NIR chromophores from small acetylenic building blocks: a Diels–Alder approach to octaalkynylphthalocyanines

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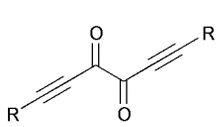
Two new routes to cross-conjugated 3,4-dimethylenehexa-1,5-diynes, both starting from dialkynyl 1,2-diones, have been devised. Whereas triisopropylsilyl-protected diketones could be diolefinated in a bis-Wittig reaction with methylenetriphenylphosphorane, their aryl-terminated congeners had to be subjected to the conditions of the Peterson olefination (trimethylsilylmethylmagnesium chloride and subsequent dehydration of the resulting diol with thionyl chloride). The reactivity of the diethynylbutadienes towards standard dienophiles was found to be low and alternative thermal reactions compete with [4 + 2] cycloadditions. However, dicyanoacetylene was shown to be an effective cycloaddition partner leading, after aromatisation, to the corresponding dicyanodiethynylbenzenes. These were cyclotetramerised with magnesium butanolate in butanol to furnish octaalkynylphthalocyanines, thereby completing a concise, three-step synthesis of these NIR chromophores of relevance to photodynamic forms of therapy.

Introduction

Organic chromophores with sizable absorptions and/or emissions at the far red end of the visible spectrum or beyond continue to play important roles as functional components in areas as diverse as laser printing, optical displays and a range of medicinal applications.[1,2] An intriguing example of the potential of near infrared (NIR) chromophores is the utilisation of selected members of this class of compounds as photosensitiser in the photodynamic treatment of various forms of cancers (photodynamic tumour therapy, PDT).[3–7] Some of the key requirements for efficient PDT agents are their accessibility by external light when embedded in organic tissue and their solubility in cellular fluids. In general, appropriately substituted nitrogen-containing macrocycles based on porphyrin[8] or phthalocyanine[9] backbones are invoked to address these points.

We are currently developing synthetic strategies for the rapid assembly of NIR chromophores from small acetylenic building blocks. In addition to the advantageous brevity and flexibility of such a modular approach, the resulting chromophores will benefit from peripheral acetylene substitution in their optical properties (bathochromically and hyperchromically shifted absorptions relative to non-acetylenic analogues) as well as in terms of their solubility, which is governed by functionalities at the acetylene termini. Acetylenic NIR chromophores should therefore be interesting candidates to be explored for their suitability as PDT agents.

We have previously devised two complementary routes to two such acetylenic building blocks, namely to the hexa-1,5-diyne-3,4-diones **1**[10,11] and to the corresponding dimiines **2**[12] and have



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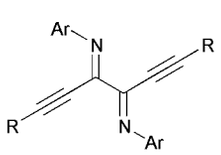

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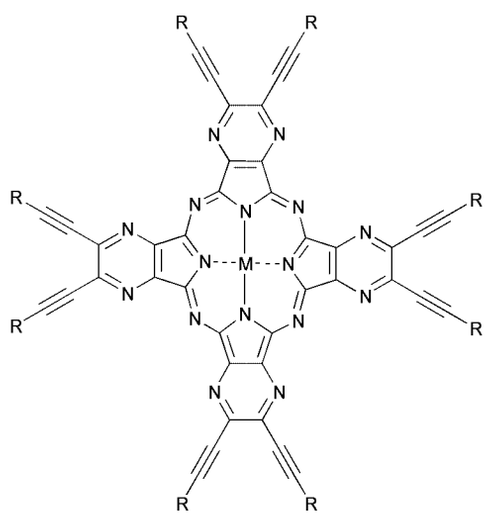
demonstrated the feasibility of our modular approach to NIR chromophores by converting the former building block into phthalocyanine-related octaalkynyltetrapyrazinoporphyrazines



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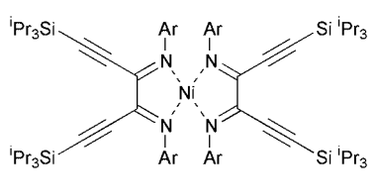

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3[13] and the latter into the highly absorbent nickel(0) dialkynyldiazabutadiene complex **4**.[14] In an effort to further extend this concept, we have now targeted the hydrocarbon π-system 3,4-dimethylenehexa-1,5-diyne **5**[15] as a third acetylenic building block in this series. The buta-1,3-diene substructure of **5** can be envisioned to participate in [4 + 2] cycloaddition reactions and can therefore aid in the construction of macrocyclic (NIR) chromophores with peripheral acetylene substitution. For example, the Diels–Alder reaction of **5** with dicyanoacetylene will furnish, after aromatization, the corresponding dicyanobenzenes, from which phthalocyanine derivatives like **6** are readily available. We disclose herein two new syntheses for

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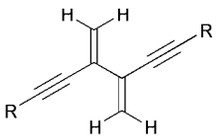
previously inaccessible derivatives of **5** and their transformation to octaalkynylphthalocyanines **6** by a novel Diels–Alder strategy with dicyanoacetylene.



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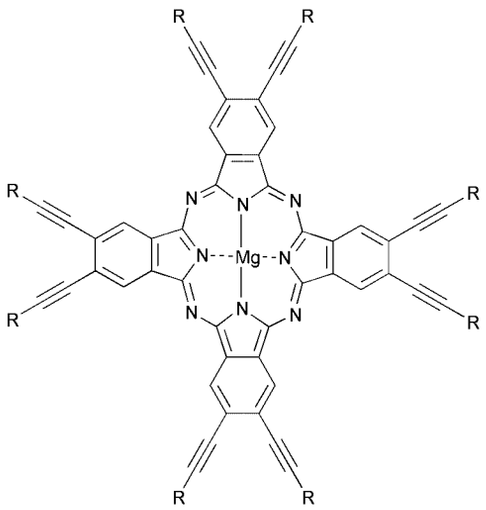

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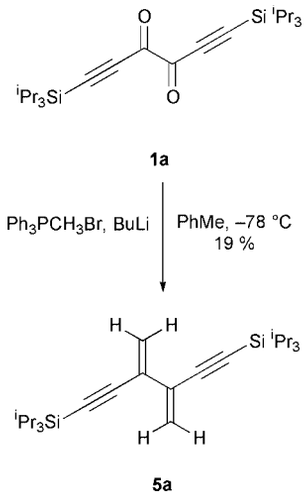
Results and discussion

