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Synthesis and Study of Oxadisilole-Fused Benzisoxazoles or Naphthisoxazoles

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Oxadisilole-fused benzisoxazoles or naphthisoxazoles were obtained through 1,3-dipolar cycloaddition of arynes with nitrile oxides in good yields at room temperature. Key to the procedure is the simultaneous in situ generation of reactive nitrile oxides from arenecarbohydroximoyl chlorides and aryne reactants from benzobis(oxadisilole) or 2,3-naphthoxadisilole. One oxadisilole-fused benzisoxazole is a new precursor of a benzyne formed by a phenyliodination/fluoride-induced elimination protocol. By using this benzyne, cycloadducts were synthesized in good yields. The de-oxadisilole reaction of some of the oxadisilole-fused benzisoxazoles could be easily conducted with a 1.0 M solution of tetrabutylammonium fluoride in THF at room temperature.

Introduction

1,3-Dipolar cycloaddition reactions (1,3-DCRs), introduced by Huisgen in the early 1960s,[1] have been largely studied as useful synthetic strategies to obtain various heterocyclic systems.[2] The idea of synthesizing benzisoxazoles by the 1,3-DCR of a benzyne with a nitrile oxide has been reported previously.[3] Benzisoxazole derivatives are associated with various biological activities, such as antipsychotic,[4] antitumor,[5] anticonvulsant,[6] antimicrobial,[7] antithrombotic[8] and antidiabetic effects.[9] Aryne is an important intermediate and synthon in organic synthesis.[10] However, most benzynes are commonly accessed in situ by fluoride-promoted *ortho*-elimination of *o*-(trimethylsilyl)-aryl triflates.[3] Aryne formation of benzoxadisilole by phenyliodination with *o*-bis(trimethylsilyl)benzene was also reported by Kitamura and Yamane.[11] Recently, we have become interested in the chemistry of arynes generated from benzobis(oxadisilole), benzotris(oxadisilole) and 2,3-naphthoxadisilole under very mild conditions. We found that benzobis(oxadisiloles) could serve as the synthetic equivalent of benzdiynes. Their applications to the synthesis of functional acenes and benzoquinones have also been reported.[12] The chemistry was further extended to the synthesis of oxadisilole-fused benzo[*d*]isoxazoline and naphtho[2,3-*d*]isoxazoline derivatives (or oxadisilole-fused benzotriazole and naphthotriazole derivatives) by 1,3-DCR of nitrones (or azides) with arynes.[13] The sequential generation of the aryne of 1,4-bis(benzyne) from 1,2,4,5-tetrakis-(trimethylsilyl)benzene has also been reported by Russell and Winling.[14] Herein, we report an efficient approach to the synthesis of oxadisilole-fused benzisoxazoles **6a**–**e** or naphthisoxazoles **10a**–**e** by using benzobis(oxadisilole) **1** or 2,3-naphthoxadisilole **7** as benzyne **3** or naphthyne **9** precursors and arenecarbohydroximoyl chlorides **4a**–**e** as starting materials for nitrile oxides **5a**–**e** at room temperature. We also found that **6d** could serve as a new precursor of benzyne **12**; trapping experiments were carried out with various carbo- and heterocyclic dienes **13a**–**c** to afford cycloadducts **14a**–**c** in good yields. Benzobis(oxadisilole) **1** can serve as the precursor for the stepwise generation of 1,4-benzdiyne **15**. We found that the de-oxadisilole reaction of **6a**,**d**,**e** could be easily conducted with a 1.0 M solution of tetrabutylammonium fluoride (TBAF) in THF at room temperature.

Results and Discussion

Preparation of Oxadisilole-Fused Benzisoxazoles and Naphthisoxazoles

The syntheses of oxadisilole-fused benzisoxazoles **6a**–**e** or naphthisoxazoles **10a**–**e** are outlined in Schemes 1 and 2. Arynes **3** and **9** were generated from benzobis(oxadisilole) (**1**) and 2,3-naphthoxadisilole (**7**), respectively, through our previously reported phenyliodination/fluoride-induced desilylation protocol.[12a,12b] Trapping of benzyne **3** and naphthyne **9** at room temperature with nitrile oxides **5a**–**e** by 1,3-DCRs afforded **6a**–**e** and **10a**–**e**, respectively, in good yields. The 1,3-dipolar nitrile oxides **5a**–**e** are reactive intermediates, commonly generated in situ from arenecarbohydroximoyl chloride counterparts **4a**–**e**, which undergo rapid dehydrohalogenation upon exposure to a suitable

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base.[15] Compounds **4a**–**e** were prepared according to literature procedures.[16]

