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Synthesis and photoactivated insecticidal activity of tetraethynylsilanes

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ABSTRACT

A series of tetraethynylsilanes (TETS) have been synthesized by reaction of silicon tetrachloride ($SiCl_4$) with Ar–C≡CLi, which was prepared in situ by treatment of Ar–C≡CH with *n*-BuLi. For these TETS thus prepared, their photoactivated insecticidal activities against the 4th-instar larvae of *Aedes albopictus* (Skuse) were evaluated to enrich the structure–activity relationship. In particular, compound 8 exhibited excellent photoactivated insecticidal activity, the LC_{50} value was 0.1346 mg L^{-1} under UV light treatment and the irradiation-generated enhancement in the activity was more than 69.58-fold, thus could be exploitable as ideal analog candidates in the search for new photoactivated insecticide leads.

1. Introduction

Compared to traditional organophosphate and carbamate pesticides, the photoactivatable insecticides act through photodynamic pathways [1,2], which are characterized by the great enhancement of their activities after absorption of light energy and have diverse biological effects including insecticidal, fungicidal, bactericidal, nematicidal, and herbicidal activities [3,4]. The main classes of photodynamic sensitizers that have been used as photoinsecticides are xanthenes, porphyrins, phenothiazines, furanocoumarins, acridines, thiophenes, and polyacetylenes [5,6].

In our work on arylene ethynylenes [7–13], we were interested in the preparation of tetraethynylsilanes $(RC{\equiv}C)_4Si$, because of their ready accessibility and stability. The attachment of a fluorophore to the silicon atom enhances the quantum yield of photoluminescence (PL), and that several TETS exhibit high quantum yields in solution have been revealed [8,9]. We envisaged such TETS could achieve high photoactivated insecticidal activities induced by four triple bonds on silicon. With this thought in mind, a series of TETS were synthesized and their photoactivated insecticidal activities against the 4th-instar larvae of *Aedes albopictus* (Skuse) were investigated, and the structure–activity correlation was also clarified [14].

2. Experimental

2.1. General

All reactions were carried out under an atmosphere of argon with freshly distilled solvents, unless otherwise noted. Tetrahydrofuran (THF) was distilled from sodium/benzophenone. Other solvents such as toluene, diisopropylamine, and CH_2Cl_2 were distilled from CaH_2. Solutions of LiHMDS and Grignard reagents in THF and diethyl ether were purchased and used without titration. A solution of *n*-BuLi in hexane was purchased and titrated by the Gilman method prior to use. Silica gel was used for column chromatography. NMR spectra were recorded at 25 °C on JEOL Lambda 300 and 500 instruments and calibrated with tetramethylsilane as an internal reference. Elemental analysis was performed on a Perkin–Elmer PE 2400 instrument. EI-MS (electron impact ionization mass spectra) were recorded on a Thermo DSQ mass spectrometer by direct inlet. IR spectra were recorded as potassium bromide pellets on an IR-Nicolet Avatrar 330 spectrometer at room temperature. UV/Vis absorption spectra were recorded on Shimadzu UV 2550 in CH_2Cl_2 at room temperature.

2.2. Synthesis

The synthesis and spectroscopic data of TETS 1–6 have been reported in our previous publications (Fig. 1) [8,9], TETS 7 was obtained from the reaction of $SiCl_4$ and $3\text{-}MeC_6H_4\text{–}C{\equiv}CLi$ in 85% yield (Scheme 1), which was prepared from commercially available $3\text{-}MeC_6H_4\text{–}C{\equiv}CH$ and *n*-BuLi in THF. The synthetic pathways of TETS 8–11 were shown in Schemes 2 and 3. TMS-protected

