Synthesis of Some Novel Class of Bis(isoxazoline) and Bis(aziridine) Derivatives

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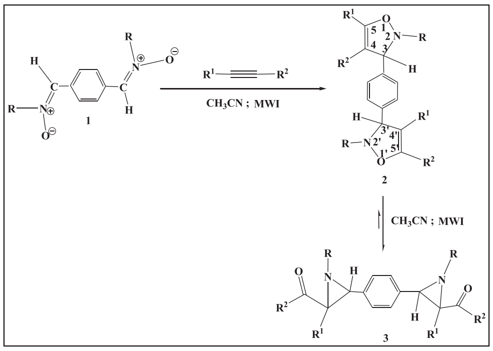

Synthesis of some new bis(isoxazoline) derivatives has been described from terepthaldehyde derived bis (nitrones) using microwave irradiation via 1,3-dipolar cycloaddition reaction. Bis(isoxazoline) derivatives in turn successfully converted into new bis(aziridine) derivatives via Baldwin rearrangement. Simple reaction methodology, non involvement of catalysts, and good to excellent yields are the important features noticed in this synthesis.

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INTRODUCTION

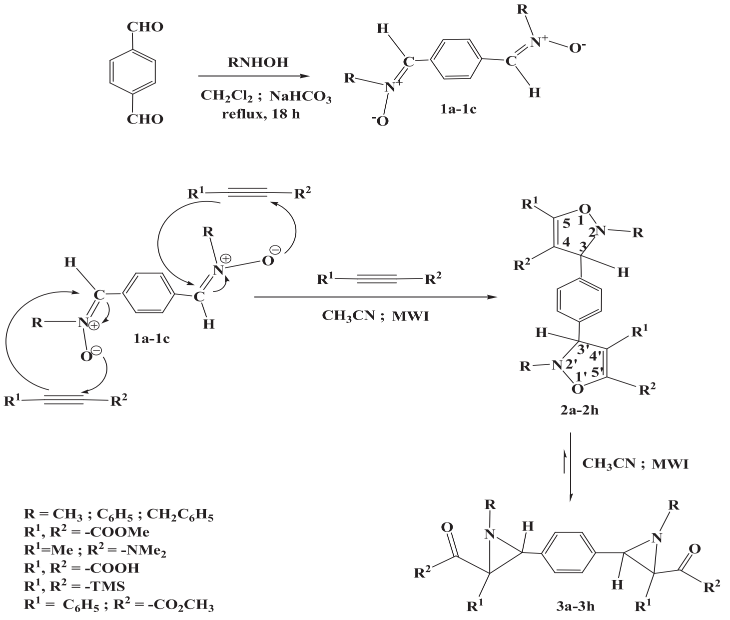
1,3-Dipolar cycloaddition reactions are an integral and weighty part of organic chemistry in pedagogy and research as well. The wealthy literature on cycloaddition reactions of nitrones for the synthesis of isoxazolidine and isoxazoline derivatives and their further applications have been widely illustrated [1–3] while synthesis of bis (isoxazolidine) and bis(isoxazoline) derivatives is challenging and needs to be explored [4–7] especially because conversions of these derivatives to aziridines via Baldwin rearrangement are found to have vast synthetic potential in this chemistry [8–10]. The chemistry of three-membered ring heterocycles, especially aziridines, has attracted the attention of synthetic chemists for more than a century because of its ability of acting as versatile species in organic synthesis [11–15]. Baldwin et al. have shown that 1,3-dipolar cycloaddition reactions of nitrones to alkynes lead to 4-isoxazolines which rearrange easily under thermal conditions to acylaziridine[16–18]. As a part of our ongoing research programme to develop new methodologies in organic synthesis [19–22], herein, we report synthesis of some new bis(isoxazoline) derivatives (2) from terepthaldehyde in good to excellent yields under microwave irradiation (Scheme 1, Table 1). Furthermore, these bis(isoxazoline) derivatives are found to have vast synthetic potential as they could be converted into synthetically more important new bis(aziridines) (3) [23–28]. The newly reported bis(isoxazoline) derivatives are obtained as single pure compound when a mixture of bis(nitrone) 1 (1 equivalent) and alkynes (2 equivalents) is exposed to microwave irradiation for 5–10 min at 115 – 130°C.

RESULTS AND DISCUSSION

To execute proposed study, terepthalaldehyde and various *N*-substituted hydroxylamines (*N-Methyl/Phenyl/Benzyl*) were employed for the synthesis of bis(nitrones) (1) following conventional methodology. This was followed by 1,3-dipolar cycloaddition reactions of bis(nitrone) 1 with different alkynes (electron deficient and electron rich) for the synthesis of a variety of bis(isoxazoline) derivatives (2) under microwave irradiation by employing reported protocol [19,29,30]. The electron deficient alkynes used in this study were acetylene dicarboxylic acid, methyl phenylpropiolate, and dimethyl acetylene dicarboxylate while electron rich alkynes were bis-(trimethylsilyl) acetylene (BTMSA) and *N,N*-dimethylaminoprop-1-yne respectively. Bis(isoxazoline) derivatives thus obtained were exposed to microwave irradiation (maintaining certain time period and temperature) to obtain a variety of new *N*-substituted bis(aziridines) (Scheme 1, Table 1).