The first members of the family of 3,4-dimethylenehexa-1,5-diynes **5** have previously been prepared by Hopf *et al.*[15] After some ill-fated attempts, it was found that a nickel-mediated coupling of selected magnesium acetylides to 2,3-dichlorobuta-1,3-diene furnished the desired target molecules. However, the procedure was found to be suitable only for the preparation of derivatives of **5** bearing simple alkyl or trimethylsilyl substituents at the acetylene termini. These substituents leave the reactive cross-conjugated π-system of **5** relatively unprotected, rendering the compounds vulnerable to polymerisation at room temperature. The authors specifically point out that more versatile aryl or more protective triisopropylsilyl substituents could not be incorporated into the backbone of **5** along this route, which instead leads to the corresponding butadiynes *via* oxidative acetylene coupling.[15] Since aryl substituents are particularly well-suited to modify the solubility of acetylenic chromophores we set out to explore synthetic alternatives to substituted dimethylenehexadiynes.

A conceptually different strategy to obtain the 3,4-dimethylenehexa-1,5-diynes could conveniently start from the acetylenic 1,2-diones **1** which we have recently made available in a single step by the copper-mediated alkynylation of oxalyl chloride[11] and which, in principle, should be amenable to diolefination. However, from the outset a transformation of this kind was deemed to be difficult in the light of the problems encountered in attempts to diolefinate simple aliphatic or aromatic diketones.[16,17] Benzil, for example, a non-acetylenic relative of **1b** and **1c**, could only be converted to 2,3-diphenylbuta-1,3-diene in 15% yield by the reaction with methylenetriphenylphosphorane.[16] It is therefore not surprising that our attempts to obtain hydrocarbons **5** from acetylenic diones using a standard bis-Wittig protocol were blessed with mixed success. The aryl-terminated alkynyl diketones **1b** and **1c**, for example, decomposed upon treatment with methylenetriphenylphosphorane in THF, and although all the starting material was consumed, no product could be isolated. The more robust triisopropylsilyl-protected acetylenic 1,2-diketone **1a**, on the other hand, did react at −78 °C in THF with the phosphorus ylide to give the desired product **5a**, but the yield of only 19% after chromatographic purification is in the same disappointingly low region as that reported for the analogous conversion of benzil (Scheme 1).



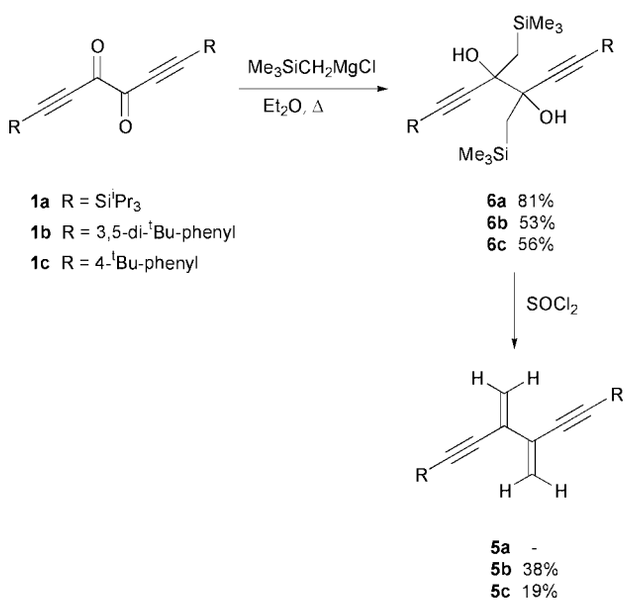
1a

Ph_3PCH_3Br, BuLi | PhMe, –78 °C, 19 %

5a

Scheme 1

While the successful preparation of **5a** is encouraging and gives access to a previously inaccessible derivative of this class of compounds, the bis-Wittig methodology is clearly not suitable for the synthesis of aryl-terminated dimethylenehexadiynes. We have therefore explored the Peterson olefination reaction[18] as an alternative route. Thus, treating the acetylenic diones **1a–c** with two equivalents of trimethylsilylmethylmagnesium chloride in refluxing Et_2O furnished the bis-ethynyl diols **6a–c** in 53–81% yield (Scheme 2). Surprisingly, all



1a R = Si^iPr_3
1b R = 3,5-di-^{t}Bu-phenyl
1c R = 4-^{t}Bu-phenyl

6a 81%
6b 53%
6c 56%

5a -
5b 38%
5c 19%

Scheme 2

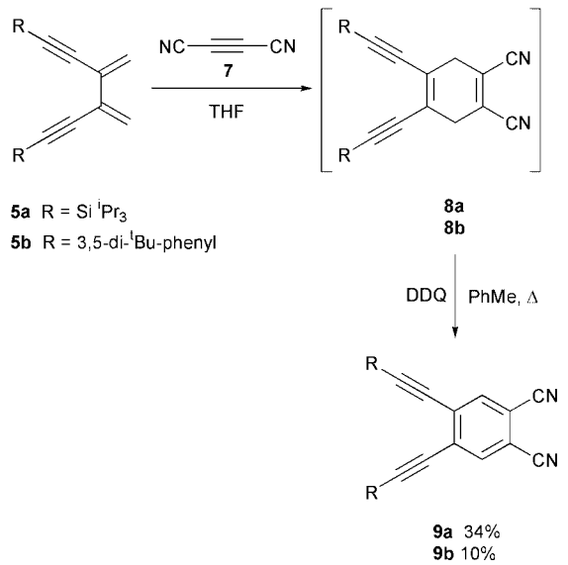
attempts to generate the CC double bonds by the formal two-fold elimination of hydroxymethylsilanes from the isolated diols **6a–c** using potassium hydride,[18] sulfuric acid,[18] or butyllithium followed by methylsulfonyl chloride[19] failed. However, and most gratifyingly, the CC double bonds of **5** could be established in a one-pot procedure by treating the alkoxide intermediates formed in the preparation of the diols **6a–c** with thionyl chloride.[18] The desired aryl dimethylenehexadiynes **5b** and **5c**, were isolated in 20% yield. The mesylate-assisted elimination to form **5a**, on the other hand, was sluggish leaving a pale

yellow oil after column chromatography that, in addition to **5a**, contained significant amounts of unidentified by-products. It therefore appears that the two methods presented here for the preparation of dimethylenehexadiynes are complementary to one another, with the Wittig reaction suitable for the triisopropylsilyl-protected derivative, and the Peterson olefination for aryl-terminated representatives.