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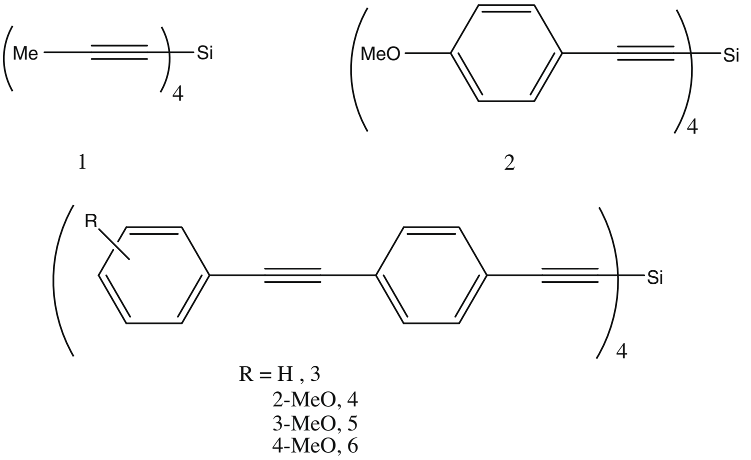
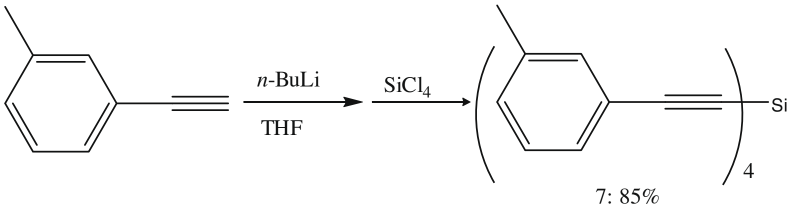
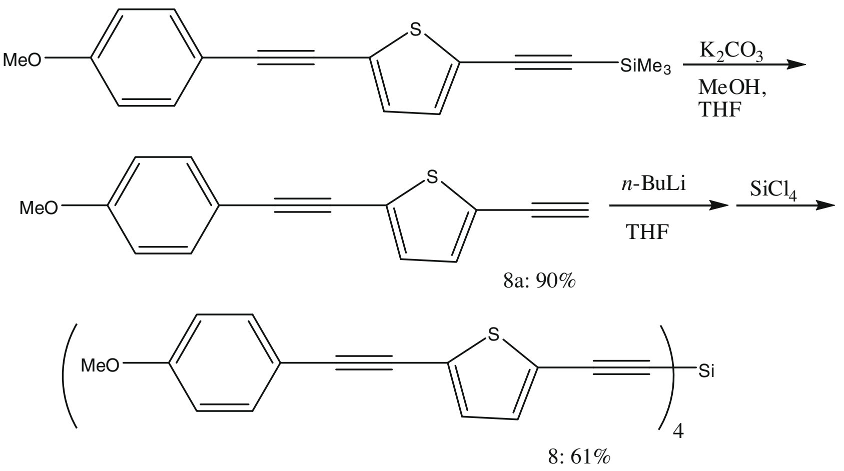


Fig. 1. Structure of TETS 1–6.



Scheme 1. Synthesis of TETS 7.