In conventional methodology, high reaction temperature and long reaction time are generally required to obtain good conversions and yields in these cycloaddition

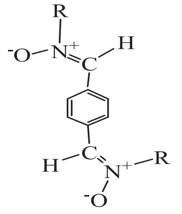
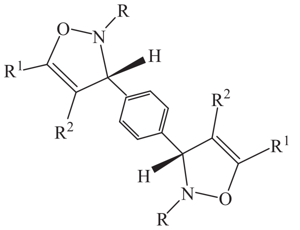
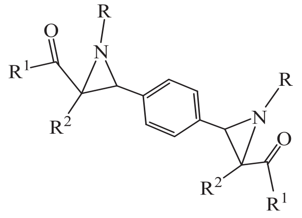
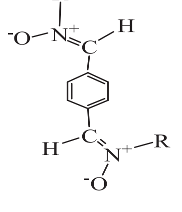
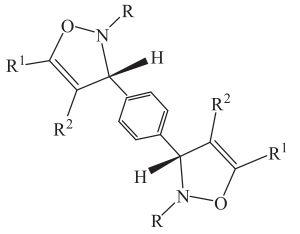
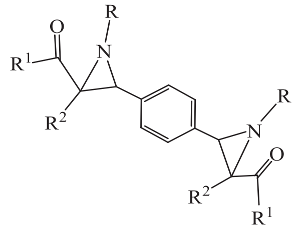
Scheme 1. Synthesis of bis(isoxazoline) and bis(aziridine) derivatives.



reactions but prolonged heating time results in a drastic drop of the yield of cycloadducts because of decomposition. A study of the reaction conditions under microwave irradiation was thus undertaken as this condition is generally faster, cleaner, and greener [20,31–33]. The results are summarized in Table 1. We also examined the effect of solvent on these reactions and also in the rearrangement 2 to **3**. Among the various polar solvents tested, water and DMSO showed a good level of conversion (90 and 68%, respectively) but, unfortunately, also induce the formation of extensive amounts of degradation products (63 and 49% transformation, respectively). As compared to the other solvents used, CH$_3$CN finally offers the better compromise in terms of efficiency (conversion, transformation,

Table 1

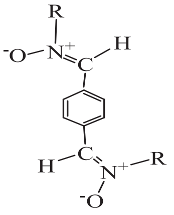
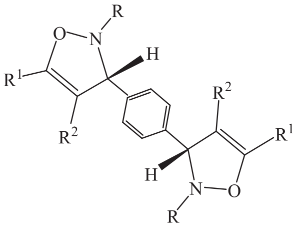
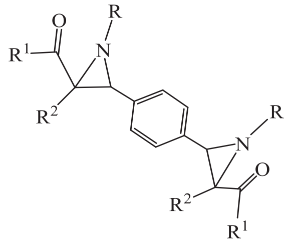
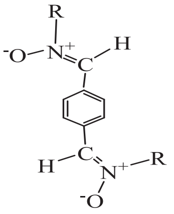
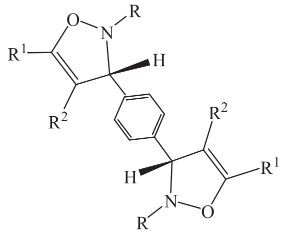
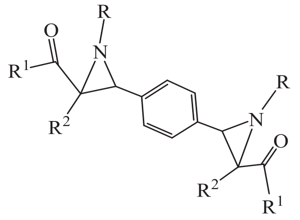
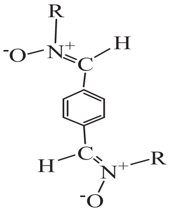
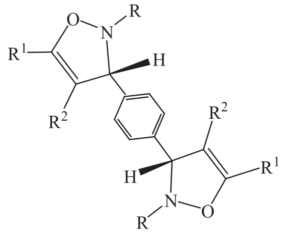
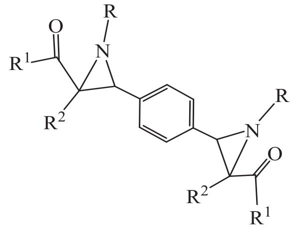
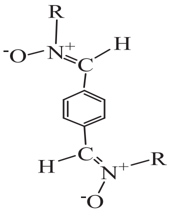
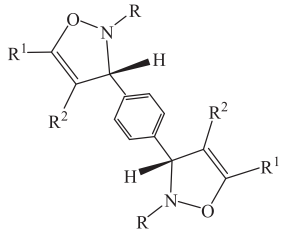
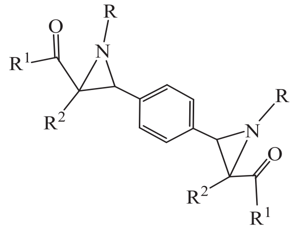
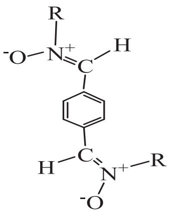
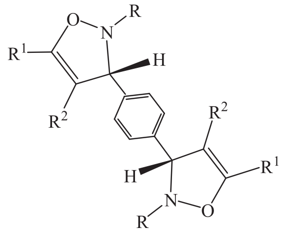
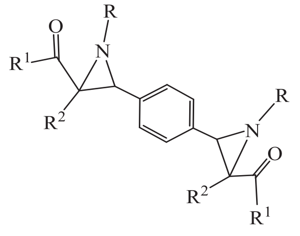
Synthesis of bis(isoxazoline) and bis(aziridine) derivatives.

Entry	Bis(nitrone)(1a–1c)	Bis(isoxazoline)^{a,c} (2a–2h)	Time (min)	Bis(aziridine)^{b,c} (3a–3h)	Time (min)
1	 1a (R = CH$_3$)	 Yield = 92% (69%) 2a R^1 = COOCH$_3$; R^2 = COOCH$_3$	5	 Yield = 78% 3a R^1 = COOCH$_3$; R^2 = COOCH$_3$	5
2	 1b (R = C$_6$H$_5$)	 Yield = 88% (67%) 2b R^1 = COOH; R^2 = COOH	6	 Yield = 75% 3b R^1 = COOH; R^2 = COOH	6

(*Continued*)

Table 1

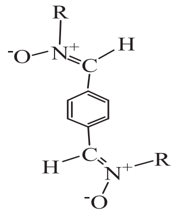
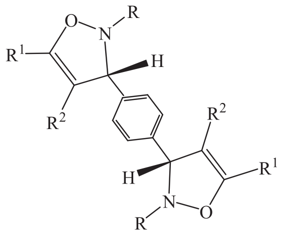
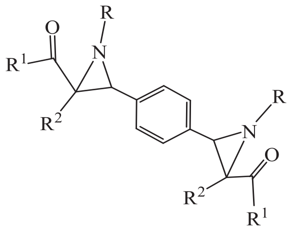
(*Continued*)