Compounds **5** were obtained either as colourless solids (**5a**, **5c**) or as a pale yellow oil (**5b**). All the derivatives rapidly turn yellow upon exposure to air, with **5a** being the most stable and **5b** being the most sensitive compound. The modest yields in the above transformations, while not at all unexpected in the light of previous work and the marked sensitivity of the material, are perhaps partially compensated by the short overall synthetic sequence and the ready availability of the starting materials. Numerous efforts to further improve the outcome of the diolefination of the acetylenic 1,2-diones **1** failed. In addition to broad variations of the reaction parameters for the above procedures, none of the titanium-based olefination protocols using either the Petasis reagent $Cp_2Ti{=}CH_2$ (prepared *in situ* from Cp_2TiMe_2 in PhMe at 60 °C)[20] or a heterogeneous mixture of $TiCl_4$–Zn–CH_2Br_2 at room temperature in CH_2Cl_2[21,22] proved to be successful.

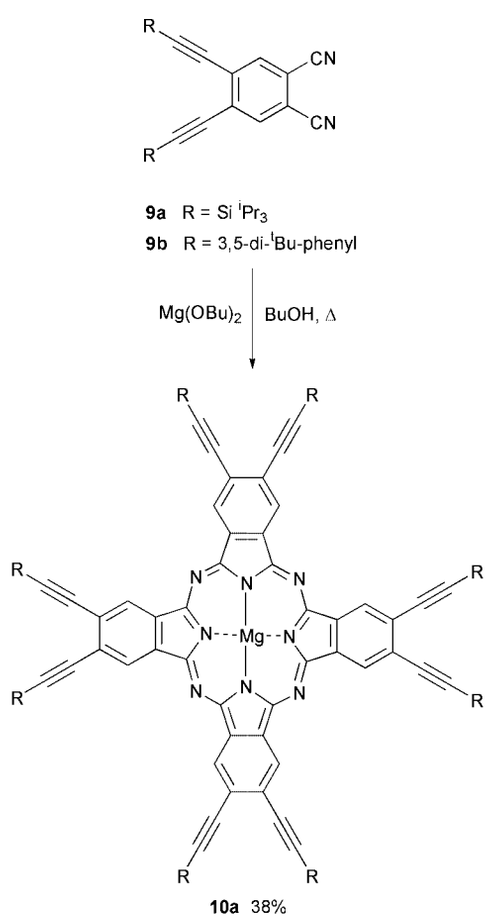
With the new 3,4-dimethylenehexa-1,5-diynes in hand, we explored their behaviour in [4 + 2] cycloaddition reactions. Much to our surprise and apparently unlike the aliphatic analogues previously prepared by Hopf *et al.*,[15] compounds **5a**–**c** turned out to be rather unreactive diene components in Diels–Alder reactions. Unfortunately, the reluctance of these compounds to take part in cycloadditions is accompanied by a marked thermal instability and by the formation of dimeric cyclooctadiene side products *via* radical routes[15] so that the use of more forcing reaction conditions is not a viable option. For example, **5c** did not react with three equivalents of dimethyl maleate in $CDCl_3$ at room temperature for 18 hours. When the mixture was heated to 60 °C **5c** decomposed within 3 hours and no cycloaddition product was detectable by ^{1}H NMR spectroscopy. Likewise, no cyclisation was observed with **5a** in the presence of either five equivalents of dimethyl acetylenedicarboxylate (toluene, reflux) or 15 equivalents of dimethyl maleate (toluene, 90 °C, 8 h). This behaviour is in marked contrast to the reported reactivity of trimethylsilyl-protected 3,4-dimethylenehexa-1,5-diene[15] in which case the reaction with identical dienophiles furnished the corresponding cyclohexene adducts in yields exceeding 40%. We suspect that the more bulky substituents at the termini of the acetylenes in **5a**–**c** render the adoption of a planar s-*cis* conformation in these compounds more difficult, thereby favouring alternative thermal pathways and polymerisation. However, by exposing **5a** in refluxing THF for 8 h or **5b** in THF for 62 h at room temperature to excess dicyanoacetylene **7**,[23,24] touted as one of the most reactive acetylenic dienophiles, we were able to isolate the corresponding cycloaddition products (Scheme 3). Again, dimerisation and polymerisation were clearly observed in both cases, despite the addition of traces of hydroquinone. The yields of isolated products are only moderate, but an increase of reaction temperature or time, or the use of Lewis acids (*e.g.* BCl_3), or conducting the reaction in 5 M ethereal lithium perchlorate solution[25] had no beneficial influence on the outcome of the experiments. Although the isolation of the 1,2-dicyano-4,5-diethynylcyclohexadienes **8** is possible, they show a pronounced tendency to aromatise in the presence of air and were best directly converted to dicyanobenzenes **9a**,**b** by treatment of the crude product of the cycloaddition reaction with DDQ in toluene.

The successful cycloaddition of dimethylenehexadiynes and dicyanoacetylene has opened up a new route to substituted dicyanobenzenes which are well established precursors for various metallated and metal-free phthalocyanine derivatives.[26] Indeed, 1,2-dicyano-4,5-diethynylbenzenes have previously been



Scheme 3

converted into octaalkynylphthalocyanines, although with different peripheral substituents.[27,28] The cyclotetramerisation of **9a** and **9b** to the corresponding phthalocyanine derivatives **10a** and **10b** proceeded smoothly by refluxing the former with magnesium butanolate in butanol and furnished the macrocycles as dark green solids in yields of 38 and 17%, respectively (Scheme 4). Noteworthy is the ease with which the two phthalocyanines



Scheme 4

can be purified and handled. Owing to the bulkiness of the substituted aryl and the triisopropylsilyl substituents, the compounds show little tendency to aggregate and are quite

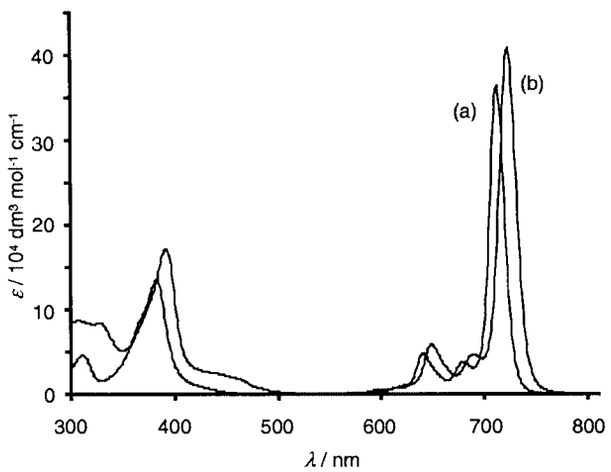


Fig. 1 UV–Vis–NIR spectrum of (a) **10a** and (b) **10b** in THF at room temperature.

soluble in common nonpolar organic solvents, properties which facilitate their purification by column and gel permeation chromatography.