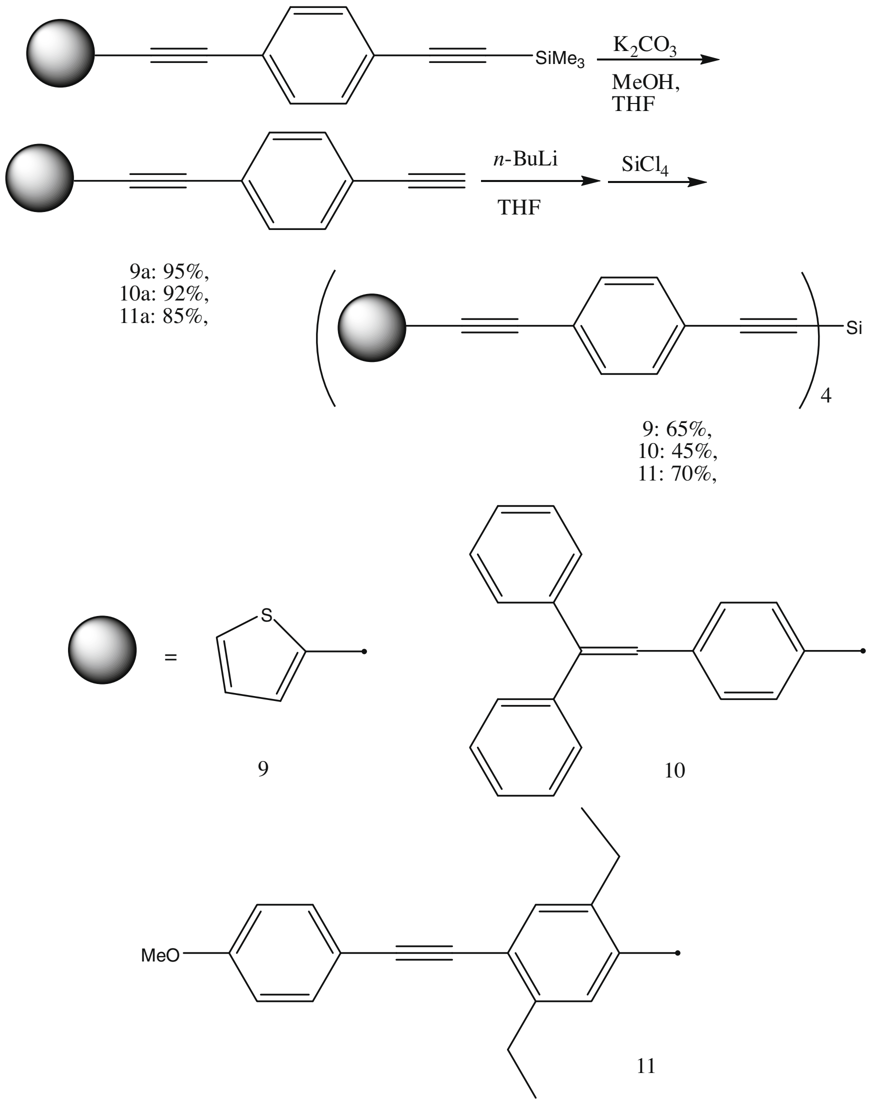


Scheme 2. Synthesis of TETS 8.

acetylenes were transformed into the corresponding terminal ethynes by desilylation with K_2CO_3 in MeOH/THF, which were used for the synthesis of TETS 8–11. All these TETS 1–11 were obtained as air-stable white solids or pale yellow solid with clear melting points.

2.2.1. TETS 11 (representative)

A solution of 1,4-diethyl-2-(2-(4-ethynyl-phenyl)ethynyl)-5-(2-(4-methoxyphenyl)ethynyl)benzene (765 mg, 1.97 mmol) in THF (20 mL) was stirred under argon and treated dropwise with a solution of n-BuLi (1.46 M in hexane, 1.32 mL, 1.92 mmol) at −78 °C. The mixture was kept at −78 °C for 10 min, warmed to room temperature for 20 min and neat tetrachlorosilane (0.05 mL, 74 mg, 0.43 mmol) was added. The solution was stirred at room temperature for 12 h and poured into water. The aqueous layer was extracted with ethyl acetate and the combined organic layer was washed with brine, dried over magnesium sulfate and filtered. After evaporation, the residue was purified by column chromatography and further purified by recrystallization to afford the desired product as white powder in a pure form (482 mg, 70%). m.p.: 260–263 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27–1.33 (m, 24H), 2.80–2.88 (m, 16H), 3.84 (s, 12H), 6.89 (d, J = 8.9 Hz, 8H), 7.38 (s, 8H), 7.46–7.52 (m, 16H), 7.62 (d, J = 8.4 Hz, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.6, 14.7, 27.1, 55.3, 86.8, 87.3, 91.0, 93.3, 94.3, 106.4, 114.0, 115.4, 121.3, 121.5, 123.2, 124.8, 131.3, 131.4, 131.5, 132.4, 132.9, 143.2, 143.4, 159.6; Anal. Calcd for $C_{116}H_{92}O_4Si$: C, 88.29;



Scheme 3. Synthesis of TETS 9–11.

H, 5.88. Found: C, 88.36; H, 5.66. EI-MS *m/z* (%): 389 (($M^+ - 28$)/4 + 2, 30), 388 (($M^+ - 28$)/4 + 1, 100). IR (KBr): $\nu = 3437$, 2961, 2156, 1598, 1507, 1243, 833, 614 cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} 353 nm (1.998×10^5 L $\text{mol}^{-1}\text{cm}^{-1}$).

TETS 7–10 were prepared according to the similar procedure, their synthetic details can be found in Supplementary data.

2.2.2. Tets 7

361 mg, 85%, m.p.: 128–131 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 12H), 7.16–7.25 (m, 8H), 7.40–7.44 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 85.8, 106.6, 121.8, 128.1, 129.5, 130.3, 133.0, 137.9. EI-MS *m/z* (%): 489 ($M^+ + 1$, 40), 488(M^+, 100), 473 ($M^+ - 15$, 44). IR (KBr): $\nu = 3422$, 3030, 2918, 2155, 1590, 1480, 1382, 1265, 1163, 926, 777, 654, 453 cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} 269 nm (1.219×10^5 L mol^{-1} cm^{-1}).