Entry	Bis(nitrone)(1a–1c)	Bis(isoxazoline)[a,c] (2a–2h)	Time (min)	Bis(aziridine)[b,c] (3a–3h)	Time (min)
3	 1c ($R = C_6H_5CH_2$)	 Yield = 88% (67%) 2c R^1 = Ph; R^2 = $COOCH_3$	6	 Yield = 74% 3c R^1 = Ph; R^2 = $COOCH_3$	6
4	 1c ($R = C_6H_5CH_2$)	 Yield = 87% (65%) 2d R^1 = TMS; R^2 = TMS	7	 Yield = 73% 3d R^1 = TMS; R^2 = TMS	7
5	 1a ($R = CH_3$)	 Yield = 86% (66%) 2e R^1 = Me; R^2 = NMe_2	7	 Yield = 70% 3e R^1 = Me; R^2 = NMe_2	7
6	 1b ($R = C_6H_5$)	 Yield = 86% (64%) 2f R^1 = $COOCH_3$; R^2 = $COOCH_3$	9	 Yield = 71% 3f R^1 = $COOCH_3$; R^2 = $COOCH_3$	9
7	 1a ($R = CH_3$)	 Yield = 85% (60%) 2 g R^1 = COOH; R^2 = COOH	10	 Yield = 72% 3 g R^1 = COOH; R^2 = COOH	10

(*Continued*)

Table 1

(*Continued*)

Entry	Bis(nitrone)(1a–1c)	Bis(isoxazoline)[a,c] (2a–2h)	Time (min)	Bis(aziridine)[b,c] (3a–3h)	Time (min)
8	 1b (R = C_6H_5)	 Yield = 84% (56%) 2 h R^1 = TMS; R^2 = TMS	10	 Yield = 71% 3 h R^1 = TMS; R^2 = TMS	10

[a] Reaction conditions: Bisnitrone (1 mmol), alkyne (2 equivalent), MWI, MeCN, 5–10 min, 115 – 130°C
[b] Isoxazoline (1 mmol), MWI, MeCN, 5–10 min, 130°C
[c] Isolated yield after purification.
Figures in the parentheses of yield indicate products obtained in conventional methodology.

and yield) and of practical convenience. Indeed, at the end of the reaction, the solvent is removed *in vacuo* and the residue is directly loaded on silica gel for purification, which avoids an aqueous workup. We have also observed that rearrangement of bis(isoxazoline) derivatives to bis (aziridines) conducted in the absence of solvent resulted in the complete degradation of the starting material. We thus next evaluated the influence of solvent (H_2O and DMSO) for this conversion but because of the formation of extensive amounts of degradation products (nearly 55–60%), this methodology was discarded. For the rearrangement of 2 to 3, the best results were obtained when the reaction was carried out in acetonitrile.

We have obtained expected fragmentation peaks in the mass spectral studies and majority of these peaks are due to the development of aziridine derivatives. Base peaks were obtained because of loss of $COOCH_3$ for dimethyl acetylene dicarboxylate, methyl phenyl propiolate while COOH, TMS, and N,N-dimethylaminoprop-1-yne (NMe_2) for acetylene dicarboxylic acid, bis-(trimethylsilyl)acetylene (BTMSA), and *N,N*-dimethylaminoprop-1-yne respectively. For all the cases, development of bis(nitrone), bis (isoxazolines) and conversions to bis(aziridine) derivatives were monitored by TLC (R_f values of bis(aziridine) derivatives were found to have lower than bis (isoxazoline) derivatives). Important signals of R, R^1, and R^2 of the bis(isoxazoline) and bis(aziridine) derivatives were obtained in the ^{1}H NMR spectrum [34] while prominent carbonyl absorptions were found in IR spectrum as well. ^{1}H NMR spectrum of the all the synthesized bis(isoxazoline) and aziridine derivatives showed that the four (4) hydrogen atoms of the phenyl ring (1,4 and 3,5 protons) linked with isoxazoline and aziridine rings are merged and obtained as single singlet signal. ^{13}C NMR spectrum of the phenyl ring carbons at ortho, meta, and para positions have been found to be merged and obtained as single signal. Exact stereochemistry of the bis(isoxazoline) and bis(aziridine) derivatives could not be assigned because of the absence of adjacent proton with respect to isoxazoline and aziridine ring proton.

CONCLUSION

In conclusion, we have reported a green chemistry protocol of the synthesis of bis(isoxazoline) derivatives and also Baldwin rearrangement of these derivatives to various new bis(aziridine) derivatives using microwave irradiation at selected temperature without involvement of any catalysts. The salient feature and the point of attraction in the present methodology are the entire syntheses that involve atom efficient green chemistry methodology which should attract synthetic chemists.

EXPERIMENTAL

^{1}H NMR spectra were recorded with a Bruker DRX 300 spectrometer (300 MHz, FT NMR) using TMS as internal standard. ^{13}C NMR spectra were recorded on the same instrument at 75 MHz. The coupling constants (*J*) are given in Hz. IR spectra were obtained with a Shimadzu FT-IR 8400 machine using KBr pellets for all the products. MS spectra were recorded with a Jeol SX-102/DA-600 (FAB) instrument, and elemental analysis was carried out using Heraus C,H and N rapid analyzer. All the reactions were monitored by TLC using 0.25-mm silica gel plates (Merck 60 F_{254} UV indicator) while column chromatography was performed with silica gel (E. Merck India) 60–200 mesh. *N*-Methylhydroxylamine, *N*-benzylhydroxylamine, dimethyl acetylenedicarboxylate, methyl phenylpropiolate, acetylenedicarboxylic acid, bis-(trimethylsilyl) acetylene (BTMSA), and *N,N*-dimethylaminoprop-1-yne etc were obtained commercially from Aldrich, Lancaster, Fluka and from Sigma-Aldrich, Switzerland and were used as received. *N*-Phenylhydroxylamine and *N*-cyclohexylhydroxylamine were prepared following standard methods available in the literature. Microwave studies were carried out in Discover Bench Mate system (Make: CEM-USA) producing continuous irradiation at 2445 MHz and infrared control system. Microwave experiments were carried out in sealed vessels with an effective magnetic stirring and reflux (which avoids all problems of non homogeneity in temperature).