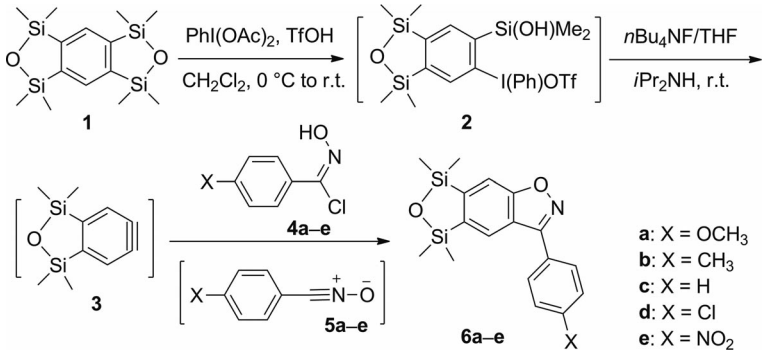
Our investigation started with the reaction of nitrile oxide **5d** generated in situ from 4-chlorobenzenehydroximoyl chloride (**4d**) with oxadisilole-fused benzyne **3** generated in situ from **1**. Phenyliodination of **1** with a 1.5:3 mixture of phenyliodium diacetate/trifluoromethanesulfonic acid (TfOH) took place readily at room temperature in dichloromethane (Scheme 1). Without isolation of the ring-opened iodination intermediate **2**, benzyne **3** could be generated in situ upon treatment with a 1.0 M solution of TBAF in THF. Trapping experiments were carried out with nitrile oxide **5d** generated in situ from **4d** (0.42 equiv.) at room temperature for 16 h to afford the oxadisilole-fused benzisoxazole **6d** in a yield of 82% in this three-step reaction (Scheme 1 and Table 1, Entry 3). Nitrile oxide **5d** is a reactive intermediate commonly generated in situ by treatment of **4d** with a base. However, with diisopropylamine as the base and CsF as the fluoride source, the desired product **6d** could only be isolated in 27% yield (Table 1, Entry 1). We observed that, with triethylamine as the base and CsF as the fluoride source, the yield of **6d** slightly increased to 30% (Table 1, Entry 2). The use of a solution of TBAF in THF as the fluoride source and iPr$_2$NH as the base gave benzisoxazole **6d** in 80% yield at room temperature after 3 h (Table 1, Entry 4). In the present case, use of 0.60 or 0.80 equiv. of **4d** at room temperature for 3 h afforded the desired product **6d** in 83 or 77% yield, respectively (Table 1, Entry 5 or 10, respectively). Finally, we found that use of 0.75 equiv. of **4d** at room temperature for 3 h improved the yield of **6d** to 87% (Table 1, Entry 7). Attempts to change the reaction time to 1, 5 or 16 h gave the desired product **6d** in 75, 81 or 84% yield, respectively (Table 1, Entries 6, 8 or 9, respectively).

Table 1. Cycloaddition of the nitrile oxide **5d**, generated from **4d**, with benzyne **3** generated from **1** (1 equiv.) by using different fluoride sources and bases at room temperature.

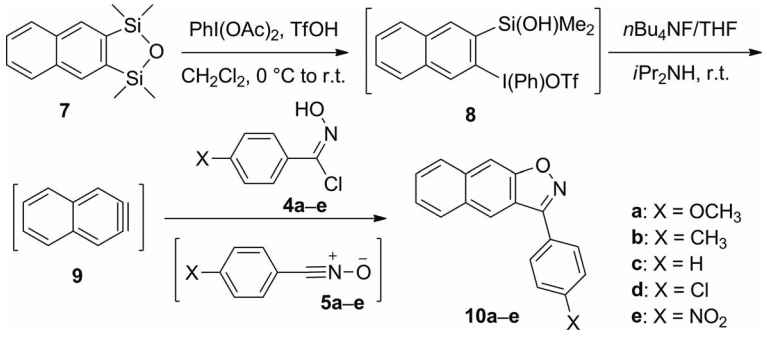
Entry	**4d** [equiv.]	Fluoride source	Base	Time [h]	Yield[a] of **6d** [%]
1	0.42	CsF	iPr$_2$NH	16	27
2	0.42	CsF	Et$_3$N	16	30
3	0.42	TBAF/THF	iPr$_2$NH	16	82
4	0.42	TBAF/THF	iPr$_2$NH	3	80
5	0.60	TBAF/THF	iPr$_2$NH	3	83
6	0.75	TBAF/THF	iPr$_2$NH	1	75
7	0.75	TBAF/THF	iPr$_2$NH	3	87
8	0.75	TBAF/THF	iPr$_2$NH	5	81
9	0.75	TBAF/THF	iPr$_2$NH	16	84
10	0.80	TBAF/THF	iPr$_2$NH	3	77

[a] Yields of purified products.