The most remarkable feature in the electronic absorption spectra of the octaalkynylphthalocyanines (Fig. 1) is their high intensity, long wavelength absorption at 713 (**10a**) and 723 nm (**10b**), respectively. The slightly bathochromically shifted absorptions of the latter indicate that fine-tuning of the spectral properties of the octaalkynylphthalocyanines by peripheral substituents is a valid possibility. Shape and intensity (ε = 372600 for **10a** and ε = 421400 dm^3 mol^{-1} cm^{-1} for **10b**) of these so-called Q-bands are characteristic for non-aggregated phthalocyanines. The bands are hyper- and bathochromically shifted compared to those of the corresponding octaalkynyltetrapyrazinoporphyrazines (*e.g.* λ_{max} = 674 nm, ε = 314600 M^{-1} l^{-1} for the octaazaanalogue of **10a**).[13] Since penetration of light through organic tissue increases with increasing wavelength,[3] the bathochromically shifted absorptions of acetylenic phthalocyanines renders them promising candidates for PDT applications and work is currently in progress to identify suitable prototypes.

Conclusion

In this work we have provided a new route to octaalkynylphthalocyanines, a class of compounds of significant interest *inter alia* in the field of photodynamic cancer therapy. The cornerstones of our approach are two new ways of preparing previously inaccessible 3,4-dimethylenehexa-1,5-diynes from dialkynyl 1,2-diones. The transformation of these buta-1,3-dienes into octaalkynylphthalocyanines was effected by a Diels–Alder [4 + 2] cycloaddition of the former with dicyanoacetylene, followed by aromatisation and cyclotetramerisation of the resulting dicyanobenzenes. While the sensitivity and the reactivity of the acetylenic dienes necessitate a compromise on yields, the overall synthetic sequence to the target chromophores is with three steps remarkably concise and does not suffer from problems arising from the presence of regioisomeric mixtures.

Experimental

^{1}H NMR spectra were recorded in $CDCl_3$ or THF–$CDCl_3$ on Bruker AMX400 and Bruker DRX500 spectrometers and are reported as follows: chemical shift, δ (ppm) [number of protons, multiplicity, coupling constant J (Hz) and assignment]. Residual protic solvent $CHCl_3$ (δ_H = 7.24 ppm) was used as the internal reference. ^{13}C NMR spectra were recorded on the same spectrometers operating at frequencies of 100.5 MHz and 126 MHz, respectively, using the central signal of $CDCl_3$ (δ_C = 77.0 ppm) as reference. Infrared spectra were recorded on Perkin Elmer 1600 FT-IR and Shimadzu 8700 FT-IR spectrometers. Mass spectra were obtained on a VG ZAB-SE (EI, FAB), a Micromass Quattro-LC (APCI) or a Fisons VG TOF Spectrometer (MALDI-TOF) using *trans*-indole-3-acrylic acid as matrix. UV–Vis–NIR spectra were recorded on a Perkin-Elmer Lambda 40. Melting points were determined on a Reichert hotstage or with the help of an electrothermal melting point apparatus (open capillaries) and are uncorrected. Elemental analyses were obtained on a Perkin-Elmer 2400 CHN analyser. Flash column chromatography was carried out under positive pressure from a compressed air line using Merck Kieselgel (230–400 mesh) unless otherwise indicated. Analytical thin layer chromatography was performed using precoated aluminium-backed plates (Merck Kieselgel 60 F254) and visualised by UV light, basic potassium permanganate solution or 50% sulfuric acid. Gel permeation chromatography (GPC) was performed on a polystyrene resin crosslinked with 1% divinylbenzene (Bio-beads 1-SX®, Bio-Rad), pre-swollen in THF. Reactions were carried out under argon in oven-dried glassware. Solvents were purified according to standard procedures[29] and were freshly distilled prior to use. The synthetic procedure for **1a** has been previously described,[11] and those for the new derivatives **1b** and **1c** are given below. 4-*tert*-Butylphenylacetylene[30] has been obtained from 4-*tert*-butylstyrene[31] and 3,5-di-*tert*-butylphenylacetylene was prepared according to ref. 32. All other reagents are available from commercial suppliers and were used as received.

1,6-Bis(3,5-di-*tert*-butylphenyl)hexa-1,5-diyne-3,4-dione 1b

Compound **1b** was prepared as for **1c** (see below). The crude product was filtered through a pad of silica (CH_2Cl_2) and recrystallised from EtOAc yielding **1b** (1.77g, 49%) as yellow needles: mp 182 °C (from EtOAc, decomp.) (Found: C, 84.5; H, 8.9. $C_{34}H_{42}O_2$ requires C, 84.6; H, 8.8%); λ_{max}(CH_2Cl_2)/nm 253 (ε/dm^3 mol^{-1} cm^{-1} 24600) and 344 (23900); ν_{max}($CHCl_3$/cm^{-1}) 3012, 2971, 2187, 1663, 1226 and 1046; δ_H (400 MHz; $CDCl_3$) 1.3 (36H, s, C(CH$_3$)$_3$), 7.5 (4H, d, J 1.8, aromatic CH), 7.6 (2H, t, J 1.8, aromatic CH); δ_C (100.5 MHz; $CDCl_3$) 31.2, 34.9, 85.4, 102.0, 118.2, 126.6, 128.2, 151.5, 173.0; *m/z* (EI, 70 eV) 482 (M$^+$, 2.5%), 241 (M$^+$/2, 100).