2.2.3. Tets 8

260 mg, 61%, m.p.: 212–215 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (s, 12H), 6.88 (d, $J = 8.9$ Hz, 8H), 7.10 (d, $J = 3.8$ Hz, 4H), 7.32 (d, $J = 3.8$ Hz, 4H), 7.46 (d, $J = 8.9$ Hz, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.3, 80.8, 90.1, 94.9, 99.6, 114.1, 114.4, 122.2, 127.2, 131.1, 133.1, 134.7, 160.1; Anal. Calcd for $C_{60}H_{36}O_4S_4Si$: C, 73.74; H, 3.71. Found: C, 73.67; H, 3.49. EI-MS *m/z* (%): 976 (M^+, 5), 275 (($M^+ - 28$)/4 + K^+, 100). IR (KBr): $\nu = 3423$, 2923, 2144, 1793, 1602, 1516, 1248, 1171, 1029, 779, 557 cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} 350 nm (1.676×10^5 L mol^{-1} cm^{-1}).

2.2.4. Tets 9

194 mg, 65%, m.p.: 282–284 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.20–7.21 (m, 4H), 7.51 (d, $J = 3.6$ Hz, 4H), 7.57–7.62 (m, 16H), 7.77 (d, $J = 5.0$ Hz, 4H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 82.9, 83.0, 84.6, 92.3, 121.4, 122.0, 122.3, 127.9, 129.4, 131.3, 132.0, 133.1; Anal. Calcd for $C_{56}H_{28}S_4Si$: C, 78.47; H, 3.29. Found: C, 78.76; H, 2.94. EI-MS *m/z* (%): 857 (M^+, 5), 856 ($M^+ - 1$, 18), 208 (($M^+ - 28$)/4 + 1, 100). IR (KBr): $\nu = 3401$, 2159, 1522, 1490, 1416, 1383, 844, 703, 590 cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} 326 nm (2.160×10^5 L mol^{-1} cm^{-1}).

2.2.5. Tets 10

246 mg, 45%, m.p.: 290–293 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (s, 4H), 7.00 (d, $J = 8.5$ Hz, 8H), 7.19–7.21 (m, 8H), 7.29–7.34 (m, 40H), 7.45 (d, $J = 8.0$ Hz, 8H), 7.57 (d, $J = 8.0$ Hz, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 87.3, 89.4, 92.2, 106.3, 120.7, 121.3, 124.5, 127.3, 127.6, 127.7, 128.2, 128.7, 129.5, 130.3, 131.2, 131.3, 132.4, 137.8, 140.0, 143.1, 143.7; Anal. Calcd for $C_{120}H_{76}Si$: C, 93.23; H, 4.96. Found: C, 93.30; H, 5.30. EI-MS *m/z* (%): 381

$((M^+ - 28)/4 + 2, 20)$, 380 $((M^+ - 28)/4 + 1, 100)$. IR (KBr): $\nu = 3425$, 3022, 2158, 1595, 1504, 1437, 1383, 835, 694, 546 cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} 352 nm (2.210×10^5 L mol^{-1} cm^{-1}).

2.3. Photoactivated insecticidal activity

Photoactivated insecticidal activity was determined as described previously [14–16]. The test insects were the 4th-instar larvae of *A. albopictus* (Skuse) which were obtained from a laboratory colony maintained in Guangdong Center for Disease Control and Prevention, Guangzhou, China. Each compound was dissolved and serially diluted with acetone. Each serial solution (0.4 mL) was added to a beaker containing 20 mL of dechlorinated water, and then 30 larvae were transferred into the beaker. Two sets of experiments were performed for each compound, one of which was for ultraviolet-treated trials, and another was held in the dark throughout the trials. After 3-h incubation in a dark room, the ultraviolet-treated groups were irradiated for 1.5 h, receiving 2074 $\mu W/cm^2$ under a light source emitting 300–400 nm with a maximum at 365 nm, and then returned to darkness for 24-h incubation. The average mortality of three replications at each concentration was calculated, and the LC_{50} value, which was defined as the concentration causing 50% mortality, was determined. All the experiments were conducted at least two times with three replicates in each case.