We further studied the 1,3-DCR of benzyne **3** generated in situ from **1** with **5a**–**e** generated in situ from **4a**–**e** (0.75 equiv.) at room temperature for 3 h. The oxadisilole-fused benzisoxazoles **6a**–**e** were formed in 70–89% yield (Scheme 1 and Table 2, Entries 1–5). As shown from the yields, this 1,3-DCR of **5a**–**e** with **3** is rather insensitive with respect to the electronic nature (X = OCH$_3$, CH$_3$, H, Cl, NO$_2$) of the substituents on the benzene rings of **5a**–**e**.



Scheme 1. Synthesis of the oxadisilole-fused benzisoxazoles **6a**–**e**.



Scheme 2. Synthesis of the naphthisoxazoles **10a**–**e**.

Furthermore, the 1,3-DCRs of **9** generated in situ from the **7** with **5a**–**e** generated in situ from **4a**–**e** at room temperature were also investigated. To our delight, the 1,3-dipolar nitrile oxides **5a**–**e** successfully participated in the cycloaddition reaction with **9** at room temperature to afford the corresponding naphthisoxazoles **10a**–**e** in moderate to good yields (Scheme 2 and Table 2, Entries 6–10).

Table 2. Cycloaddition of **5a**–**e** generated from **4a**–**e** (0.75 equiv.) with **3** or **9** generated from **1** (1 equiv.) or **7** (1 equiv.) at room temperature.

Entry	Arenecarbohydroximoyl chloride	X	Aryne	Product	Yield[a] [%]
1	**4a**	OCH_3	**3**	**6a**	89
2	**4b**	CH_3	**3**	**6b**	82
3	**4c**	H	**3**	**6c**	70
4	**4d**	Cl	**3**	**6d**	87
5	**4e**	NO_2	**3**	**6e**	71
6	**4a**	OCH_3	**9**	**10a**	87
7	**4b**	CH_3	**9**	**10b**	75
8	**4c**	H	**9**	**10c**	54
9	**4d**	Cl	**9**	**10d**	84
10	**4e**	NO_2	**9**	**10e**	34

[a] Yields of purified products.

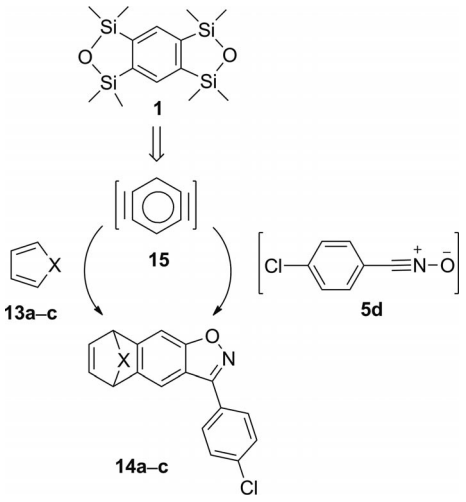
Benzyne 12 from the Oxadisilole-Fused Benzisoxazole 6d

The oxadisilole-fused benzisoxazole **6d** is a new precursor of benzyne **12** obtained by a phenyliodination/fluoride-induced elimination protocol. Trapping experiments of **12** were carried out with various carbo- and heterocyclic dienes **13a**–**c**. Cycloadducts **14a**–**c** were synthesized by the Diels–Alder reactions outlined in Scheme 3. Phenyliodination of **6d** with a 3:4 mixture of $PhI(OAc)_2$/TfOH took place readily at room temperature in CH_2Cl_2. Without isolation of intermediate **11** or **11′**, benzyne **12** could be generated in situ upon treatment with KF and a catalytic amount of TBAF. Cycloadducts **14a**–**c** were obtained by trapping experiments of **12** with various dienes **13a**–**c** [furan, *N*-(*tert*-butoxycarbonyl)pyrrole (*N*-Boc-pyrrole) and cyclopentadiene] in good isolated yields (Scheme 3 and Table 3). With the generation of **12** from **6d**, we have demonstrated that **1** is a synthetic equivalent of 1,4-benzdiyne **15**.[12b] As depicted in Scheme 4, the stepwise generated 1,4-benzdiyne was first treated with nitrile oxide **5d** and then with other dienes **13a**–**c** to build up a series of cycloadducts **14a**–**c**.

Table 3. Cycloaddition of dienes **13a**–**c** with **12** generated from **6d**.

Entry	Diene	X	Product	Yield[a] of **14** [%]
1	**13a**	O	**14a**	92
2	**13b**	*N*-Boc	**14b**	71
3	**13c**	CH_2	**14c**	79

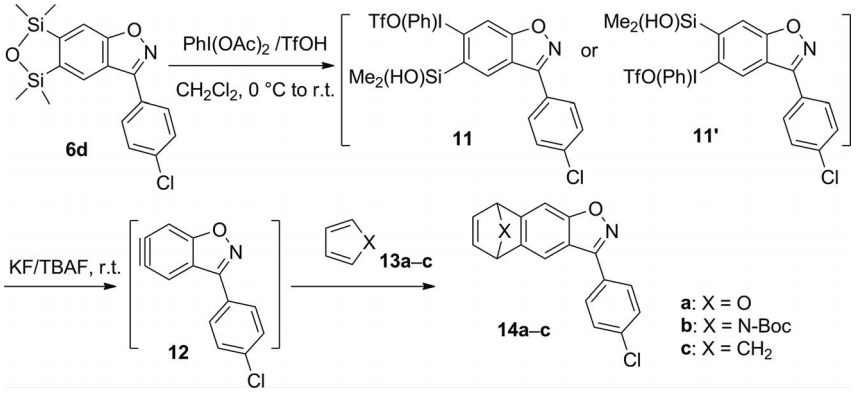
[a] Yields of purified products.