1,6-Bis(4-*tert*-butylphenyl)hexa-1,5-diyne-3,4-dione 1c

To a cooled (0 °C) solution of 4-*tert*-butylphenylacetylene (2.63 g, 16.6 mmol) in THF (20 ml) was added BuLi (10.4 ml of a 1.6 M solution in hexane, 16.6 mmol). The solution was stirred for 10 min and then transferred *via* cannula into a cooled (0 °C) solution of CuBr (2.39 g, 16.6 mmol) and LiBr (2.89 g, 33.3 mmol) in THF (100 ml). The resulting yellow suspension was stirred for 15 min at that temperature before a precooled (0 °C) solution of oxalyl chloride (0.96 g, 7.6 mmol) in THF (20 ml) was added dropwise. Stirring was continued for an additional 10 min and the reaction was hydrolysed by the addition of saturated aqueous ammonium chloride (80 ml) and 1 M HCl (20 ml). The layers were separated and the aqueous layer was extracted with Et_2O (100 ml). The combined organic layers were dried over $MgSO_4$ and the solvents were evaporated to leave a brown oil. This was filtered through a pad of silica (Et_2O) furnishing the crude product as a brown solid. Recrystallisation from EtOH yielded **1c** (1.56g, 56%) as yellow needles: mp 142–143 °C (from EtOH) (Found: C, 84.6; H, 7.0. $C_{26}H_{26}O_2$ requires C, 84.3; H, 7.0%); λ_{max}(CH_2Cl_2)/nm 255 (ε/dm^3 mol^{-1} cm^{-1} 20200) and 338 (19400); ν_{max}($CHCl_3$/cm^{-1}) 3031, 2972, 2190, 1664 and 1210; δ_H (400 MHz; $CDCl_3$) 1.3 (18H, s, C(CH$_3$)$_3$), 7.5 (4H, d, J 8.5, aromatic CH), 7.6 (4H, d, J 8.5, aromatic CH); δ_C (100.5 MHz; $CDCl_3$) 31.0, 35.2, 86.2, 100.8, 116.1, 125.9, 133.8, 155.8, 172.7; *m/z* (EI, 70 eV) 370 (M$^+$, 0.4%), 185 (M$^+$/2, 100).

1,6-Bis(triisopropylsilyl)-3,4-bis(trimethylsilylmethyl)hexa-1,5-diyne-3,4-diol 6a

To a refluxing solution of diketone **1a**[11] (500 mg, 1.2 mmol) in Et_2O (10 ml) was added dropwise over 5 min Me_3SiCH_2MgCl (2.6 ml of a 1.0 M solution in Et_2O, 2.6 mmol). Heating under reflux was continued for 1 h. The mixture was cooled to room temperature and quenched by the addition of saturated aqueous ammonium chloride solution (25 ml). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 25 ml). The combined organic layers were dried ($MgSO_4$) and the solvent evaporated *in vacuo* to leave a pale yellow oil, which was purified by flash chromatography (5% EtOAc in hexanes), yielding diol **6a** as a mixture of diastereomers. Diastereomer A: (282 mg, 39%) pale yellow oil, diastereomer B (301 mg, 42%) white solid: mp 92–93 mp °C (from pentane); ν_{max}($CHCl_3$/cm^{-1}) 3439, 2943, 2166, 1464, 1246, 997 and 847; δ_H (400 MHz; $CDCl_3$) diastereomer A: 0.1 (18H, s, $Si(CH_3)_3$), 1.1 (42H, s, $Si(CH(CH_3)_2)_3$), 1.1–1.3 (4H, br m, CH_2), 2.5 (2H, s, OH); diastereomer B: 0.1 (18H, s, $Si(CH_3)_3$), 1.1 (42H, s, $Si(CH(CH_3)_2)_3$), 1.2 (2H, d, *J* 14.5, CH_aH$_b$), 1.4 (2H, d, *J* 14.5, CH$_a$$H_b$), 2.5 (2H, s, OH); δ_C (100.5 MHz; $CDCl_3$) diastereomer A: 0.2, 11.2, 18.7, 77.6, 87.0, 110.1 (the CH_2 carbon was not observed); diastereomer B: 0.2, 11.2, 18.6, 26.1 (br), 78.5, 87.1, 108.7; *m*/*z* (FAB) 617.4018 ($C_{32}H_{66}O_2Si_4Na$ requires 617.4038; *m*/*z* (APCI$^+$) 617.5 ([M + Na]$^+$, 100%).

1,6-Bis(3,5-di-*tert*-butylphenyl)-3,4-bis(trimethylsilylmethyl)-hexa-1,5-diyne-3,4-diol 6b

Diol **6b** was prepared starting from **1b** using the procedure described for **6a**. The crude brown oil obtained was purified by flash chromatography (CH_2Cl_2–hexanes 1 : 1) yielding **6b** (288 mg, 53%) as a white solid (only one diastereoisomer observed): mp 138–141 °C (from hexanes) (Found: C, 76.5; H, 10.3. $C_{42}H_{66}O_2Si_2$ requires C, 76.5; H, 10.1%); ν_{max}(KBr/cm^{-1}) 3523, 2964, 2193, 1591, 1246, 1032, 876 and 704; δ_H (400 MHz; $CDCl_3$) 0.2 (18H, s, $Si(CH_3)_3$), 1.3 (36H, s, $C(CH_3)_3$), 1.4 (2H, d, *J* 14.5, CH_aH$_b$), 1.5 (2H, d, *J* 14.5, CH$_a$$H_b$), 2.7 (2H, s, OH), 7.3 (4H, d, *J* 1.8, aromatic CH), 7.4 (2H, t, *J* 1.8, aromatic CH); δ_C (100.5 MHz; $CDCl_3$) 0.2, 25.5 (br), 31.3, 34.7, 78.5, 87.2, 89.3, 121.6, 122.9, 125.8, 150.8; *m*/*z* (EI, 70 eV) 658 (M$^+$, 2.5%), 329 (M$^+$/2, 14.7), 239 (M$^+$/2 − $Si(CH_3)_3OH$, 100).

