**, 38–39 °C/0.05 mmHg. [c] Decomposition upon distillation *in vacuo*. [d] Yields of isolated pure allylamine, isolated *via* precipitation as the hydrochloride and regeneration of the base [e] Lit.[9] bp 100 °C/0.5 mmHg.

known for the corresponding cyclopropane and oxirane derivatives, the conversion into allylic amines was investigated (Scheme 3). Sonication of 2-(bromomethyl)aziridines **8** in aqueous methanol at room temp. in the presence of a zinc–copper couple,[10]† resulted in a clean reaction leading to allylamines **9**. No side reactions, *e.g.* ring opening of the aziridine *via* C–C bond cleavage, were observed, but the lower yields are certainly due to absorption phenomena and the aqueous solubility of allylamines (*cf.* workup). Efforts to improve the rearrangement by the use of the corresponding iodo compounds, *i.e.* 2-(iodomethyl)aziridines **10**, were without success as less clean reaction mixtures and lower yields resulted from the sonication process. 2-(Iodomethyl)aziridines **10** were synthesized by reaction of the bromo compounds **8** with sodium iodide in acetone. The conversion of 2-(bromomethyl)-aziridines **8** can be interpreted as occurring *via* single-electron-transfer from the metal to the substrate, followed by loss of bromide from the radical anion **11** to form a radical **12**. It may be expected that the carbon centred radical rearranges into the aminyl radical **13** which further gives the final allylamines **9**. An alternative mechanism consists of the additional capture of an electron by radical **12** to generate the corresponding carbanion, which gives an anionic ring opening to the same end products. This new reaction of 2-(bromomethyl)aziridines **8** is the aza-analogue of the sonochemical cleavage of 2,3-epoxyalkylhalides.[10,11]



Scheme 3

Received, 24th January 1994; Com. 4/00411F

Footnote

† Zinc powder was washed three times with 3% aqueous hydrogen chloride and five times with distilled water. After filtration and drying *in vacuo* (P_2O_5), zinc powder (0.98 g; 0.015 mol) and copper(I) iodide were stirred for 5 min with 8 ml water and 12 ml methanol in a sonication apparatus (Bransonic 12; 48 KHz ± 10%).[10] To the black suspension was added 0.005 mol of 2-(bromomethyl)aziridine **8** and sonication was continued for 4 h. After treatment with ammonium chloride (aq) and filtration, the filtrate was extracted four times with dichloromethane, dried ($MgSO_4$) and evaporated to give crude allylamine **9**. Purification is performed by conversion into the hydrochloride (HCl–diethyl ether), filtration and regeneration of the free base (6 mol dm^{-3} NaOH, CH_2Cl_2). Flash chromatography may be executed but is usually not necessary.

References

1 A. L. J. Beckwith and K. U. Ingold, in *Rearrangements in the Ground and Excited States*, ed. P. de Mayo, Academic Press, NY, 1980.
2 P. Dowd and W. Zhang, *Chem. Rev.*, 1993, **93**, 2091.
3 D. H. R. Barton, R. S. H. Motherwell and W.B. Motherwell, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2363.
4 A. Johns and J. A. Murphy, *Tetrahedron Lett.*, 1988, **29**, 837.
5 R. C. Gash, F. MacCorquodale and J. C. Walton, *Tetrahedron*, 1989, **45**, 5531.
6 P. Galatsakis, S. D. Millan and T. Faber, *J. Org. Chem.*, 1993, **58**, 1215.
7 J. M. Dickinson and J. A Murphy, *Tetrahedron*, 1992, **48**, 1317.
8 A. L. Schwan and M. D. Refrik, *Tetrahedron Lett.*, 1993, **34**, 4901.
9 J. A. Deyrup and C. L. Moyer, *J. Org. Chem.*, 1970, **35**, 3424.
10 L. A. Sarandeses, A. Mourino and J.-L. Luche, *J. Chem. Soc. Chem. Commun.*, 1991, 818.
11 L. A. Sarandeses and J.-L. Luche, *J. Org. Chem.*, 1992, **57**, 2757.