Scheme 4. Benzobis(oxadisilole) **1** as the synthetic equivalent of 1,4-benzdiyne **15** for the preparation of cycloadducts **14a**–**c**.

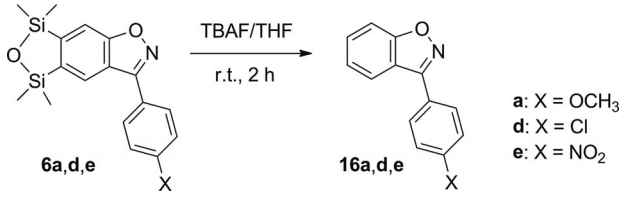
De-oxadisilole Reaction of Oxadisilole-Fused Benzisoxazoles 6a,d,e

We were delighted to find that benzisoxazole derivatives **16a**,**d**,**e** could be easily obtained from oxadisilole-fused benzisoxazoles **6a**,**d**,**c** with a 1.0 M solution of TBAF in THF by de-oxadisilole reactions. Reactions were completed at room temperature within 2 h to give the target products



Scheme 3. Benzyne **12** generation and trapping experiments.

16a,**d**,**e** in good yields (Scheme 5 and Table 4). This easy de-oxadisilole reaction proceeded smoothly under the chosen reaction conditions.



Scheme 5. Synthesis of benzisoxazole derivatives **16a**,**d**,**e**.

Table 4. Synthesis of **16a**,**d**,**e** from **6a**,**d**,**e** at room temperature.

Entry	Reactant	X	Product	Yield[a] of **16** [%]
1	**6a**	OCH_3	**16a**	56
2	**6d**	Cl	**16d**	72
3	**6e**	NO_2	**16e**	63

[a] Yields of purified products.

The structures of compounds **6a**–**e**, **10a**–**e**, **14a**–**c** and **16a**,**d**,**e** were established by ^1H and ^{13}C NMR spectroscopy, MS, IR spectroscopy, elemental analysis and high-resolution (HR) MS.

Conclusions

Oxadisilole-fused benzisoxazoles **6a**–**e** or naphthisoxazoles **10a**–**e** were obtained through the 1,3-DCR of benzyne (**3**) or naphthyne (**9**) generated in situ from benzobis(oxadisilole) (**1**) or 2,3-naphthoxadisilole (**7**) with nitrile oxides **5a**–**e** generated in situ from arenecarbohydroximoyl chlorides **4a**–**e** in good yields at room temperature. Oxadisilole-fused benzisoxazole **6d** is a new precursor of benzyne **12** through the phenyliodination/fluoride-induced elimination protocol. Cycloaddition of **12** with various dienes **13a**–**c** afforded cycloadducts **14a**–**c** in good yields. In the overall transformations, benzobis(oxadisilole) (**1**) served as a synthetic equivalent of 1,4-benzdiyne (**15**). We also found an easy de-oxadisilole method for oxadisilole-fused benzisoxazoles **6a**,**d**,**e** to give benzisoxazole derivatives **16a**,**d**,**e** in the presence of TBAF/THF in good yields at room temperature. These reactions could offer great opportunities for the synthesis of important heterocyclic compounds.

Experimental Section

General Methods: Purification was effected by silica gel column chromatography (200–300 mesh silica gel) using mixtures of reagent-grade EtOAc/petroleum ether (PE, 60–80 °C) as the eluents. NMR spectra were recorded at 500 MHz for ^1H and 125 MHz for ^{13}C with $CDCl_3$ as the solvent by using a Bruker DRX-500 NMR spectrometer. Chemical shifts are reported in ppm on the δ scale relative to the residual resonance of $CHCl_3$ (δ =7.26 ppm for ^1H, and 77.16 ppm for the central peak of the triplet in ^{13}C). Coupling constants (J) are reported in Hz. IR spectra were recorded with an FTIR spectrometer and expressed in cm^{-1} (KBr disc). Low-resolution mass spectra were obtained with a Finnigan MAT SSQ-710 spectrometer in EI mode and are reported as m/z values. High-resolution mass spectra were recorded with a Finnigan MAT-8430 instrument. Element analyses were performed at the Shanghai University.

