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A strategy for the preparation of cyclic polyarenes based on single electron transfer-promoted photocyclization reactions

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Abstract Single electron transfer (SET)-promoted photocyclization reactions of substrates comprised of benzylsilane tethered to phthalimides were subjected to an exploratory study in order to probe a new approach for the preparation of cyclic polyarenes. The results show that UV irradiation of the substrates leads to efficient photochemical reactions that are initiated by SET from benzylsilane moieties to the excited phthalimide acceptor. Ensuing desilylation reactions of the benzylsilane cation radical moieties in the intermediate zwitterionic biradicals and proton transfer gives biradical precursors of the cyclic polyarene products. The observations made in this effort suggests that SET photochemical methods, which have been employed earlier to generate cyclic poly-ethers, -thioethers and -amides, serve as a useful method to access potentially interesting macrocyclic targets.

Keywords SET photochemistry · Cyclic polyarenes · Benzylsilanes · Phthalimides

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Introduction

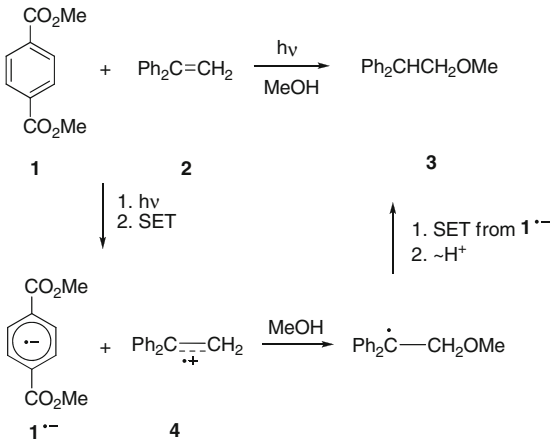
Outside the areas of electrochemistry and electron impact mass spectrometry, little was known prior to the early 1970s about the operation and implications of single electron transfer (SET) in ground or excited state reactions of organic substances. Several significant observations were made during the decade that had a major impact on understanding the rates of SET and the role in governing the nature of organic chemical reactions. The key earlier work by Marcus [1], which defined the energetic requirements of SET, led to studies by Rehm and Weller [2], which demonstrated the relationship that exists between the free energies and rate constants for excited state SET. The Rehm–Weller formulation, arising from studies of fluorescence quenching rates, served as the foundation for understanding what at that time was a unique and rarely encountered phenomenon in organic photochemistry. More importantly, the effort gave photochemists the ability to predict when SET processes would occur with rates that are competitive with those of other excited state decay pathways. Particularly important in this regard are what have become to be known as the Weller equations (Eq. 1), a set of relationships that interrelate the redox ($E_{1/2}(+)$ and $E_{1/2}(-)$) and excited state ($E_{0,0}$) properties of electron donors and acceptors to the free energies (ΔG^{o}_{SET}) and then the activation free energies ($\Delta G^{\ddagger}_{SET}$) and rate constants ($k_{SET}$) for excited state SET (Eqs. 2 and 3). Thus, by using these equations, one was now easily able to determine the free energy change (ΔG^{o}_{SET}) for an intermolecular SET process occurring, for example, between an electron donor having a known oxidation potential ($E_{1/2}(+)$) and an excited state acceptor with a known reduction potential ($E_{1/2}(-)$) and excited state energy ($E_{0,0}$). Importantly, the Weller equations showed that when ΔG^{o}_{SET} is negative for SET in an excited state donor–acceptor pair the rate constant for SET (k_{SET}) approaches the diffusion controlled limit (ca. $1 \times 10^{9}\ M^{-1}\ s^{-1}$), a value which is in the regime of typical excited state decay processes, including intersystem crossing, radiationless decay, light emission and chemical reactions. Thus, in cases where ΔG^{o}_{SET} is negative, SET-promoted pathways that proceed through ion radical intermediates would take place efficiently in photochemical processes.

$$\Delta G^{o}_{SET} = E_{1/2}(+) - E_{1/2}(-) - E_{0,0} + AE_{Coulombic} \quad (1)$$

$$\Delta G^{\ddagger}_{SET} = (\Delta G^{o}_{SET}/2) + ((\Delta G^{o}_{SET}/2) + (\Delta G^{\ddagger}(0))^{2})^{1/2} \quad (2)$$

$$k_{SET} = k_{o}\exp - (\Delta G^{\ddagger}_{SET}/\ RT) \quad (3)$$

Another equally important observation that contributed significantly to this area was made by Arnold and his coworkers [3] in the early 1970s. It was only about a decade earlier that organic chemists began to understand the mechanistic basis of organic photochemical reactions that take place directly from excited state species. Examples of this are found in the important investigations carried out by Zimmerman and his coworkers [4], which led to formulations of organic chemical (arrow pushing) mechanisms for interesting photochemical processes, like the cross-conjugated cyclohexadienone and di-π-methane rearrangements.

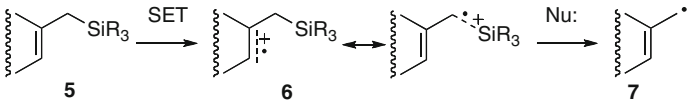


Scheme 1

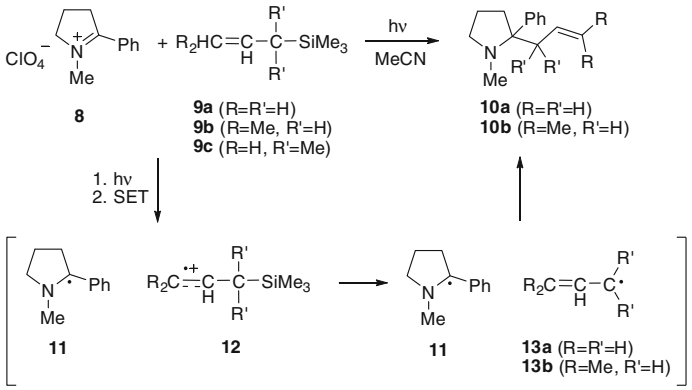
The key observation made by Arnold arose in a study of the methyl *p*-acetylbenzoate (**1**) sensitized photoreaction of 1,1-diphenylethene (**2**, Scheme 1), where the ether **3** is generated when methanol is used as solvent. This and other observations led Arnold and his coworkers to propose that an SET pathway is followed in this process, in which the excited state of **1** serves as the SET acceptor and the alkene as the electron donor and, in addition, that a key step in product formation is nucleophilic capture of the cation radical intermediate **4** by methanol [3].