Representative experimental procedure for the synthesis of bis (nitrone) 1a (entry 1,Table 1; R = CH_3). Terephthalaldehyde (1.34 g, 10 mmol) was added to a solution of *N*-methylhydroxylamine hydrochloride (2.09 g, 25 mmol) in CH_2Cl_2 (20 mL) in a 50-mL R.B flask. $NaHCO_3$ (2.52 g, 30 mmol) was added and the mixture heated at reflux for 18 h. The solution was filtered in hot condition and the inorganic solid washed with warm $CHCl_3$. The bis(nitrone) crystallized from the filtrate as a white solid and was collected at the vacuum pump (1.42 g, 74%, m.p > 250°C).

Spectroscopic data for bis(nitrone) 1a: N-methyl(4-{[methyl (oxido)iminio]methyl{phenyl)methylideneamine N-oxide. R_f = 0.50; FT-IR (KBr): υ_{max} 3130 (s), 3010 (m), 2970 (m), 2246 (m), 1690 (s), 1630 (s), 1610 (s), 1515 (s), 1310 (m), 1176 (s), 1150 (s), 782 (s) cm^{-1}; ^1H NMR ($CDCl_3$): 8.24 (s, 4H, Ar—H), 7.40 (s, 2H, 2 × $CH{=}N^+$), 3.89 (s, 6H, 2 × CH_3); ^{13}C NMR ($CDCl_3$): δ 134.66 (2 × $CH{=}N^+$), 131.81, 130.54 (1,4 Ar—C), 128.29, 127.52 (2,6 and 3,5 Ar—C), 54.58 (2 × CH_3); FAB-MS (*m/z*): 192 (M^+), 176 (M-O), 134 (M-$CHNOCH_3$); *Anal.* Calcd. for $C_{10}H_{12}O_2N_2$: C, 62.47; H, 6.30; N, 14.58. Found: C, 62.33; H, 6.24; N, 14.35%.

General experimental procedure for the synthesis of bis (isoxazoline) derivatives (2a–2h) under microwave irradiation (entry 1, Table 1; R = CH_3). Bis(nitrone) 1a (0.41 mmol, 80 mg) and dimethyl acetylene dicarboxylate (0.82 mmole, 116 mg) were dissolved in acetonitrile (10 mL) and were heated in a sealed vessel at 115°C during 5 min under microwave irradiation (400 W, temperature-controlled mode). The progress of the reaction was monitored by TLC (R_f = 0.58).The resulting reaction mixture was concentrated under vacuum, and the crude material was directly purified by column chromatography on silica gel (ethyl acetate/hexane) to afford pure bis(isoxazoline) 2a (Table 1, entry 1, 92%) as a colourless gummy mass. Same methodology was adopted for the synthesis of other bis (isoxazoline) derivatives 2b–2h (Scheme 1, Table 1, entry 2–8).

Spectroscopic data for bis(isoxazoline) 2a (Table 1, entry 1): (3R,3′R)-tetramethyl 3,3′-(1,4-phenylene)bis(2-methyl-2,3-dihydroisoxazole-4,5-dicarboxylate. FT-IR (KBr): υ_{max} 3036 (s), 2255 (m), 1760 (s), 1710 (s), 1600 (s), 1520 (s), 1440 (s), 1324 (m), 1314 (s), 1260 (m), 1170 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.60 (s, 4H, Ar—H), 5.20 (s, 2H, 2 × 3-H), 3.80 (s, 12H, 4 × —$COOCH_3$), 2.52 (s, 6H, 2 × N—CH_3); ^{13}C NMR ($CDCl_3$): δ 172.54 ($2\times\underline{CO}OCH_3$), 171.13 ($2\times\underline{CO}OCH_3$), 134.28, 133.87 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 131.13, 130.45 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings), 88.62 (2 × 5-C), 77.43 (2 × 3-C), 59.79 (2 × 4-C), 52.20 (2 × CH_3), 38.58 ($2\times$—$COO\underline{CH_3}$), 36.62 ($2\times$—$COO\underline{CH_3}$); FAB–MS (*m/z*): 476 (M^+), 460, 400, 386, 276, 185 (B.P), 75, 59; *Anal.* Calcd. for $C_{22}H_{24}O_{10}N_2$: C, 55.44; H, 5.07; N, 5.88. Found: C, 55.39; H, 5.02; N, 5.74%.

General experimental procedure for the synthesis of bis (aziridine) derivatives (3a–3h) under microwave irradiation (entry 1, Table 1). Bis(isoxazoline) 2a (0.25 mmol, 120 mg) was dissolved in acetonitrile (10 mL) and was heated in a sealed vessel at 130°C during 5 min under microwave irradiation (400 W, temperature-controlled mode). The progress of the reaction was monitored by TLC (R_f = 0.52). The resulting reaction mixture was concentrated under vacuum, and the crude material was directly purified by column chromatography on silica gel (ethyl acetate/hexane) to afford pure bis(aziridine) 3a (Table 1, entry 1, 78%) as a pale yellow gummy mass. Same methodology was adopted for the synthesis of other bis(aziridine) derivatives 3b–3h (Scheme 1, Table 1, entry 2–8).