3. Results and discussion

At 100 mg L^{-1}, the mortality of 4th-instar larvae of *A. albopictus* (Skuse) in the light treatments was shown in Table 1, only three TETS 3, 8, 9 and α-terthienyl showed potent toxicity (100%), larvicidal activities of other eight TETS were very low ($\leqslant$38%) even at so high concentration (100 mg L^{-1}). Unsubstituted TETS 3 gave a good insecticidal activity, when methoxy group was introduced at the terminal phenyl ring, the toxicities of TETS 4–6 were very low comparable to that of TETS 3, which indicated that the attaching of electron donor substituent (methoxy group) did not promote insecticidal activity. Similarly, when phenyleneethynylenes were substituted by diphenylethenyl terminal [17], the toxicity of TETS 10 was also very low. While the lower toxicity of longer TETS 11 revealed enhancement of the conjugated system could not increase the corresponding insecticidal activity. Notably, shorter TETS 1, 2, 7 gave no insecticidal activity.

To gain further insight into the three TETS 3, 8, 9 and α-terthienyl with potent toxicity, their photoactivated insecticidal activities were discussed in detail (see Table 2). The LC_{50} values of active compounds 3, 8, 9 and α-terthienyl under UV light were 5.2665, 0.1346, 5.4277 and 0.0843 mg L^{-1}, respectively, while in the dark, those of TETS 3, 8, 9 and α-terthienyl were 9.6266, 9.3667, 52.9240 and 31.3566 mg L^{-1}, respectively, so the irradiation-generated enhancement in the activities of TETS 3, 8, 9 was more than 1.82, 69.58, 9.75-fold, respectively, TETS 8 exhibited the excellent photoactivated insecticidal activity. When four thiophene rings were attached on the same slicon atom with the triple bond, the photoactivated insecticidal activity was increased significantly.

Table 1
Toxicities of TETS 1–11 and α-terthienyl to 4th-instar larvae of *Aedes albopictus* (Skuse) at 100 mg L^{-1} in the light treatment.

Compound	Mortality ± SD (%)
1	0.0000 ± 0.0000
2	0.0000 ± 0.0000
3	100.0000 ± 0.0000
4	32.0000 ± 1.5275
5	38.0000 ± 1.7321
6	9.6000 ± 0.5508
7	0.0000 ± 0.0000
8	100.0000 ± 0.0000
9	100.0000 ± 0.0000
10	10.0000 ± 0.8386
11	28.0000 ± 0.6429
α-terthienyl	100.0000 ± 0.0000

Table 2
Photoactivated insecticidal activities of active compounds 3, 8, 9 and α-terthienyl to 4th-instar larvae of *Aedes albopictus* (Skuse).

Compound	LC_{50} ± SD (mg L^{-1})
Light	
3	5.2665 ± 0.0017
8	0.1346 ± 0.0069
9	5.4277 ± 0.0079
α-terthienyl	0.0843 ± 0.0038
Dark	
3	9.6266 ± 0.0603
8	9.3667 ± 0.7552
9	52.9240 ± 8.0585
α-terthienyl	31.3566 ± 0.5009

Because the light-dependent toxicity results from photooxidation of various substrates leading to membrane damage, enzyme inactivation, cell death, and other biological function losses, it could be predicted that weeds, bacteria, fungi, nematodes, and other organisms would also be sensitive to these compounds in the presence of light due to their common targets [14]. Prolonging illumination time can always improve the phototoxicity of photosensitizer, we can presume that the photolarvicidal effect of these active compounds would be more potent when applied in open field conditions [18,19].

4. Conclusions

A series of TETS have been successfully synthesized in moderated yields, and their photoactivated insecticidal activities against the 4th-instar larvae of *A. albopictus* (Skuse) were determined. TETS 3, 8, 9 exhibited higher activities. When four thiophene rings were attached on the same silicon atom with the triple bond, TETS 8 displayed the highest photoactivated insecticidal activity. The relationship analysis between structure and activity showed the thiophene ring played a very important role, which is a promising strategy in the search for new photoactivated insecticide leads.

5. Abbreviations

TETS	tetraethynylsilanes
NMR	nuclear magnetic resonance
SD	standard deviation
LC_{50}	median inhibitory concentration

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jphotobiol.2009.11.003.

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