The results of Arnold's seminal studies suggested that a new family of excited state reactions could be designed by taking into account the rates of SET and the chemical properties of ion radicals. Thus, shortly after that time, several research groups initiated efforts to discover new photochemical reactions that are driven by excited state SET with the hope that these processes would add to the growing repertoire of reactions that could be used to prepare organic substances. In the early 1980s, independently and nearly simultaneously groups headed by Mizuno [5, 6] and Mariano [7, 8] recognized that SET-promoted photochemical reactions, in which allyl and benzyl silanes participate as electron donors, might serve as both efficient and useful preparative methods. Both groups reasoned that in these processes, SET from the silicon-containing substrates **5** (Scheme 2) to excited state acceptors would be facilitated by the presence of electropositive trialkylsilyl groups that stabilize the forming cation radical intermediates **6**. In addition, this thermodynamic stabilization would be coupled to kinetic destabilization brought about by distribution of the charged radical center into the C–Si bond. As a consequence, the allyl- and benzyl-silane cation radicals would be subject to nucleophile-induced C–Si bond cleavage to generate the corresponding allylic and benzylic radicals **7**.

One of the first reported photochemical processes in which this pathway operates is found in the reports by Mariano et al. [7, 8] describing the photoaddition reactions of allylsilanes to 2-phenyl-1-pyrrolinium perchlorate (**8**) (Scheme 3). For example, these workers found that irradiation of **8** in an acetonitrile solution containing



Scheme 2



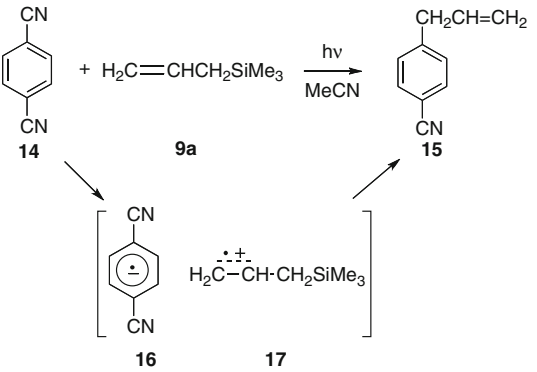
Scheme 3

trimethylallylsilane (**9a**) results in formation of the 2-allylpyrrolidine adduct **10a**. The proposed mechanistic pathway for this process involves initial SET from **9a** to the singlet excited state of **8**, giving the allylsilane cation radical **12** which then undergoes acetonitrile-promoted desilylation to generate the radical pair **11** + **13a**. Coupling of the radicals then provides adduct **10a**. This mechanistic proposal was consistent with the finding that photoaddition of the prenylsilanes **9b** and **9c** to pyrrolinium salt **10b** lead to generation of the same adduct **10b**, demonstrating that the same allyl radical intermediate **13b** was involved in both processes.

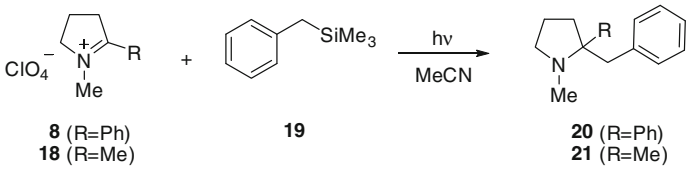
At nearly the same time, the group headed by Mizuno [5, 6] observed that allylsilanes participate in photoaddition reactions with electron-deficient cyano-arenes and -alkenes. One example arising from their earlier work is photoaddition of trimethylallysilane **9a** to 1,4-dicyanobenzene (**14**), which produces adduct **15** via pathway where initial SET generates the ion radical pair **16** + **17** (Scheme 4). Desilylation of the allylsilane cation radical followed by radical coupling and loss of HCN then forms **15**.

Benzylsilanes were also observed to participate as electron donors in photoinduced SET reaction pathways [5, 9, 10]. As with those derived from allylsilanes, benzylsilane cation radicals undergo nucleophile-promoted desilylation in processes that generate benzyl radicals. Examples of photochemical reactions that are driven by this chemical behavior are found in the photoadditions of trimethylbenzylsilane (**19**) to 2-methyl- and 2-phenyl-2-pyrrolinium perchlorates **8** and **18** that produce adducts **20** and **21** through routes that involve SET following excitation of either the pyrrolinium salt (for **8**) or benzylsilane (for **18**) (Scheme 5) [9, 10].