Spectroscopic data for bis(aziridine) 3a (Table 1, entry 1): dimethyl 3,3′-(1,4-phenylene)bis(2-(2-methoxy-2-oxoacetyl)-1-methylaziridine-2-carboxylate. FT-IR (KBr): υ_{max} 3028 (s), 2985 (m), 1766 (s), 1720 (s), 1660 (s), 1590 (m), 1520 (s), 786 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.53 (s, 4H, Ar—H), 4.86 (s, 2H, 2 × aziridine protons), 3.92 (s, 6H, 2 × —$COOCH_3$, linked with aziridine rings), 3.70 (s, 6H, 2 × —$COOCH_3$, linked with keto group), 2.68 (s, 6H, 2 × N—CH_3); ^{13}C NMR ($CDCl_3$): δ 174.10 (2 × C=O), 170.74 ($2\times$—$C\underline{O}OCH_3$, linked with aziridine rings), 169.20 ($2\times$—$C\underline{O}OCH_3$, linked with keto group), 130.80, 130.23 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 128.15, 127.30 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings), 60.24 (2 × aziridine ring carbons), 54.24 (2 × aziridine ring carbons), 48.60 (2 × CH_3), 35.06 ($2\times$—$COO\underline{CH_3}$, linked with aziridine rings), 33.18 ($2\times$—$COO\underline{CH_3}$, linked with keto group); FAB–MS (*m/z*): 476 (M^+), 461, 417, 400, 386, 276, 200, 76, 75, 59; *Anal.* Calcd. for $C_{22}H_{24}O_{10}N_2$: C, 55.44; H, 5.07; N, 5.88. Found: C, 55.26; H, 4.92; N, 5.61%.

Spectroscopic data of bis(isoxazoline) and bis(aziridine) derivatives. ***Spectroscopic data for bis(isoxazoline) 2b (Table 1, entry 2): (3R,3′R)-3,3′-(1,4-phenylene)bis(2-phenyl-2,3-dihydro isoxazole-4,5-dicarboxylic acid.*** Gray gummy liquid (88%), FT-IR (KBr): υ_{max} 3285 (s), 3080 (s), 2250 (m), 1760 (s), 1685 (s), 1585 (s), 1545 (s), 1360 (m), 1285 (m), 1015 (m), 880 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.13 (s, 2H, 2 × —COOH), 10.06 (s, 2H, 2 × —COOH), 7.05 (s, 4H, Ar—H), 6.84–6.68 (m, 10H, $2\times$Ar—H), 5.42 (s, 2H, $2\times$3-H); ^{13}C NMR ($CDCl_3$): δ 174.27 ($2\times\underline{CO}OH$), 173.45 ($2\times\underline{CO}OH$), 136.54, 135.42 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 133.25, 132.72 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings), 129.44, 128.70 ($2\times$1,4 Ar—C; N-phenyl carbons), 128.12, 127.83 ($2\times$2,6 and 3,5 Ar—C; N-phenyl carbons), 85.71 ($2\times$5-C), 78.32 ($2\times$3-C), 57.14 ($2\times$4-C); FAB–MS (*m/z*): 544 (M^+), 467, 466, 310, 234, 77; *Anal.* Calcd. for $C_{28}H_{20}O_{10}N_2$: C, 61.75; H, 3.70; N, 5.14. Found: C, 61.63; H, 3.57; N, 5.03%.

Spectroscopic data for bis(aziridine) 3b (Table 1, entry 2): dimethyl 3,3′-(1,4-phenylene)bis(2-(2-methoxy-2-oxoacetyl)-1-methylaziridine-2-carboxylate. Dark gray gummy mass (75%), FT-IR (KBr): υ_{max} 3280 (s), 3076 (s), 2250 (m), 1765 (s), 1754 (s), 1682 (s), 1660 (s), 1585 (s), 1540 (s), 1364 (m), 1282 (m), 1016 (m), 870 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 10.20 (s, 2H, $2\times$—COOH), 10.05 (s, 2H, $2\times$—COOH), 7.14 (s, 4H, Ar—H), 6.77–6.62 (m, 10H, $2\times$Ar—H), 4.90 (s, 2H, $2\times$aziridine protons); ^{13}C NMR ($CDCl_3$): δ 175.50 ($2\times$C=O), 174.27 ($2\times\underline{CO}OH$), 173.45 ($2\times\underline{CO}OH$), 135.80, 135.26 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 132.88, 132.51 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings), 130.12, 129.42 ($2\times$1,4 Ar—C; N-phenyl carbons), 128.30, 127.67 ($2\times$2,6 and 3,5 Ar—C; N-phenyl carbons), 67.20 ($2\times$aziridine ring carbons), 60.43 ($2\times$aziridine ring carbons); FAB–MS (*m/z*): 544 (M^+), 499, 466, 394, 310, 234, 77, 45; *Anal.* Calcd. for $C_{28}H_{20}O_{10}N_2$: C, 61.75; H, 3.70; N, 5.14. Found: C, 61.54; H, 3.74; N, 5.10%.

Spectroscopic data for bis(isoxazoline) 2c (Table 1, entry 3): (3R,3′R)-dimethyl 3,3′-(1,4-phenylene)bis(2-benzyl-5-phenyl-2,3-dihydroisoxazole-4-carboxylate. Colourless liquid. Yield 88%; FT-IR (KBr): υ_{max} 3065 (s), 1740 (s), 1660 (s), 1590 (s), 1490 (m), 1480 (m), 1355 (m), 1290 (m), 1020 (m), 830 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.80 (s, 4H, Ar—H), 7.54–7.35 (m, 10H, $2\times$Ar—H, phenyl protons linked with C_5 and $C_{5'}$ carbons), 7.12–6.94 (m, 10H, $2\times CH_2C_6H_5$), 5.13 (s, 2H, $2\times$3-H), 3.74 (s, 4H, $2\times CH_2C_6H_5$), 3.30 (s, 6H, $2\times$–$COOCH_3$); ^{13}C NMR ($CDCl_3$): δ 174.54 ($2\times\underline{CO}OCH_3$), 134.07, 133.85 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 133.14, 133.03 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings), 130.92, 130.64 ($2\times$1,4 Ar—C; phenyl carbons linked with C_5 and $C_{5'}$ carbons), 129.75, 129.57 ($2\times$2,6 and 3,5 Ar—C; phenyl carbons linked with C_5 and $C_{5'}$ carbons), 128.77, 128.64 ($2\times$1,4 Ar—C; phenyl carbons linked with benzyl carbons), 128.15, 127.97 ($2\times$2,6 and 3,5 Ar—C; phenyl carbons linked with benzyl carbons), 83.80 ($2\times$5-C), 74.46 ($2\times$3-C), 59.32 ($2\times$4-C), 32.16 ($2\times\underline{CH_2}C_6H_5$), 28.12 ($2\times$—$COO\underline{CH_3}$); FAB–MS (*m/z*): 664 ($M^+$), 587, 559, 370, 294, 91, 77; *Anal.* Calcd. for $C_{42}H_{36}O_6N_2$: C, 75.87; H, 5.45; N, 4.21. Found: C, 75.79; H, 5.38; N, 4.23%.