Oxadisilole-Fused Benzisoxazoles 6a–e and Naphthisoxazoles 10a–e: TfOH (0.27 mL, 3.0 mmol) was added by means of a syringe to a stirred solution of $PhI(OAc)_2$ (493 mg, 1.5 mmol) in dichloromethane (10 mL) at 0 °C under N_2. The mixture was stirred under N_2 at 0 °C for 0.5 h and at room temperature for 1.5 h. The clear yellow solution was cooled again to 0 °C followed by dropwise addition of a solution of the benzobis(oxadisilole) **1** (or 2,3-naphthoxadisilole **7**) (1.0 mmol) in dichloromethane (5 mL). The mixture was stirred at 0 °C for 0.5 h and at room temperature for 3–6 h. The clear yellow solution was cooled again to 0 °C, iPr$_2$NH (0.35 mL, 2.5 mmol) and arenecarbohydroximoyl chlorides **4a**–**e** (0.75 mmol) were added followed by a solution of TBAF (1.0 M in THF, 4.5 mL, 4.5 mmol). The mixture was stirred under N_2 at room temperature for 3 h. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of 5–10% EtOAc in PE (60–80 °C) as the eluent to afford cycloadducts **6a**–**e** and **10a**–**e**.

3-(4-Methoxyphenyl)-5,6-oxadisilole-Fused Benzisoxazole (6a): Yield: 237 mg, 89%. Colourless solid. M.p. 119–120 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.43 (s, 6 H, $SiMe_2$), 0.44 (s, 6 H, $SiMe_2$), 3.91 (s, 3 H, OMe), 7.11 (d, J = 8.5 Hz, 2 H, Ar-H), 7.80 (d, J = 1.0 Hz, 1 H, Ar-H), 7.93 (d, J = 8.5 Hz, 2 H, Ar-H), 8.08 (d, J = 1.0 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 1.1, 1.5, 55.5, 112.4, 114.8, 121.5, 122.4, 125.3, 129.6, 142.4, 150.4, 156.9, 161.4, 164.9 ppm. IR (KBr): $\tilde{\nu}$ = 3443, 3042, 2953, 2849, 1611, 1584, 1480, 1254, 1093, 927, 835, 795 cm^{-1}. HRMS (MALDI-TOF): calcd. for $C_{18}H_{21}NO_3Si_2$ $[M + H]^+$ 356.1132; found 356.1133.

3-(4-Methylphenyl)-5,6-oxadisilole-Fused Benzisoxazole (6b): Yield: 209 mg, 82%. Colourless solid. M.p. 86–89 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.42 (s, 6 H, $SiMe_2$), 0.44 (s, 6 H, $SiMe_2$), 2.47 (s, 3 H, Me), 7.40 (d, J = 8.0 Hz, 2 H, Ar-H), 7.81 (d, J = 0.5 Hz, 1 H, Ar-H), 7.87 (d, J = 8.0 Hz, 2 H, Ar-H), 8.07 (d, J = 0.5 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 1.1, 1.4, 21.6, 112.4, 122.4, 125.3, 126.2, 128.1, 130.0, 140.6, 142.4, 150.4, 157.2, 164.9 ppm. IR (KBr): $\tilde{\nu}$ = 3443, 3030, 2956, 1596, 1433, 1256, 1086, 930, 794 cm^{-1}. MS (EI): m/z (%) = 339 (100) $[M^+]$, 324 (73). HRMS (MSI-TOF): calcd. for $C_{18}H_{21}NO_2Si_2$ $[M + Na]^+$ 362.1009; found 362.1031.

3-Phenyl-5,6-oxadisilole-Fused Benzisoxazole (6c): Yield: 171 mg, 70%. Colourless solid. M.p. 102–105 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.44 (s, 6 H, $SiMe_2$), 0.45 (s, 6 H, $SiMe_2$), 7.56–7.61 (m, 3 H, Ar-H), 7.83 (d, J = 1.0 Hz, 1 H, Ar-H), 7.98–8.00 (m, 2 H, Ar-H), 8.10 (d, J = 1.0 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 1.1, 1.5, 112.5, 122.3, 125.3, 128.3, 129.1, 129.3, 130.4, 142.6, 150.6, 157.3, 165.0 ppm. IR (KBr): $\tilde{\nu}$ = 3442, 3052, 2960, 1598, 1447, 1252, 1092, 933, 796 cm^{-1}. HRMS (MALDI-TOF): calcd. for $C_{17}H_{19}NO_2Si_2$ $[M + H]^+$ 326.1031; found 326.1027.