3,4-Bis(trimethylsilylmethyl)-1,6-bis(4-*tert*-butylphenyl)hexa-1,5-diyne-3,4-diol 6c

Diol **6c** was prepared starting from **1c** using the procedure described for **6a**. The crude brown solid obtained was purified by flash chromatography (15% EtOAc in hexanes) yielding **6c** (255 mg, 56%) as a white solid (only one diastereomer observed): mp 172–175 °C (from Et_2O–hexanes) (Found: C, 74.65; H, 9.2. $C_{34}H_{50}O_2Si_2$ requires C, 74.7; H, 9.2%); ν_{max}-($CHCl_3$/cm^{-1}) 3553, 3017, 2968, 2222, 1505, 1365, 1249, 1018 and 838; δ_H (400 MHz; $CDCl_3$) 0.2 (18H, s, $Si(CH_3)_3$), 1.3 (18H, s, $C(CH_3)_3$), 1.3 (2H, d, *J* 14.6, CH_aH$_b$), 1.4 (2H, d, *J* 14.4, CH$_a$$H_b$), 2.6 (2H, s, OH), 7.3 (8H, m, aromatic CH); δ_C (100.5 MHz; $CDCl_3$) 0.2, 25.3 (br), 31.1, 34.8, 78.3, 86.2, 89.9, 119.6, 125.3, 131.3, 151.7; *m*/*z* (EI, 70 eV) 546 (M$^+$, 6.7%), 273 (M$^+$/2, 35.9), 183 (M$^+$/2 − $Si(CH_3)_3OH$, 100).

1,6-Bis(triisopropylsilyl)-3,4-dimethylenehexa-1,5-diyne 5a

To a cooled (0 °C) suspension of methyltriphenylphosphonium bromide (1.03 g, 2.87 mmol) in THF (40 ml) was added BuLi (1.79 ml of a 1.6 M solution in hexanes, 2.87 mmol). The reaction was stirred for 45 min at room temperature. The resulting orange solution was cooled to −78 °C and a solution of diketone **1a** (600 mg, 1.4 mmol) in THF (6 ml) was added dropwise. The mixture was stirred for an additional 30 min at this temperature until the TLC control indicated that all the starting material had been consumed. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (50 ml) and extracted with hexanes (50 ml). The layers were separated, the organic layer was dried ($MgSO_4$) and the solvents were evaporated *in vacuo* leaving a dark brown oil which was subjected to flash chromatography (hexanes) yielding **5a** (110 mg, 19%) as a white solid. The compound turns yellow upon exposure to air: mp 50–52 °C (from hexanes) (Found: C, 74.8; H, 11.2. $C_{26}H_{46}Si_2$ requires C, 75.3; H, 11.2%); λ_{max}(CH_2Cl_2)/nm 229 (ε/dm^3 mol^{-1} cm^{-1} 15700) and 247 (19800); ν_{max}(KBr/cm^{-1}) 2943, 2864, 2156, 1462, 1167, 993, 950, 907, 881 and 664; δ_H (400 MHz; $CDCl_3$) 1.1 (42H, s, $Si(CH(CH_3)_2)_3$), 5.7 (2H, s, CH_aH$_b$), 6.1 (2H, s, CH$_a$$H_b$); δ_C (100.5 MHz; $CDCl_3$) 11.2, 18.6, 94.2, 103.2, 125.1, 129.0; *m*/*z* (EI, 70 eV) 414 (M$^+$, 13.4%), 371 (M$^+$ − C_3H_7, 86.1), 329 (M$^+$ − C_6H_{13}, 100).

1,6-Bis(3,5-di-*tert*-butylphenyl)-3,4-dimethylenehexa-1,5-diyne 5b

To a refluxing solution of diketone **1b** (800 mg, 1.66 mmol) in Et_2O (20 ml) was added dropwise over 5 min Me_3SiCH_2MgCl (3.32 ml of a 1.0 M solution in Et_2O, 3.32 mmol). Heating was continued for 1 h. The reaction mixture was cooled to 0 °C and thionyl chloride (0.24 ml, 3.32 mmol) was added *via* syringe. After stirring at this temperature for 1 h the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (40 ml) and extracted with Et_2O (40 ml). The organic extract was washed with water (40 ml) and brine (40 ml), dried ($MgSO_4$) and the solvent was evaporated *in vacuo* to leave a brown oil. This was subjected to flash chromatography (10% CH_2Cl_2 in hexane) yielding compound **5b** (300 mg, 38%) as a yellowish oil which was prone to polymerisation upon exposure to air and upon heating: λ_{max}(CH_2Cl_2)/nm 260 (ε/dm^3 mol^{-1} cm^{-1} 21600), 273 (22100), 288 (20200) and 332sh (7200); ν_{max}($CHCl_3$/cm^{-1}) 3007, 2904, 2870, 2208, 1589, 1477, 1367, 1250, 1142, 907 and 877; δ_H (400 MHz; $CDCl_3$) 1.3 (36H, s, $C(CH_3)_3$), 5.9 (2H, s, CH_aH$_b$), 6.2 (2H, s, CH$_a$$H_b$), 7.37 (4H, d, *J* 1.9, aromatic CH), 7.43 (2H, t, *J* 1.8, aromatic CH); δ_C (100.5 MHz; $CDCl_3$) 31.3, 34.8, 84.7, 93.6, 121.8, 123.0, 124.3, 125.8, 129.0, 150.9; *m*/*z* (FAB) 479.3660 (MH$^+$), $C_{36}H_{47}$ requires 479.3678; *m*/*z* (EI, 70 eV) 478 (M$^+$, 51.20%), 219 (100), 147 (100).