Spectroscopic data for bis(aziridine) 3c (Table 1, entry 3): dimethyl 3,3′-(1,4-phenylene)bis(2-benzoyl-1-benzylaziridine-2-carboxylate. Gray gummy liquid. Yield 74%; FT-IR (KBr): υ_{max} 3070 (s), 1744 (s), 1714 (s), 1622 (s), 1590 (s), 1484 (m), 1475 (m), 1358 (m), 1282 (m), 1016(m), 850 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.23 (s, 4H, Ar—H), 7.06–6.90 (m, 20H, $4\times$Ar—H), 4.82 (s, 2H, $2\times$aziridine protons), 3.82 (s, 4H, $2\times CH_2C_6H_5$), 3.34 (s, 6H, $2\times$–$COOCH_3$); ^{13}C NMR ($CDCl_3$): δ 174.68 ($2\times$C=O), 172.80 ($2\times\underline{CO}OCH_3$), 133.00, 132.74 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 132.06, 131.90 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings), 130.68, 130.52 ($2\times$1,4 Ar—C; phenyl carbons linked with C_5 and $C_{5'}$ carbons), 129.24, 129.10 ($2\times$2,6 and 3,5 Ar—C; phenyl carbons linked with C_5 and $C_{5'}$ carbons), 128.61, 128.30 ($2\times$1,4 Ar—C; phenyl carbons linked with benzyl carbons), 127.83, 127.29 ($2\times$2,6 and 3,5 Ar—C; phenyl carbons linked with benzyl carbons), 60.46 ($2\times$aziridine ring carbons), 57.54 ($2\times$aziridine ring carbons); 37.70 ($2\times\underline{CH_2}C_6H_5$), 27.94 ($2\times$—$COO\underline{CH_3}$); FAB–MS (*m/z*): 664 ($M^+$), 559, 514, 468, 370, 294, 105, 91, 77; *Anal.* Calcd. for $C_{42}H_{36}O_6N_2$: C, 75.87; H, 5.45; N, 4.21. Found: C, 75.60; H, 5.27; N, 4.17%.

Spectroscopic data for bis(isoxazoline) 2d (Table 1, entry 4): 1,4-bis((R)-2-benzyl-4,5-bis(trimethylsilyl)-2,3-dihydroisoxazol-3-yl)benzene. Yellow sticky liquid. Yield 87%; FT-IR (KBr): υ_{max} 3073 (s), 2255 (m), 1665 (s), 1585 (s), 1500 (m), 1470 (m), 1350 (m), 1282 (m), 1025 (m), 860 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.16 (s, 4H, Ar—H), 7.05–6.92 (m, 10H, $2\times$Ar—H), 5.02 (s, 2H, $2\times$3-H), 3.43 (s, 4H, $2\times CH_2C_6H_5$), 0.82 (s, 36H, $4\times SiMe_3$); ^{13}C NMR ($CDCl_3$): δ 136.66, 134.80 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 132.54, 131.89 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings),129.70, 129.64 ($2\times$1,4 Ar—C; phenyl carbons linked with benzyl carbons), 128.75, 128.43 ($2\times$2,6 and 3,5 Ar—C; phenyl carbons linked with benzyl carbons), 80.67 ($2\times$5-C), 75.90 ($2\times$3-C), 56.44 ($2\times$4-C), 31.75 ($2\times\underline{CH_2}C_6H_5$), 0.12 ($4\times SiMe_3$ carbons); FAB–MS (*m/z*): 684 (M^+), 607, 583, 380, 304, 91, 77; *Anal.* Calcd. for $C_{38}H_{56}Si_4O_2N_2$: C, 66.62; H, 8.23; N, 4.09. Found: C, 66.50; H, 8.12; N, 4.12%.

Spectroscopic data for bis(aziridine) 3d (Table 1, entry 4): (3,3′-(1,4-phenylene)bis(1-benzyl-2-(trimethylsilyl)aziridine-3,2-diyl))bis((trimethylsilyl)methanone. Gray gummy liquid. Yield 73%; FT-IR (KBr): υ_{max} 3085 (s), 1760 (s), 1710 (s), 1665 (s), 1584 (s), 1500 (m), 1475 (m), 1356 (m), 1285 (m), 1014 (m), 865 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.03 (s, 4H, Ar—H), 6.87–6.74 (m, 10H, $2\times$Ar—H), 4.54 (s, 2H, $2\times$aziridine protons), 2.65 (s, 4H, $2\times CH_2C_6H_5$), 0.80 (s, 36H, $4\times SiMe_3$); ^{13}C NMR ($CDCl_3$): δ 173.48 ($2\times$C=O), 135.90, 135.34 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 133.68, 132.72 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings),130.54, 130.23 ($2\times$1,4 Ar—C; phenyl carbons linked with benzyl carbons), 128.78, 128.16 (2 × 2,6 and 3,5 Ar—C; phenyl carbons linked with benzyl carbons), 57.54 (2 × aziridine ring carbons), 55.75 (2 × aziridine ring carbons), 34.42 (2 × $\underline{CH_2}C_6H_5$), 0.15 (4 × $SiMe_3$ carbons); FAB–MS (*m/z*): 684 (M^+), 611, 607, 583, 520, 492, 380, 304, 101, 91, 77; *Anal.* Calcd. for $C_{38}H_{56}Si_4O_2N_2$: C, 66.62; H, 8.23; N, 4.09. Found: C, 66.43; H, 8.14; N, 4.10%.