3-(4-Chlorophenyl)-5,6-oxadisilole-Fused Benzisoxazole (6d): Yield: 235 mg, 87%. Colourless solid. M.p. 117–120 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.43 (s, 6 H, $SiMe_2$), 0.44 (s, 6 H, $SiMe_2$), 7.57 (d, J = 8.5 Hz, 2 H, Ar-H), 7.82 (d, J = 0.5 Hz, 1 H, Ar-H), 7.92 (d, J = 8.5 Hz, 2 H, Ar-H), 8.04 (d, J = 0.5 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 1.1, 1.5, 112.6, 122.0, 125.0, 127.6, 129.5, 129.6, 136.6, 142.9, 150.9, 156.4, 165.0 ppm. IR (KBr): $\tilde{\nu}$ = 3444, 3058, 2957, 1601, 1433, 1252, 1094, 942, 794 cm^{-1}. MS (EI): m/z (%) = 359 (78) $[M^+]$, 344 (100).

$C_{17}H_{18}ClNO_2Si_2$ (359.96): calcd. C 56.72, H 5.04, N 3.89; found C 56.43, H 5.04, N 3.86.

3-(4-Nitrophenyl)-5,6-oxadisilole-Fused Benzisoxazole (6e): Yield: 197 mg, 71%. Colourless solid. M.p. 203–204 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.44 (s, 6 H, $SiMe_2$), 0.45 (s, 6 H, $SiMe_2$), 7.87 (s, 1 H, Ar-H), 8.07 (s, 1 H, Ar-H), 8.19 (d, J = 9.0 Hz, 2 H, Ar-H), 8.46 (d, J = 9.0 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 1.1, 1.5, 112.8, 121.5, 124.50, 124.58, 129.2, 135.4, 143.6, 149.0, 151.4, 155.5, 165.3 ppm. IR (KBr): $\tilde{\nu}$ = 3442, 3080, 2959, 1601, 1522, 1250, 1087, 941, 795 cm^{-1}. MS (EI): *m*/*z* (%) = 370 (18) [M$^+$], 355 (65), 209 (100). $C_{17}H_{18}N_2O_4Si_2$ (370.51): calcd. C 55.11, H 4.90, N 7.56; found C 54.97, H 5.06, N 7.35.

3-(4-Methoxyphenyl)naphth[2,3-*d*]isoxazole (10a): Yield: 180 mg, 87%. Colourless solid. M.p. 188–189 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, OMe), 7.13 (d, J = 8.5 Hz, 2 H, Ar-H), 7.48 (t, J = 7.5 Hz, 1 H, Ar-H), 7.58 (t, J = 7.5 Hz, 1 H, Ar-H), 7.98 (d, J = 8.5 Hz, 2 H, Ar-H), 8.02–8.04 (m, 3 H, Ar-H), 8.45 (s, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.6, 105.1, 114.8, 121.3, 122.0, 122.2, 124.8, 127.7, 128.1, 129.3, 129.7, 130.6, 134.2, 157.0, 160.1, 161.5 ppm. IR (KBr): $\tilde{\nu}$ = 3444, 3052, 2974, 1608, 1463, 1255, 1030, 870, 753 cm^{-1}. HRMS (MALDI-TOF): calcd. for $C_{18}H_{13}NO_2$ [M + H]$^+$ 276.1019; found 276.1019.

3-(4-Methylphenyl)naphth[2,3-*d*]isoxazole (10b): Yield: 146 mg, 75%. Colourless solid. M.p. 158–159 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.49 (s, 3 H, Me), 7.42 (d, J = 8.0 Hz, 2 H, Ar-H), 7.46–7.49 (m, 1 H, Ar-H), 7.56–7.59 (m, 1 H, Ar-H), 7.97–8.00 (m, 4 H, Ar-H), 8.02 (d, J = 8.0 Hz, 1 H, Ar-H), 8.45 (s, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.7, 105.1, 122.0, 122.2, 124.8 126.1, 127.7, 128.1, 128.2, 129.4, 130.1, 130.6, 134.3, 140.9, 157.4, 160.2 ppm. IR (KBr): $\tilde{\nu}$ = 3447, 3052, 2920, 1611, 1505, 1463, 1245, 1099, 870, 752 cm^{-1}. MS (EI): *m*/*z* (%) = 259 (100) [M$^+$], 231 (64), 91 (16). $C_{18}H_{13}NO$ (259.31): calcd. C 83.37, H 5.05, N 5.40; found C 83.25, H 5.10, N 5.36.

3-Phenylnaphth[2,3-*d*]isoxazole (10c): Yield: 100 mg, 54%. Colourless solid. M.p. 139–140 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.51 (m, 1 H, Ar-H), 7.58–7.65 (m, 4 H, Ar-H), 7.99–8.09 (m, 5 H, Ar-H), 8.48 (s, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 105.2, 122.0, 124.9, 127.7, 127.8 128.2, 128.3, 129.2, 129.36, 129.37, 130.6, 130.7, 134.3, 157.5, 160.2 ppm. IR (KBr): $\tilde{\nu}$ = 3443, 3052, 2964, 1633, 1501, 1462, 1246, 1100, 865, 748 cm^{-1}. HRMS (MALDI-TOF): calcd. for $C_{17}H_{11}NO$ [M + H]$^+$ 246.0917; found 246.0913.