Since the time of these early studies, many new SET-promoted photochemical reactions have been discovered, some of which have been employed in the synthesis



Scheme 4



8 (R=Ph)
18 (R=Me)

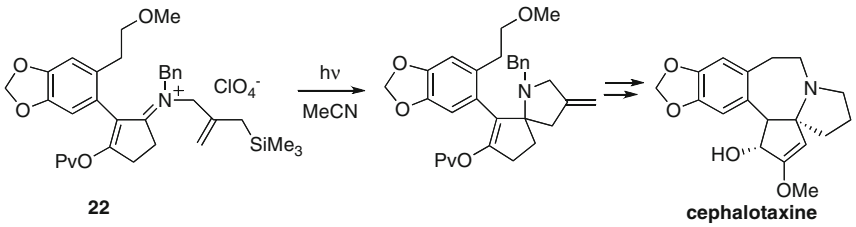
19

20 (R=Ph)
21 (R=Me)

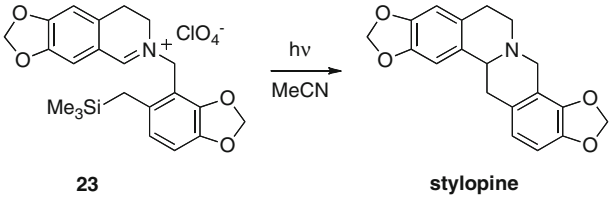
Scheme 5

of biologically important naturally occurring substances. Two examples of the preparatively useful SET photochemical processes involving allyl- and benzylsilanes are the photocyclization reaction of the *N*-allysilane containing iminium salt **22**, which serves as a cornerstone of a route for the synthesis of the harringtonine alkaloid cephalotaxine (Scheme 6) [11], and the photoinduced conversion of the *N*-benzyl-dihydroisoquinolinium salt **23**, the key final step in a concise sequence for the synthesis of the protoberberine alkaloid stylopine (Scheme 7) [12]. In addition, the role played by desilylation of cation radicals of many other silicone-containing electron donors, including α-silyl-ethers, -thioethers, -amine, -amides and -sulfonamides, in preparatively useful SET-promoted photochemical reactions has been demonstrated [13–16]. A specific example that can be used to point out the preparative potential of SET photochemical processes of this type is the photomacrocyclization reaction of the phthalimide **24**, containing a polyether tethered trimethylsilyl ether group (Scheme 8) [17]. In this system, excitation of the phthalimide acceptor chromophore is followed by chain-assisted SET to form the intermediate zwitterionic biradical **26**, which following methanol-induced desilylation and proton transfer produces the biradical intermediate **27** that couple to generate the macrocyclic polyether **25**. Despite the complexity of this system and the great distance that exists between the reactive centers, the macrocyclic polyether (crown ether) containing product is generated in a quite acceptable 53% yield.

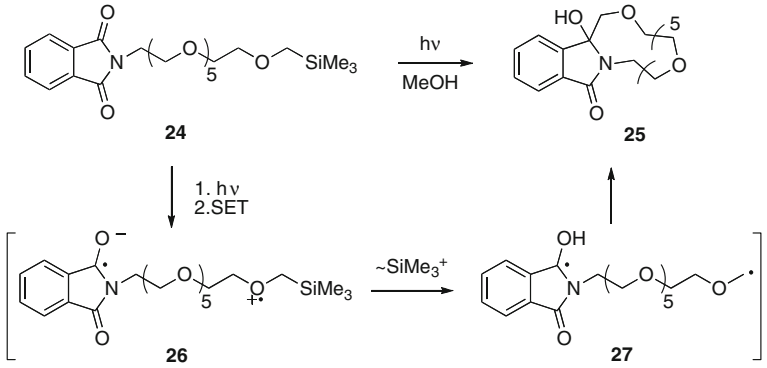
The results obtained from previous mechanistic and synthetic investigations of the SET photochemistry of α-silyl substituted electron donors have recently encouraged us to explore reactions of new types of donor–acceptor systems that



Scheme 6



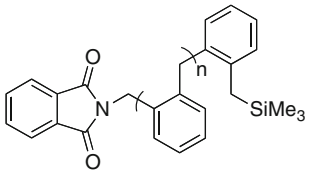
Scheme 7



Scheme 8

serve as useful synthetic methods for the preparation of novel macrocyclic substances [18, 19]. Among a number of α-silyl electron donor candidates that can be employed in SET-promoted photocyclization reactions, benzylsilanes would be an interesting group owing to the fact that the processes would generate macrocyclic polyarenes. As stated above, earlier studies demonstrated that, as a consequence of their low oxidation potentials ($E_{1/2}(+)$ = ca. + 1.6 V), benzylsilanes [20] would participate (e.q., k_{SET} ca. 1×10^{10} M^{-1} s^{-1}) as electron donors with excited states of electron acceptors like phthalimides ($E^{S1}_{1/2}(-)$ = ca. + 2.3 V, $E^{T1}_{1/2}(-)$ = ca. + 1.6 V) [21–23] that have appropriate reduction potentials. In addition, desilylation of benzyl silane radical cations should take place rapidly to form benzyl radicals that can undergo C–C bond forming reactions.

In order to probe the synthetic potential of the SET-promoted photochemical reactions of systems comprised of benzylsilanes tethered to electron acceptors, we



28 (n = 0)
29 (n = 1)
30 (n = 2)

Scheme 9

have prepared and investigated the phthalimide derivatives **28–30** shown in Scheme 9. The results of this effort are described below.

Experimental

General procedures

^{1}H- and ^{13}C-NMR (200 MHz) spectra were recorded on $CDCl_3$ solutions and chemical shifts are reported in parts per million relative to $CHCl_3$ peak (7.24 ppm for ^{1}H-NMR and 77.0 ppm for ^{13}C-NMR) as an internal standard. Preparative photochemical reactions were conducted with an apparatus consisting of a 450-W Hanovia medium vapor pressure mercury lamp surrounded by a Pyrex glass filter in a water-cooled quartz immersion well surrounded by the solution being irradiated. The photolysis solutions were purged with nitrogen before and during irradiations. The photolysates were concentrated under reduced pressure giving residues, which were subjected to silica gel column chromatography. High resolution (HRMS) mass spectra were obtained by use of electron impact ionization unless otherwise noted. All starting materials used in the photoreactions derived from commercial sources. All new compounds described were isolated as oils in >90% purity (by NMR analysis) unless noted otherwise.