Spectroscopic data for bis(isoxazoline) 2e (Table 1, entry 5): (3R,3′R)-3,3′-(1,4-phenylene)bis(N,N,2,5-tetramethyl-2,3-dihydroisoxazol-4-amine. Deep yellow liquid. Yield 86%; FT-IR (KBr): υ_{max} 3035 (s), 2250 (m), 1680 (s), 1580 (s), 1510 (m), 1465 (m), 1315 (m), 1245 (s), 1005 (m), 858 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.48 (s, 4H, Ar—H), 4.93 (s, 2H, 2 × 3-H), 2.80 (s, 12H, 2 × NMe_2), 2.12 (s, 6H, 2 × N—CH_3), 1.63 (s, 6H, 2 × CH_3); ^{13}C NMR ($CDCl_3$): δ 134.76, 134.37 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 133.50, 133.13 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings), 83.70 (2 × 5-C), 73.47 (2 × 3-C), 55.60 (2 × 4-C), 39.52 (2 × NMe_2), 30.21 (2 × N—CH_3), 20.43 (2 × CH_3); FAB–MS (*m/z*): 358 (M^+), 343, 342, 242, 217, 141, 126; *Anal.* Calcd. for $C_{20}H_{30}O_2N_4$: C, 66.99; H, 8.43; N, 15.63. Found: C, 66.84; H, 8.32; N, 15.53%.

Spectroscopic data for bis(aziridine) 3e (Table 1, entry 5): 1,1′-(3,3′-(1,4-phenylene)bis(2-(dimethylamino)-1-methylaziridine-3,2-diyl))diethanone. Brown sticky liquid. Yield 70%; FT-IR (KBr): υ_{max} 3042 (s), 2244 (m), 1755 (s), 1715 (s), 1660 (s), 1575 (s), 1510 (m), 1460 (m), 1315 (m), 1250 (s), 1008 (m), 846 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.40 (s, 4H, Ar—H), 4.76 (s, 2H, 2 × aziridine protons), 2.74 (s, 12H, 2 × NMe_2), 2.10 (s, 6H, 2 × N—CH_3), 1.57 (s, 6H, 2 × $COCH_3$); ^{13}C NMR ($CDCl_3$): δ 174.06 (2 × C=O), 132.96, 132.57 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 131.34, 131.10 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings), 54.95 (2 × aziridine carbons), 52.64 (2 × aziridine carbons), 37.78 (2 × NMe_2), 31.60 (2 × N—CH_3), 22.43 (2 × $CO\underline{CH_3}$); FAB–MS (*m/z*): 358 (M^+), 343, 342, 300, 289, 272, 242, 217, 141, 126, 43; *Anal.* Calcd. for $C_{20}H_{30}O_2N_4$: C, 66.99; H, 8.43; N, 15.63. Found: C, 66.90; H, 8.36; N, 15.44%.

Spectroscopic data for bis(isoxazoline) 2f (Table 1, entry 6): (3R,3′R)-tetramethyl 3,3′-(1,4-phenylene)bis(2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylate. Pale yellow liquid. Yield 86%; FT-IR (KBr): υ_{max} 3018 (s), 2246 (m), 1763 (s), 1710 (s), 1605 (s), 1532 (s), 1436 (s), 1320 (m), 1254 (m), 1184 (s), 776 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.85 (m, 2 × 5H), 6.94 (s, 4H, Ar—H), 5.68 (s, 2H, 2 × 3-H), 3.37 (s, 12H, 4 × —$COOCH_3$); ^{13}C NMR ($CDCl_3$): δ 171.86 (2 × $\underline{CO}OCH_3$), 169.35 (2 × $\underline{CO}OCH_3$),137.53, 137.59 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 135.62, 135.71 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings), 132.60, 129.86 (2 × 1,4 Ar—C; N-phenyl carbons), 127.64, 127.42 (2 × 2,6 and 3,5 Ar—C; N-phenyl carbons), 86.12 (2 × 5-C), 75.48 (2 × 3-C), 61.23 (2 × 4-C), 39.52 (2 × —$COO\underline{CH_3}$), 37.80 (2 × —$COO\underline{CH_3}$); FAB–MS (*m/z*): 600 (M^+), 523, 482, 446, 338, 262 (B.P), 77, 59; *Anal.* Calcd. for $C_{32}H_{28}O_{10}N_2$: C, 63.98; H, 4.69; N, 4.66. Found: C, 63.90; H, 4.57; N, 4.60%.

Spectroscopic data for bis(aziridine) 3f (Table 1, entry 6): diphenyl 3,3′-(1,4-phenylene)bis(2-(2-methoxy-2-oxoacetyl)-1-phenylaziridine-2-carboxylate. Yellow liquid. Yield 71%; FT-IR (KBr): υ_{max} 3035 (s), 2980 (m), 1763 (s), 1726 (s), 1660 (s), 1585 (m), 1535 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.42 (m, 2 × 5H), 6.50 (s, 4H, Ar—H), 4.74 (s, 2H, 2 × aziridine protons), 3.80 (s, 6H, 2 × —$COOCH_3$, linked with aziridine rings), 3.53 (s, 6H, 2 × —$COOCH_3$, linked with keto group); ^{13}C NMR ($CDCl_3$): δ 173.11 (2 × C=O), 172.06 (2 × —$C\underline{O}OCH_3$, linked with aziridine rings), 170.15 (2 × —$C\underline{O}OCH_3$, linked with keto group), 130.80, 130.23 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 129.80, 129.56 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings), 128.06, 127.90 (2 × 1,4 Ar—C; N-phenyl carbons), 127.24, 127.03 (2 × 2,6 and 3,5 Ar—C; N-phenyl carbons), 62.62 (2 × aziridine ring carbons), 59.46 (2 × aziridine ring carbons), 37.12 (2 × —$COO\underline{CH_3}$, linked with aziridine rings), 35.47 (2 × —$COO\underline{CH_3}$, linked with keto group); FAB–MS (*m/z*): 600 (M^+), 523, 513, 436, 338, 262 (B.P), 87, 77, 59; *Anal.* Calcd. for $C_{32}H_{28}O_{10}N_2$: C, 63.98; H, 4.69; N, 4.66. Found: C, 63.81; H, 4.54; N, 4.52%.