3-(4-Chlorophenyl)naphth[2,3-*d*]isoxazole (10d): Yield: 176 mg, 84%. Colourless solid. M.p. 175–176 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.51 (m, 1 H, Ar-H), 7.51–7.61 (m, 3 H, Ar-H), 7.99–8.04 (m, 5 H, Ar-H), 8.42 (s, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 105.3, 121.5, 121.6, 125.0 127.4, 127.9, 128.1, 129.3, 129.5, 129.6, 130.7, 134.3, 136.8, 156.5, 160.2 ppm. IR (KBr): $\tilde{\nu}$ = 3446, 3052, 2922, 1634, 1463, 1216, 1092, 826, 744 cm^{-1}. HRMS (MALDI-TOF): calcd. for $C_{17}H_{10}ClNO$ [M + H]$^+$ 280.0528; found 280.0524.

3-(4-Nitrophenyl)naphth[2,3-*d*]isoxazole (10e): Yield: 74 mg, 34%. Pale brown solid. M.p. >271 °C. ^{1}H NMR (500 MHz, DMSO): δ = 7.60 (t, J = 7.5 Hz, 1 H, Ar-H), 7.71 (t, J = 7.5 Hz, 1 H, Ar-H), 8.17 (d, J = 8.0 Hz, 1 H, Ar-H), 8.26 (d, J = 8.0 Hz, 1 H, Ar-H), 8.40 (s, 1 H, Ar-H), 8.47–8.53 (m, 4 H, Ar-H), 8.95 (s, 1 H, Ar-H) ppm. ^{13}C NMR (125 MHz, DMSO): δ = 105.1, 120.3, 122.6, 124.5, 125.3, 128.0, 128.2, 129.46, 129.51, 130.6, 134.0, 134.1, 148.8, 155.7, 159.5 ppm. IR (KBr): $\tilde{\nu}$ = 3453, 3088, 1630, 1604, 1526, 1347, 853, 754 cm^{-1}. HRMS (MALDI-TOF): calcd. for $C_{17}H_{10}N_2O_3$ [M + H]$^+$ 291.0769; found 291.0764.

Cycloadducts 14a–c from Benzyne 12 Generated from Oxadisilole-Fused Benzisoxazole 6d: Trifluoromethanesulfonic acid (0.36 mL, 4.0 mmol) was added by means of a syringe to a stirred solution of $PhI(OAc)_2$ (987 mg, 3.0 mmol) in dichloromethane (10 mL) at 0 °C. The mixture was stirred under N_2 at 0 °C for 0.5 h and at room temperature for 1.5 h. The clear yellow solution was cooled again to 0 °C followed by dropwise addition of a solution of **6d** (359 mg, 1.0 mmol) in dichloromethane (5 mL). The mixture was stirred at 0 °C for 0.5 h and at room temperature for 3 h. The clear yellow solution was cooled again to 0 °C, the diene [furan (0.76 mL, 10 mmol), *N*-(*tert*-butoxycarbonyl)pyrrole (1.6 mL, 10 mmol) or cyclopentadiene (0.82 mL, 10 mmol)] was added followed by KF (232 mg, 4.0 mmol) and TBAF (1.0 M in THF, 0.2 mL, 0.2 mmol). The mixture was stirred under N_2 at room temperature for 16 h. The organic solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of 10–15% EtOAc in PE (60–80 °C) as the eluent to afford cycloadducts **14a**–**c**.

3-(4-Chlorophenyl)-5,8-dihydro-5,8-epoxynaphth[2,3-*d*]isoxazole (14a): Yield: 272 mg, 92%. Pale brown solid. M.p. 157–158 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.80 (d, J = 6.5 Hz, 2 H, O-C-H), 7.03–7.07 (m, 2 H, C=C-H), 7.48–7.50 (m, 3 H, Ar-H), 7.57 (s, 1 H, Ar-H), 7.81 (d, J = 8.0 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 81.9, 82.2, 104.1, 112.4, 116.9, 127.5, 129.3, 129.5, 136.3, 142.1, 143.3, 144.9, 152.3, 156.7, 163.9 ppm. IR (KBr): $\tilde{\nu}$ = 3444, 3023, 1599, 1464, 1336, 1090, 845 cm^{-1}. MS (EI): *m*/*z* (%) = 295 (42) [M$^+$], 266 (100); 267 (100). $C_{17}H_{10}ClNO_2$ (295.72): calcd. C 69.05, H 3.41, N 4.74; found C 69.14, H 3.44, N 4.75.