1,6-Bis(4-*tert*-butylphenyl)-3,4-dimethylenehexa-1,5-diyne 5c

Diene **5c** was prepared starting from **1c** using the procedure described for **5b**. Removal of the solvents left a brown oil which was filtered through a pad of silica (washed with 150 ml of hexanes) to furnish a yellow solid. This was washed with a small amount of hexanes to give pure **5c** (113 mg, 19%) as a white solid. The compound turns yellow upon exposure to air and polymerizes upon heating above 130 °C. λ_{max}(CH_2Cl_2)/nm 261 (ε/dm^3 mol^{-1} cm^{-1} 66600), 276 (72300), 291 (62100) and 336 (3000); ν_{max}($CHCl_3$/cm^{-1}) 3011, 2965, 2210, 1504, 1364, 1268, 1104, 906 and 837; δ_H (400 MHz; $CDCl_3$) 1.3 (18H, s, $C(CH_3)_3$), 5.8 (2H, s, CH_aH$_b$), 6.2 (2H, s, CH$_a$$H_b$), 7.3 (4H, d, *J* 8.4, aromatic CH), 7.4 (4H, d, *J* 8.4, aromatic CH); δ_C (100.5 MHz; $CDCl_3$) 31.1, 34.8, 85.2, 92.6, 119.8, 124.1, 125.4, 128.9, 131.3, 151.8; *m*/*z* (FAB) 367.2417 (MH$^+$), $C_{28}H_{31}$ requires 367.2426; *m*/*z* (EI, 70 eV) 366 (M$^+$, 84.2%), 351 (M$^+$ − CH_3, 100).

Dicyanoacetylene 7[23,24]

A three-neck flask, fitted with a mechanical stirrer and a glass tube leading to a cold trap (−78 °C) was charged with tetrahydrothiophene 1,1-dioxide (70 ml, previously dried by distillation from phosphorus pentaoxide) and phosphorus pentaoxide (17 g, 0.06 mol). The apparatus was thoroughly flushed with argon before a homogeneous suspension of acetylenedicarboxamide (5 g, 0.045 mol) in tetrahydrothiophene 1,1-dioxide (25 ml) was added dropwise under vigorous stirring

over 30 min at 110 °C and a pressure of *ca.* 12 Torr. After the addition was complete, the temperature was raised to 120 °C and the mixture stirred for another 15 min. During this period, **7** condensed in the cold trap as colourless needles (*ca.* 2.0 g). The material turns black within a few minutes upon exposure to air but was stable for weeks when stored in an atmosphere of argon at −20 °C. δ_C (100.5 MHz; $CDCl_3$) 55.1, 103.1.

4,5-Bis(triisopropylsilylethynyl)phthalonitrile 9a

A solution of diene **5a** (260 mg, 0.628 mmol), dicyanoacetylene **7**[23,24] (190 mg, 2.50 mmol) and hydroquinone (15 mg) in THF (5 ml) was heated under reflux. After 5 h another two equivalents of dicyanoacetylene (95 mg, 1.26 mmol) were added. After 8 h, TLC control indicated that all the starting material had been consumed. The solvent was evaporated *in vacuo* and the dark brown residue taken up in toluene (5 ml). DDQ (712 mg 3.14 mmol) was added and the solution was heated under reflux for 24 h. The solvent was evaporated and the residue subjected to flash chromatography (CH_2Cl_2–hexanes 1:1) yielding **9a** (105 mg, 34%) as a white solid: mp 117–118 °C (from pentane) (Found: C, 73.6; H, 9.25; N, 5.8. $C_{30}H_{44}N_2Si_2$ requires C, 73.7; H, 9.1; N, 5.7%); $\lambda_{max}(CH_2Cl_2)$/nm 230sh (ε/dm^3 mol^{-1} cm^{-1} 15700), 254sh (32800), 268 (52600), 311 (20300) and 339sh (5500); $\nu_{max}(CHCl_3/cm^{-1})$ 2949, 2864, 2235, 1581, 1464, 1254, 1069, 997, 883 and 833; δ_H (400 MHz; $CDCl_3$) 1.1 (42H, s, $Si(CH(CH_3)_2)_3$), 7.8 (2H, s, aromatic CH); δ_C (126 MHz; $CDCl_3$) 11.2, 18.6, 102.0, 104.5, 114.0, 114.5, 130.4, 138.0; *m*/*z* (EI, 70 eV) 488 (M^+, 4.0%), 445 ($M^+ - C_3H_7$, 80.6), 403 ($M^+ - C_6H_{13}$, 100).

4,5-Bis(3,5-di-*tert*-butylphenylethynyl)phthalonitrile 9b

Phthalonitrile **9b** was prepared starting from **5b** using a procedure analogous to that described for **9a**. The reaction time in THF was 62 h at room temperature. The dark brown oil obtained was subjected to flash chromatography (CH_2Cl_2–hexanes 1:1) yielding **9b** (30 mg, 10%) as a white solid: mp 248–251 °C (from hexane, decomp.) (Found: C, 86.7; H, 7.95; N, 4.8. $C_{40}H_{44}N_2$ requires C, 86.9; H, 8.0; N, 5.1%); $\lambda_{max}(CH_2Cl_2)$/nm 240 (ε/dm^3 mol^{-1} cm^{-1} 32400), 281 (56200), 315 (35700) and 357 (27700); $\nu_{max}(CHCl_3/cm^{-1})$ 3007, 2964, 2240, 2210, 1591, 1469, 1248, 1063 and 907; δ_H (400 MHz; $CDCl_3$) 1.3 (36H, s, $C(CH_3)_3$), 7.36 (4H, d, *J* 1.8, aromatic CH), 7.44 (2H, t, *J* 1.8, aromatic CH), 7.9 (2H, s, aromatic CH); δ_C (100.5 MHz; $CDCl_3$) 31.2, 34.8, 84.4, 101.9, 113.8, 114.8, 120.5, 124.5, 126.1, 131.2, 136.3, 151.2; *m*/*z* (EI, 70 eV) 552 (M^+, 90.2%), 57 ($[C(CH_3)_3]^+$, 100).

[2,3,9,10,16,17,23,24-Octakis(triisopropylsilylethynyl)-phthalocyaninato]magnesium(II) 10a

A mixture of phthalonitrile **9a** (20.0 mg, 41 μmol) and a solution of $Mg(OBu)_2$ in BuOH (0.5 ml of a 1.0 M solution previously prepared by heating a suspension of Mg turnings (97.5 mg, 4.0 mmol) and a crystal of iodine in BuOH (4.0 ml) under reflux for 4 h) was heated under reflux for 2 h. The solvent was evaporated in a Kugelrohr apparatus leaving a dark green solid, which was purified first by flash chromatography (10% EtOAc→20% EtOAc in hexanes), then by GPC with THF as eluent yielding **10a** (7.7 mg, 38%) as a dark green solid (Found: C, 71.2; H, 9.15; N, 5.2. $C_{120}H_{176}N_8Si_8Mg{\cdot}2H_2O$ requires C, 71.5; H, 9.0; N, 5.55%); λ_{max}(THF)/nm 261 (ε/dm^3 mol^{-1} cm^{-1} 61200), 279 (41200), 311 (47300), 382 (138900), 641 (49500), 680 (39100), 713 (372600); δ_H (400 MHz; THF–$CDCl_3$) 1.3 (168H, s, $Si(CH(CH_3)_2)_3$), 9.5 (8H, s, aromatic CH); δ_C (100.5 MHz; THF–$CDCl_3$) 11.1, 18.1, 96.0, 106.2, 125.4, 127.6, 137.4, 152.8; *m*/*z* (MALDI-TOF) 2001 ($[M + Na]^+$ requires 2000.2, 100%).