2-(2′-Bromobenzyloxy)tetrahydropyran **34**

To a CH_2Cl_2 (80 mL) solution containing 3,4-dihydropyran (3.0 g, 35.7 mmol) and 2-bromobenzyl alcohol **33** (6.0 g, 32.1 mmol) was added *p*-TsOH (0.12 g, 0.7 mmol) at 0 °C. The solution was warmed to and stirred at room temperature for 2.5 h and then diluted with 5% K_2CO_3 and extracted with CH_2Cl_2. The organic layers were dried and concentrated in vacuo to give a residue that was subjected to column chromatography (CH_2Cl_2) to yield **34** (8.7 g, 100%) as a colorless oil: ^{1}H NMR ($CDCl_3$) 1.52–1.94 (6H, m), 3.54–3.61 (1H, m), 3.89–3.97 (1H, m), 4.58 (1H, d, $J = 13.5$ Hz), 4.74–4.80 (1H, m), 4.83 (1H, d, $J = 13.2$ Hz), 7.12–7.17 (1H, m), 7.32 (1H, t, $J = 7.4$ Hz) and 7.53 (2H, m); ^{13}C NMR ($CDCl_3$) 19.9, 26.0, 31.1, 62.7, 69.1, 98.9, 123.3, 127.9, 129.3, 129.6, 133.0, 138.3; HRMS (FAB) *m/z* 271.0305 (M^++H, $C_{12}H_{16}BrO_2$ requires 271.0334).

2-((Tetrahydropyranyl)oxymethyl)phenyl boronic acid **35**

To a solution of anhydrous THF (80 mL) containing **34** (4.5 g, 16.6 mmol) was added 2.5 M *n*-BuLi (8.0 mL, 20.0 mmol) at −78 °C. After stirring for 30 min at −78 °C. $B(OMe)_3$ (5.6 mL, 49.8 mmol) was added dropwise and the mixture was warmed to and stirred at room temperature for 1 h. After addition of 80 mL of H_2O, the solution was extracted with diethyl ether. The ether layer was dried and concentrated in vacuo to give a residue that was subjected to column chromatography (EtOAc: hexane 1:2) to yield **35** (2.1 g, 53%) as a white crystalline solid: ^{1}H NMR ($CDCl_3$) 1.86–1.56 (6H, m), 3.57–3.54 (1H, m), 3.91–3.88 (1H, m), 5.14 (3H, s), 6.91 (1H, b), 7.40–7.35 (3H, m), 7.52–7.47 (1H, m) and 7.81–7.79 (1H, m); ^{13}C NMR ($CDCl_3$) 20.32, 26.02, 31.27, 63.58, 71.86, 95.38, 121.71, 127.84, 131.26, 131.67 and 154.09.

2-(Trimethylsilylmethyl)benzyl bromide **36**

To a solution of anhydrous ether (50 mL) containing PPh_3 (11.3 g, 43.1 mmol) and CBr_4 (14.3 g, 43.1 mmol) was added the known [10] 2-(trimethylsilylmethyl)benzyl alcohol **(32)** (7.0 g, 36.0 mmol) at 0 °C. The solution was stirred for 24 h at room temperature followed by filtration. The filtrate was concentrated in vacuo giving a residue that was subjected to column chromatography (hexane) to yield **36** (7.45 g, 80%) as a colorless oil: ^{1}H NMR ($CDCl_3$) 0.04 (9H, s), 2.28 (2H, s), 4.49 (2H, s) and 7.01–7.33 (4H, m); ^{13}C NMR ($CDCl_3$) −0.8, 24.0, 33.6, 125.4, 129.4, 130.4, 131.2, 134.6, 140.5; HRMS (FAB) *m/z* 256.0285 (M^+, $C_{11}H_{17}BrSi$ requires 256.0283).

2-(*o*-(Silylmethyl)benzyl)benzyloxy tetrahydropyran **37**

To a solution of toluene (15 mL) containing boronic acid **35** (0.9 g, 3.81 mmol) and benzyl bromide **36** (1.0 g, 3.97 mmol) were added 1 M aq. Na_2CO_3 (4.8 mL) and tetrakis(triphenylphosphine)palladium (0) (300 mg, 6.8 mol%). After 4 h stirring at 80 °C, the mixture was cooled to room temperature and filtered. The filtrate was extracted with diethyl ether. The ether extract was dried and concentrated in vacuo to give a residue that was subjected to column chromatography (diethyl ether: hexane 1:15) to yield **37** (0.77 g, 57%) as a yellow oil: ^{1}H NMR ($CDCl_3$) 0.04 (9H, s), 1.48–1.92 (6H, m), 2.12 (2H, s), 3.50–3.57 (1H, m), 3.86–3.3.94 (1H, m), 4.00 (2H, s), 4.52 and 4.82 (2H, two d, $J = 12.3$ *Hz*), 4.71 (1H, t, $J = 3.4$ *Hz*), 6.84–7.48 (8H, m); ^{13}C NMR ($CDCl_3$) δ −1.0, 19.6, 23.7, 25.7, 30.8, 36.0, 62.3, 67.38, 98.1, 124.5, 126.3, 126.4, 128.2, 129.2, 129.3, 129.8, 130.0, 136.6, 136.8, 139.3, 139.4; HRMS (FAB) *m/z* 369.2252 (M^++H, $C_{23}H_{33}O_2Si$ requires 369.2250).