***N*-(*tert*-Butoxycarbonyl)-3-(4-chlorophenyl)-5,8-dihydro-5,8-iminonaphth[2,3-*d*]isoxazole (14b):** Yield: 280 mg, 71%. Pale yellow solid. M.p. 147–149 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, CMe_3), 5.58 (s, 2 H, N-C-H), 7.01 (s, 2 H, C=C-H), 7.50–7.52 (m, 3 H, Ar-H), 7.61 (s, 1 H, Ar-H), 7.82–7.84 (m, 2 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.3, 66.2, 81.3, 104.6, 113.3, 116.8, 127.6, 129.4, 129.6, 136.5, 141.7, 144.4, 151.6, 154.9, 156.7, 163.7 ppm. IR (KBr): $\tilde{\nu}$ = 3435, 3069, 2976, 1697, 1464, 1338, 1168, 834 cm^{-1}. HRMS: calcd. for $C_{22}H_{19}N_2O_3Cl$ [M]$^+$ 394.1085; found 394.1084.

3-(4-Chlorophenyl)-5,8-dihydro-5,8-methanonaphth[2,3-*d*]isoxazole (14c): Yield: 232 mg, 79%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.31 (d, J = 7.5 Hz, 1 H, CH_2), 2.43 (d, J = 7.5 Hz, 1 H, CH_2), 3.97 (s, 1 H, CH_2-C-H), 3.99 (s, 1 H, CH_2-C-H), 6.77–6.82 (m, 2 H, C=C-H), 7.46 (s, 1 H, Ar-H), 7.50 (d, J = 8.5 Hz, 2 H, Ar-H), 7.55 (s, 1 H, Ar-H), 7.85 (d, J = 8.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 49.6, 50.4, 68.6, 104.7, 113.1, 116.6, 128.1, 129.3, 129.4, 129.5, 129.6, 136.1, 142.2, 143.3, 148.2, 155.9, 156.4, 163.8 ppm. IR (KBr): $\tilde{\nu}$ = 3386, 3048, 2935, 1604, 1464, 1341, 1092, 834 cm^{-1}. HRMS: calcd. for $C_{18}H_{12}NOCl$ [M]$^+$ 293.0610; found 293.0607.

Benzisoxazole Derivatives 16a,d,e from Oxadisilole-Fused Benzisoxazole 6a,d,e: TBAF (1.0 M in THF, 2.0 mL, 2.0 mmol) was added to a solution of oxadisilole-fused benzisoxazole derivatives **6a**,**d**,**e** (1.0 mmol) in dichloromethane (10 mL) under N_2. The mixture was stirred at room temperature for 2 h. The organic solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of 5–10% EtOAc in PE (60–80 °C) as the eluent to afford benzisoxazole derivatives **16a**,**d**,**e**.

3-(4-Methoxyphenyl)-1,2-benzisoxazole (16a): Yield: 126 mg, 56%. Colourless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.90 (s, 3 H, OMe), 7.08 (d, J = 8.5 Hz, 2 H, Ar-H), 7.37 (t, J = 7.5 Hz, 1 H, Ar-H), 7.58 (t, J = 7.5 Hz, 1 H, Ar-H), 7.63 (d, J = 8.5 Hz, 1 H,

Ar-H), 7.92 (d, J = 8.5 Hz, 3 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.6, 110.3, 114.7, 120.7, 121.5, 122.4, 123.9, 129.6, 129.8, 157.0, 161.3, 163.9 ppm. LRMS (EI): m/z (%) = 225 (100) [M^+], 197 (27), 105 (72).

3-(4-Chlorophenyl)-1,2-benzisoxazole (16d): Yield: 165 mg, 72%. Colourless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.42 (m, 1 H, Ar-H), 7.54–7.56 (m, 2 H, Ar-H), 7.60–7.63 (m, 1 H, Ar-H), 7.66–7.68 (m, 1 H, Ar-H), 7.89–7.93 (m, 3 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 110.5, 120.3, 122.1, 124.2, 127.6, 129.4, 129.6, 130.1, 136.6, 156.5, 164.1 ppm. MS (EI): m/z (%) = 229 (100) [M^+], 201 (41), 166 (37).

3-(4-Nitrophenyl)-1,2-benzisoxazole (16e): Yield: 151 mg, 63%. Pale brown solid. ^{1}H NMR (500 MHz, DMSO): δ = 7.56 (t, J = 7.5 Hz, 1 H, Ar-H), 7.79 (t, J = 7.5 Hz, 1 H, Ar-H), 7.92 (d, J = 8.5 Hz, 1 H, Ar-H), 8.20 (d, J = 8.5 Hz, 1 H, Ar-H), 8.33 (d, J = 8.5 Hz, 2 H, Ar-H), 8.45 (d, J = 8.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (125 MHz, DMSO): δ = 110.4, 119.2, 122.5, 124.5, 125.0, 129.3, 131.0, 134.2, 148.6, 155.4, 163.5 ppm. MS (EI): m/z (%) = 240 (100) [M^+], 212 (20), 194 (24).

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