[2,3,9,10,16,17,23,24-Octakis(3,5-di-*tert*-butylphenylethynyl)-phthalocyaninato]magnesium(II) 10b

Phthalocyanine **10b** was prepared starting from phthalonitrile **9b** as described for **10a**. The crude product was purified by flash chromatography (eluting first with CH_2Cl_2, then with 10% Et_2O in CH_2Cl_2), followed by GPC (THF), yielding **10b** (4.0 mg, 17%) as dark green solid. λ_{max}(THF)/nm 255 (ε/dm^3 mol^{-1} cm^{-1} 65900), 278 (87700), 307 (89700), 391 (177100), 649 (60600), 689 (48300), 723 (421400). δ_H (400 MHz; THF–$CDCl_3$) 1.3 (144H, s, $C(CH_3)_3$), 7.5 (8H, s, aromatic CH), 7.6 (16H, s, aromatic CH), 9.6 (8H, s, aromatic CH); δ_C (100.5 MHz; THF–$CDCl_3$) 29.9, 33.5, 86.9, 95.3, 121.6, 121.9, 124.9, 125.4, 125.6, 136.8, 149.7, 152.6; *m*/*z* (MALDI-TOF) 2254 ($[M + Na]^+$ requires 2256.4, 100%).

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References

1 J. Fabian, H. Nakazumi and M. Matsuoka, *Chem. Rev.*, 1992, **92**, 1197.
2 *Infrared Absorbing Dyes*, ed. M. Matsuoka, Plenum Press, New York, 1990.
3 R. Bonnett, *Chem. Soc. Rev.*, 1995, 19.
4 L. Milgrom and S. MacRobert, *Chem. Br.*, March 1998, 45.
5 M. Ochsner, *Photochem. Photobiol.*, 1997, **39**, 1.
6 M. Ochsner, *Arzneim. Forsch.*, 1997, **47(II)**, 1185.
7 R. Bonnett, *Rev. Contemp. Pharmacother.*, 1999, **10**, 1.
8 B. Franck and A. Nonn, *Angew. Chem.*, 1995, **107**, 1941.
9 I. Rosenthal, in *Phthalocyanines—Properties and Applications*, ed. C. C. Leznoff and A. B. P. Lever, VCH, Weinheim, 1996, vol. 4, pp. 481–514.
10 R. Faust and C. Weber, *Liebigs Ann. Chem.*, 1996, 1235.
11 R. Faust, C. Weber, V. Fiandanese, G. Marchese and A. Punzi, *Tetrahedron*, 1997, **53**, 14655.
12 R. Faust, B. Göbelt, C. Weber, C. Krieger, M. Gross, J.-P. Gisselbrecht and C. Boudon, *Eur. J. Org. Chem.*, 1999, 205.
13 R. Faust and C. Weber, *J. Org. Chem.*, 1999, **64**, 2571.
14 R. Faust, B. Göbelt and C. Weber, *J. Organomet. Chem.*, 1999, **578**, 193.
15 H. Hopf, M. Theurig, P. G. Jones and P. Bubenitschek, *Liebigs Ann. Chem.*, 1996, 1301.
16 A. de Groot, B. Evenhuis and H. Wynberg, *J. Org. Chem.*, 1968, **33**, 2214.
17 T. Niemi, P. L. Coe and S. J. Till, *J. Chem. Soc.*, *Perkin Trans. 1*, 2000, 1519.
18 D. J. Ager, *Synthesis*, 1984, 384.
19 F. A. Carey and J. R. Toler, *J. Org. Chem.*, 1976, **41**, 1966.
20 N. A. Petasis and E. I. Bzoweij, *J. Am. Chem. Soc.*, 1990, **112**, 6392.
21 L. Lombardo, *Tetrahedron Lett.*, 1982, **23**, 4293.
22 K. Takai, Y. Hotta, K. Oshima and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1698.
23 H. Hopf and B. Witulski, in *Modern Acetylene Chemistry*, ed. P. J. Stang and F. Diederich, Wiley-VCH, Weinheim, 1995, pp. 33–66.
24 V. Jäger, in *Methoden der Organischen Chemie* (*Houben-Weyl*), ed. E. Müller, Thieme, Stuttgart, 1977, vol. V/2a, 677.
25 P. A. Grieco, J. J. Nunes and M. D. Gaul, *J. Am. Chem. Soc.*, 1990, **112**, 4595.
26 C. C. Leznoff, in *Phthalocyanines—Properties and Applications*, ed. C. C. Leznoff and A. B. P. Lever, VCH Publishers, Weinheim, 1989, vol. 1, pp. 1–54.
27 D. S. Terekhov, K. J. M. Nolan, C. R. McArthur and C. C. Leznoff, *J. Org. Chem.*, 1996, **61**, 3034.
28 C. C. Leznoff, Z. Li, H. Isago, A. M. D'Ascanio and D. S. Terekhov, *J. Porphyrins Phthalocyanines*, 1999, **3**, 406.
29 D. D. Perrin and W. L. F. Armarego, *Purification of Laboratory Chemicals*, Pergamon Press, Oxford, 1988.
30 R. W. Bott, C. Eaborn and D. R. A. Wilson, *J. Chem. Soc.*, 1965, 384.
31 *Organization*, ed. H. J. O. Beezer, 19th edn., Johann Ambrosius Barth, Heidelberg, pp. 269, 249.
32 D. Philp, V. Gramlich, P. Seiler and F. Diederich, *J. Chem. Soc.*, *Perkin Trans. 2*, 1995, 875.