2-(2′-(Trimethylsilylmethyl)benzyl)benzyl alcohol **38**

To a solution of MeOH (10 mL) containing **37** (0.2 g, 0.54 mmol) was added *p*-toluenesulfonic acid (10 mg, 0.06 mmol) at room temperature. After stirring for 2 h, the mixture was extracted with aq. $NaHCO_3$ and diethyl ether. The organic

layer was dried and concentrated in vacuo to give a residue that was subjected to column chromatography (diethyl ether:hexane 1:15) to yield **38** (0.15 g, 100%) as a colorless oil: ^{1}H NMR ($CDCl_3$) 0.06 (9H, s), 2.14 (2H, s), 4.01 (2H, s), 4.68 (2H, b) and 6.80–7.46 (8H, m); ^{13}C NMR ($CDCl_3$) −0.6, 24.2, 36.5, 64.0, 125.0, 126.8, 127.3, 128.8, 128.8, 129.9, 130.1, 130.7, 137.2, 139.2, 139.5, 139.89; HRMS (EI) *m/z* 284.1596 (M^+, $C_{18}H_{24}OSi$ requires 284.1596).

2-(2′-(Trimethylsilylmethyl)benzyl)benzyl bromide **39**

To a solution of anhydrous ether (40 mL) containing triphenylphosphine (1.67 g, 6.37 mmol) and CBr_4 (2.11 g, 6.36 mmol) was added **38** (1.51 g, 5.31 mmol). The solution was stirred for 2 h at room temperature and filtered. Concentration of the filtrate in vacuo gave a residue that was subjected to column chromatography (hexane) to yield **39** (1.52 g, 83%) as a yellowish oil: ^{1}H NMR ($CDCl_3$) 0.10 (9H, s), 2.17 (2H, s), 4.11 (2H, s), 4.55 (2H, s) and 6.91–7.43 (8H, m); ^{13}C NMR ($CDCl_3$) −0.6, 24.2, 32.8, 36.4, 125.1, 127.0, 127.5, 129.9, 129.9, 130.5, 130.7, 131.1, 136.5, 136.5, 140.1, 140.3; HRMS (FAB) *m/z* 346.0750 (M^+, $C_{18}H_{23}BrSi$ requires 346.0752).

2-(2′-(2′-(Trimethylsilylmethyl)benzyl)benzyl)benzyl alcohol **41**

To a solution of toluene (20 mL) containing boronic acid **35** (0.92 g, 3.9 mmol) and benzyl bromide **39** (1.42 g, 4.09 mmol) were added 1 M aq. Na_2CO_3 (4.8 mL) and tetrakis(triphenylphosphine)-palladium(0) (310 mg, 6.9 mol%). The resulting solution was stirred for 4 h at 80 °C and filtered. The filtrate was extracted with diethyl ether, giving an ether layer that was dried and concentrated in vacuo to give a residue (1.5 g) containing coupled product **40**. To the residue were added MeOH (30 mL) and TsOH (100 mg, 0.6 mmol) and the resulting solution was stirred for 2 h at room temperature. The residue obtained by concentration of the solution in vacuo was extracted with aq. $NaHCO_3$ and diethyl ether. The ether extract was dried and concentrated in vacuo to give a final residue that was subjected to column chromatography (EtOAc : hexane 1:5) to yield **41** (1.14 g, 78%) as a yellowish oil: ^{1}H NMR ($CDCl_3$) −0.03 (9H, s), 2.04 (2H, s), 3.88 (2H, s), 4.04 (2H, s), 4.59 (2H, s), 6.86–7.44 (12H, m); ^{13}C NMR ($CDCl_3$) −0.7, 24.2, 36.1, 37.3, 64.0, 125.0, 126.8, 127.2, 127.3, 127.4, 128.7, 128.9, 129.9, 130.1, 130.2, 130.4, 130.5, 136.9, 138.7, 139.2, 139.5, 139.9; HRMS (FAB) *m/z* 397.1965 (M^++Na, $C_{25}H_{30}OSiNa$ requires 397.1964).

Benzylsilane linked phthalimides **28–30**

To solutions of anhydrous THF (50 mL) containing the benzyl alcohol **32** (0.8 g, 4.12 mmol), **38** (1.4 g, 4.92 mmol), and **41** (1.0 g, 2.67 mmol) were added phthalimide (0.73 g, 4.96 mmol for **32**, 0.87 g, 5.91 mmol for **38**, 0.47 g, 3.19 mmol for **41**) and diisopropyl azodicarboxylate (DIAD) (1.0 g, 4.95 mmol for **32**, 1.19 g, 5.88 mmol for **38**, 0.65 g, 3.21 mmol for **41**). The resulting solutions were stirred for 15 h at room temperature and concentrated in vacuo to give residues

that were subjected to column chromatography (diethyl ether:hexane 2:5 for **28**, EtOAc:hexane 1:2 for **29**, EtOAc:hexane 1:5 for **30**). The isolated substances were purified by recrystallization (hexane) to yield **28** (0.65 g, 70%), **29** (1.13 g, 55%) and **30** (0.58 g, 43%).

28: ^{1}H NMR ($CDCl_3$) 0.06 (9H, s), 2.39 (2H, s), 4.80 (2H, s), 6.98–7.23 (4H, m), 7.70–7.73 (2H, m), 7.82–7.87 (2H, m); ^{13}C NMR ($CDCl_3$) −1.5, 23.3, 39.4, 123.3, 124.4, 127.4, 128.5, 129.5, 132.1, 132.3, 134.0, 138.8, 168.3; HRMS (EI) *m/z* 323.1340 (M^+, $C_{19}H_{21}NO_2Si$ requires 323.1342).

29: ^{1}H NMR ($CDCl_3$) 0.10 (9H, s), 2.22 (2H, s), 4.18 (2H, s), 4.87 (2H, s), 6.73–7.42 (8H, m), 7.66–7.69 (2H, m), 7.79–7.82 (2H, m); ^{13}C NMR ($CDCl_3$) −0.6, 24.0, 37.0, 39.7, 123.8, 124.9, 126.5, 127.3, 128.6, 129.4, 129.6, 130.9, 132.6, 134.4, 135.2, 137.0, 138.9, 139.7, 168.6; HRMS (EI) *m/z* 413.1812 (M^+, $C_{26}H_{27}NO_2Si$ requires 413.1811).