Spectroscopic data for bis(isoxazoline) 2g (Table 1, entry 7): (3R,3′R)-3,3′-(1,4-phenylene)bis(2-methyl-2,3-dihydroisoxazole-4,5-dicarboxylic acid. White liquid. Yield 85%; FT-IR (KBr): υ_{max} 3280 (s), 3073 (s), 2235 (m), 1755 (s), 1684 (s), 1590 (s), 1540 (s), 1358 (m), 1280 (m), 1018 (m), 805 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.05 (s, 2H, 2 × —COOH), 9.96 (s, 2H, 2 × —COOH), 6.80 (s, 4H, Ar—H), 5.42 (s, 2H, 2 × C_3H), 2.08 (s, 6H, 2 × N—CH_3); ^{13}C NMR ($CDCl_3$): δ 173.78 (2 × $\underline{CO}OH$), 173.20 (2 × $\underline{CO}OH$), 134.69, 133.80 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 131.78, 130.80 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings), 80.64 (2 × 5-C), 77.30 (2 × 3-C), 55.85 (2 × 4-C), 51.30 (2 × N—CH_3); FAB–MS (*m/z*): 420 (M^+), 405, 330, 248, 172, 76; *Anal.* Calcd. for $C_{18}H_{16}O_{10}N_2$: C, 51.41; H, 3.83; N, 6.66. Found: C, 51.33; H, 3.60; N, 6.47%.

Spectroscopic data for bis(aziridine) 3g (Table 1, entry 7): dimethyl 3,3′-(1,4-phenylene)bis(2-(2-methoxy-2-oxoacetyl)-1-methylaziridine-2-carboxylate. Gray liquid. Yield 72%; FT-IR (KBr): υ_{max} 3282 (s), 3070 (s), 2255 (m), 1762 (s), 1756 (s), 1680 (s), 1660 (s), 1580 (s), 1540 (s), 1360 (m), 865 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.12 (s, 2H, 2 × —COOH), 10.00 (s, 2H, 2 × —COOH), 6.90 (s, 4H, Ar—H), 5.10 (s, 2H, 2 × aziridine protons), 2.08 (s, 6H, 2 × N—CH_3); ^{13}C NMR ($CDCl_3$): δ 173.38 (2 × C=O), 172.20 (2 × $\underline{CO}OH$), 171.70 (2 × $\underline{CO}OH$),134.62, 134.13 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 132.21, 132.10 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings), 65.75 (2 × aziridine ring carbons), 61.54 (2 × aziridine ring carbons), 50.23 (2 × N—CH_3); FAB–MS (*m/z*): 420 (M^+), 405, 360, 347, 332, 73, 45; *Anal.* Calcd. for $C_{18}H_{16}O_{10}N_2$: C, 51.41; H, 3.83; N, 6.66. Found: C, 51.30; H, 3.63; N, 6.44%.

Spectroscopic data for bis(isoxazoline) 2h (Table 1, entry 8): 1,4-bis((R)-2-benzyl-4,5-bis(trimethylsilyl)-2,3-dihydroisoxazol-3-yl)benzene. Yellow gummy liquid. Yield 84%; FT-IR (KBr): υ_{max} 3078 (s), 2256 (m), 1660 (s), 1583 (s), 1500 (m), 1480 (m), 1354 (m), 1280 (m), 1020 (m), 850 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.06 (s, 4H, Ar—H), 6.80–6.62 (m, 10H, 2 × Ar—H), 4.86 (s, 2H, 2 × 3-H), 1.13 (s, 36H, 4 × $SiMe_3$); ^{13}C NMR ($CDCl_3$): δ 135.34, 135.18 (1,4 Ar—C; phenyl ring carbons linked with isoxazoline rings), 133.62, 133.40 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with isoxazoline rings),130.68,130.52 (2 × 1,4 Ar—C; phenyl carbons), 128.48, 127.90 (2 × 2,6 and 3,5 Ar—C; phenyl carbons), 83.55 (2 × 5-C), 76.43 (2 × 3-C), 55.60 (2 × 4-C), 1.05 (4 × $SiMe_3$ carbons); FAB–MS (*m/z*): 656 (M^+), 583, 579, 510, 367, 289, 77; *Anal.* Calcd. for $C_{36}H_{52}Si_4O_2N_2$: C, 65.85; H, 7.92; N, 4.56. Found: C, 65.74; H, 7.82; N, 4.47%.

Spectroscopic data for bis(aziridine) 3h (Table 1, entry 8): (3,3′-(1,4-phenylene)bis(1-phenyl-2-(trimethylsilyl)aziridine-3,2-diyl))bis((trimethylsilyl)methanone. Gray liquid. Yield 71%; FT-IR (KBr): υ_{max} 3080 (s), 1766 (s), 1710 (s), 1664 (s), 1580 (s), 1475 (m), 1355 (m), 1280 (m), 1010 (m), 860 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.95 (s, 4H, Ar—H), 6.80–6.63 (m, 10H, 2 × Ar—H), 4.65 (s, 2H, 2 × aziridine protons), 0.96 (s, 36H, 4 × $SiMe_3$); ^{13}C NMR ($CDCl_3$): δ 174.35 (2 × C=O), 136.23, 136.12 (1,4 Ar—C; phenyl ring carbons linked with aziridine rings), 133.47, 133.14 (2,6 and 3,5 Ar—C; phenyl ring carbons linked with aziridine rings),128.80,128.68 (2 × 1,4 Ar—C; phenyl carbons), 127.66, 127.53 (2 × 2,6 and 3,5 Ar—C; phenyl carbons), 55.79 (2 × aziridine ring carbons), 53.65 (2 × aziridine ring carbons), 0.84 (4 × $SiMe_3$ carbons); FAB–MS (*m/z*): 656 (M^+), 579, 506, 478, 101,77, 73; *Anal.* Calcd. for $C_{36}H_{52}Si_4O_2N_2$: C, 65.85; H, 7.92; N, 4.56. Found: C, 65.74; H, 7.69; N, 4.42%.

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