30: ^{1}H NMR ($CDCl_3$) 0.02 (9H, s), 2.12 (2H, s), 3.97 (2H, s), 4.20 (2H, s), 4.82 (2H, s), 6.74–7.48 (12H, m), 7.63–7.68 (2H, m), 7.71–7.76 (2H, m); ^{13}C NMR ($CDCl_3$) −0.7, 24.2, 36.6, 37.1, 40.1, 123.8, 125.0, 126.7, 126.9, 127.4, 128.8, 129.3, 129.7, 129.8, 130.4, 130.6, 131.0, 132.6, 134.4, 135.3, 136.9, 138.6, 139.0, 139.5, 140.1, 168.5; HRMS (FAB) *m/z* 503.2279 (M^+, $C_{33}H_{33}NO_2Si$ requires 503.2281).

Photoreaction of phthalimide **28**

A nitrogen-purged solution of MeOH (200 mL) containing phthalimide **28** (250 mg, 0.77 mmol) was irradiated for 1 h by using Pyrex filtered light. The photolysate was concentrated in vacuo to give a residue that was subjected to extraction with diethyl ether. The organic extract was dried, concentrated in vacuo. The residue was recrystallized by using EtOAc to give **42** (40 mg, 0.159 mmol, 23%) as a white solid and the mother liquor was concentrated in vacuo to give a residue that was subjected to column chromatography ($CHCl_3$) to give **45** (110 mg, 72%), a known substance whose ^{1}H NMR spectroscopic properties closely match those previously reported [24].

42: ^{1}H NMR ($CDCl_3$) 2.89 and 3.51 (2H, two d, $J = 15.9$ *Hz*), 4.07 (1H, s), 4.33 and 5.02 (2H, two d, $J = 17.4$ *Hz*), 7.17–7.69 (8H, m); ^{13}C NMR ($CDCl_3$) δ 39.9, 40.1, 86.3, 122.3, 124.1, 127.1, 127.5, 127.7, 130.2, 130.3, 131.1, 131.2, 133.0, 148.6; HRMS (FAB) *m/z* 251.0928 (M^+, $C_{16}H_{13}NO_2$ requires 251.0946).

45: ^{1}H NMR ($CDCl_3$) 5.02 (2H, s), 6.38 (1H, s), 7.13–7.24 (4H, m), 7.47 (1H, t, $J = 7.2$ *Hz*), 7.55 (1H, t, $J = 7.2$ *Hz*), 7.69 (1H, d, $J = 7.8$ *Hz*) and 7.85 (1H, d, $J = 7.2$ *Hz*); ^{13}C NMR ($CDCl_3$) 43.5, 104.0, 120.8, 123.7, 127.3, 127.9, 128.5, 128.6, 129.8, 129.9, 130.8, 132.0, 134.5, 135.1, 166.7; HRMS (FAB) *m/z* 233.0839 (M^+, $C_{16}H_{11}NO$ requires 233.0841).

Photoreaction of phthalimide **29**

A solution of **29** (250 mg, 0.60 mmol) in MeOH (200 mL) was irradiated by using Pyrex filtered light for 1 h. The photolysate was concentrated in vacuo to give a residue that was extracted with CH_2Cl_2. The organic layer was dried, concentrated

in vacuo to give a white solid. The resulting solid was dissolved in MeOH and the solution was filtered. The filtrate was concentrated in vacuo to give a white solid **43** (170 mg, 92%): ^{1}H NMR ($CDCl_3$) 3.54 (1H, s), 3.49 and 4.75 (2H, two d, $J = 14.1$ *Hz*), 3.73 and 4.41 (2H, two d, $J = 13.8$ *Hz),* 4.06 and 4.14 (2H, two d, $J = 14.4$ *Hz*), 6.35 (1H, d, $J = 7.8$ *Hz*), 6.56–6.61 (1H, m), 6.89–6.94 (1H, m), 7.12–7.22 (2H, m), 7.38–7.44 (4H, m), 7.60–7.72 (2H, m), 7.84 (1H, d, $J = 7.2$ *Hz*); HRMS (FAB) *m/z* 342.1492 (M^++H, $C_{23}H_{20}NO_2$ requires 342.1494).

Photoreaction of phthalimide **30**

A solution of **30** (250 mg, 0.50 mmol) in MeOH (200 mL) was irradiated for 40 min by using Pyrex filtered light. The photolysate was concentrated in vacuo to give a residue that was extracted with CH_2Cl_2. The organic extract was dried and concentrated in vacuo to give a residue. The residue was dissolved in a minimum amount of $CHCl_3$ and then diluted with an excess of hexane to form a white solid. The solid was collected by filtration to yield **44** (90 mg, 42%): ^{1}H NMR ($CDCl_3$) 2.76 (1H, s), 2.96 and 3.58 (2H, two d, $J = 15.3$ *Hz*), 3.83 and 4.75 (2H, two d, $J = 15.6$ *Hz*), 4.01 and 4.96 (2H, two d, $J = 15.6$ *Hz*), 4.58 and 4.63 (2H, two d, $J = 15.2$ *Hz*), 6.64 (1H, d, $J = 7.5$ *Hz*), 6.96 (1H, t, $J = 7.2$ *Hz*) and 7.04–7.81 (14H, m); HRMS (FAB) *m/z* 432.1967 (M^++H, $C_{30}H_{26}NO_2$ requires 432.1964).

Dehydration reactions of **42–43** giving **45–46**

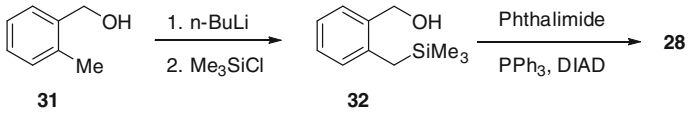
To acetonitrile solutions (15 mL) containing the cyclic amidols **42** (100 mg, 0.4 mmol) and **43** (100 mg, 0.29 mmol) was added *p*-toluenesulfonic acid (30 mg, 0.18 mmol) and the resulting solutions were stirred for 24 h at room temperature. The solutions were extracted with diethyl ether and aq. $NaHCO_3$. The ether layers were dried and concentrated in vacuo to give residues which were either subjected to column chromatography ($CHCl_3$) for the case in which **45** is formed (84 mg, 90%) or to recrystallization ($CHCl_3$) for the cases of **46** (95 mg, 100%). Enamide **45** was found to have ^{1}H NMR properties that closely match those previously reported [24].

46: ^{1}H NMR ($CDCl_3$) 3.70 and 4.48 (2H, two d, $J = 14.7$ *Hz*), 4.58 and 4.71 (2H, two d, $J = 14.7$ *Hz*), 6.78 (1H, s), 7.19–7.38 (7H, m), 7.44–7.49 (2H, m), 7.57–7.62 (1H, m), 7.79–7.84 (2H, m); ^{13}C NMR ($CDCl_3$) δ 39.1, 45.8, 105.2, 119.8, 123.6, 127.0, 127.4, 128.8, 128.9, 129.3, 129.6, 130.8, 131.2, 132.3, 132.4, 134.88, 136.0, 138.1, 138.3, 139.1, 140.6, 169.5; HRMS (FAB) *m/z* 323.1309 (M^+, $C_{23}H_{17}NO$ requires 323.1310).

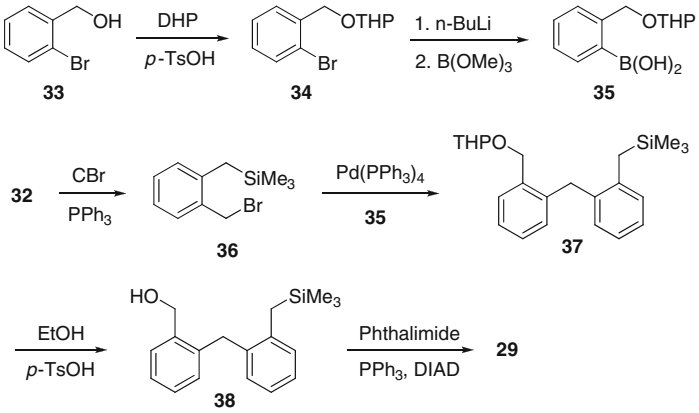
Results and discussion

Synthesis of trimethylsilylbenzyl tethered phthalimides **28–30**

The synthetic pathways utilized to prepare the phthalimide derivatives **28–30** were initiated by base-promoted introduction of the trimethylsilyl group at the benzylic



Scheme 10

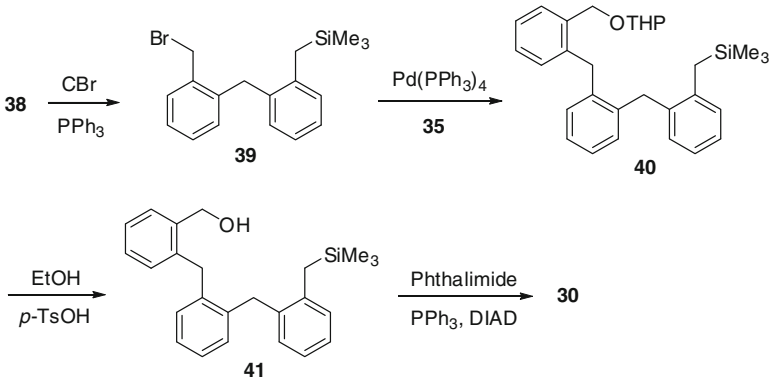


Scheme 11

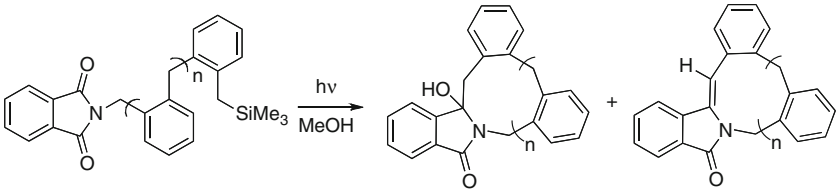
position of the *o*-methylbenzylalcohol **31** by utilizing the known procedure [12] (Scheme 10). The resulting alcohol **32** along with phthalimide were then coupled by using a Mitsunobu reaction, which resulted in formation of the mono-phenyl tethered phthalimide **28**. Preparation of the di- and tri-benzyl units needed to produce **29** and **30**, respectively, was initiated by formation of the THP protected boronic acid **35** starting with *o*-bromobenzyl alcohol (**33**) (Scheme 11) via the intermediate bromoarene **34**. Palladium-induced coupling of **35** with the benzylic bromide **36**, formed from the corresponding benzyl alcohol **32**, gave the diarylmethane adduct **37** which was subjected to alcohol deprotection furnishing **38**. Mitsunobu reaction between **38** and phthalimide gave rise to the bis-arene tethered phthalimide **29**. Finally, alcohol **38** was transformed into the corresponding bromide **39**, which underwent palladium coupling with boronic acid **35** to yield the tribenzyl intermediate **40** (Scheme 12). Alcohol deprotection of **40** gave benzylic alcohol **41**, which underwent Mitsunobo coupling with phthalimde to generate the tri-arene tethered phthalimide **30**.

Photoreactions of phthalimides **28–30**

Photoreactions of benzylsilane-tethered phthalimides **28–30** were carried out by irradiation (Pyrex, $\lambda > 290$ nm) of MeOH solutions of the substrates. Photoreaction of **28** carried out in this manner led to high yielding formation of the cyclic amidol **42** (23%) and enamide **45** (72%), the latter of which arises by dehydration of **42** (Scheme 13). Both of these substances have been described previously in



Scheme 12



28 (n = 0)
29 (n = 1)
30 (n = 2)

42 (n = 0, 23%)
43 (n = 1, 92%)
44 (n = 2, 42%)

45 (n = 0, 72%)
46 (n = 1, 0%)
47 (n = 2, 0%)

Scheme 13

Kanaoka's report on the photochemistry of *N*-2-methylbenzyl-phtalimides (see below) [24]. In contrast, the cyclic amidols **43**–**44** are formed as sole products in photoreactions of the respective bis- and tris-arene containing phthalimides **29** and **30**. The amidols **43** and **44** undergo quantitative conversion to enamides **46** and **47**, respectively, when treated with *p*-toluene sulfonic acid in MeCN.

Importantly, all spectroscopic data, including ^{1}H- and ^{13}C-NMR, and HRMS, were in full accord with the structures assigned to the photoproducts. An unusual feature of the ^{1}H NMR spectroscopic data for enamide **46** led us to gain additional information for its exact structural assignment. Specifically, the two sets of benzylic protons both appear as two sets of doublet with germinal coupling constants (3.70 and 4.48 ppm; 2H, two d, $J = 14.7$ *Hz*, 4.58 and 4.71; 2H, two d, $J = 14.7$ *Hz*) in this spectrum, suggesting that they are diastereotopically related. Although this phenomenon could be a consequence of restricted rotation about the benzylic C–C bonds in both the Z and E-stereoisomers of **46**, it was expected that the rotation would be more restricted in the latter isomer. However, that the stereochemistry of **46** is Z and not E was demonstrated by utilizing X-ray crystallographic analysis (Fig. 1).

A common mechanism is at work in the photocyclization reactions of the benzylsilane terminated phthalimide displayed in Scheme 14. In each case, sequential, methanol-promoted desilylation and proton transfer takes place on the

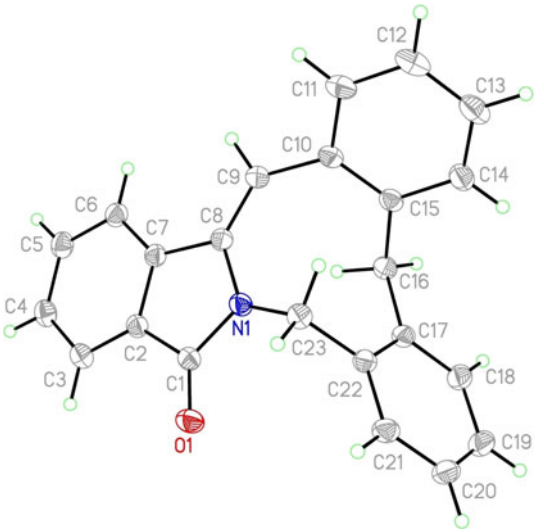
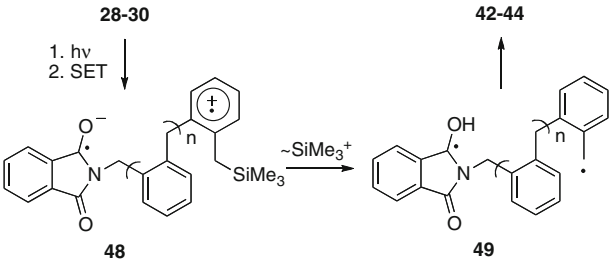


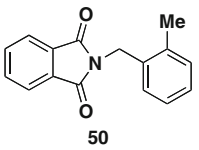
Fig. 1 Ortep plot of the X-ray crystallographic data of enamide **46**



Scheme 14

intermediate zwitterionic biradicals **48** (Scheme 14) that are formed by either direct or intervening arene ring assisted SET from the benzylsilane donor site to the electronically excited phthalimide. This process gives rise to biradicals **49**, which undergo cyclization to generate the cyclic amidol products. It should be noted that the oxidation potentials of dialkylbenzenes that mimic the central arene rings in **29** and **30** are sufficiently low ($E_{1/2}(+)$ ca. +2.4 V) [25] to make them reasonably efficient electron donors to the phthalimide singlet ($E^{S1}_{1/2}(-)$ = ca. + 2.3 V) excited states. As a result, the internal arene rings can also serve as electron donor sites that may facilitate long-range SET and the formation of the reactive zwitterionic biradical intermediates.

It is interesting to compare the photocyclization reaction of the benzyltrimethylsilane containing substrate **28** to its analog **50** (Scheme 15) that lacks the trimethylsilyl group. Indeed, analog **50** is known to participate in a related sequential SET–proton transfer pathway that results in formation of the biradical intermediate **49** ($n = 0$). Kanaoka and his coworkers observed that irradiation of **50**



50

Scheme 15

in acetonitrile solutions promotes production of the cyclic amidol **42** as the exclusive product but in only 18% yield. This yield contrasts dramatically with that observed for the phtocyclization reaction of **28**, which produces the same amidol **42** and derived enamide **45** in a combined yield of 95%.

Conclusion

Although preliminary, the results of the investigation described above show that the SET photochemistry of benzylsilane terminated, arene-linked phthalimides serves as a key step in routes for the preparation of cyclic polyarenes. Thus, similar to the conclusions made in earlier studies of poly-donor-linked, silylmethyl ether terminated phthalimide systems, in reactions of the arene linked substrates, SET from the internal arene donor site(s) may facilitate long-range SET required to form the reactive benzylsilane cation radical center. This mechanistic feature as well as preparative applications of the process will be goals of our continuing investigations in this area.

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