A Facile Synthesis of New Tetrapyrrole Macrocyclic Derivatives. Formation of Bimetallic Transition Metal Complexes

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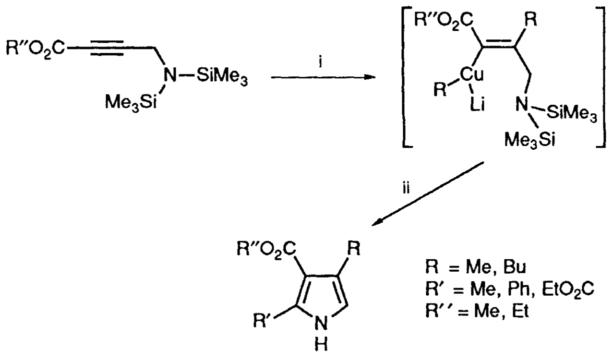
The reaction of Me(hexynyl)CuLi with $(Me_3Si)_2NCH_2{-}C{\equiv}C{-}CO_2Et$ followed by treatment with a diacid dichloride gave a facile access to *meta*-dipyrrolyl benzene or 2,6-dipyrrolyl pyridine derivatives, which were cyclised to tetrapyrrolic macrocycles **7** and **9**; further reactions with $Pd(acac)_2$ or $Ni(acac)_2$ led to bimetallic complexes.

Porphyrin macrocycles constitute an important class of compounds of particular interest owing to their role in biological systems.[1] Recent work has been devoted to the design of new porphyrin ligands with specific properties, or new structural analogues of porphyrins.[2] The synthesis of homoporphyrins as well as penta- and hexa-pyrrolic macrocycles has been reported. Our current interest in the use of aminosilanes for the synthesis of nitrogen heterocycles[3,4] led us to investigate the synthesis of nitrogen macrocyclic compounds. We recently reported a one-pot synthesis of pyrroles from bis(trimethylsilyl)aminomethyl propiolate **1** on addition of organocuprate reagents and reaction with an acid chloride,[4] Scheme 1. The substituted pyrroles obtained with a free 5-position could easily allow the preparation of dipyrrolylmethane derivatives and are, therefore, relevant to the porphyrin field. We report here a facile route to new polyheterocyclic and tetrapyrrolic macrocycles.

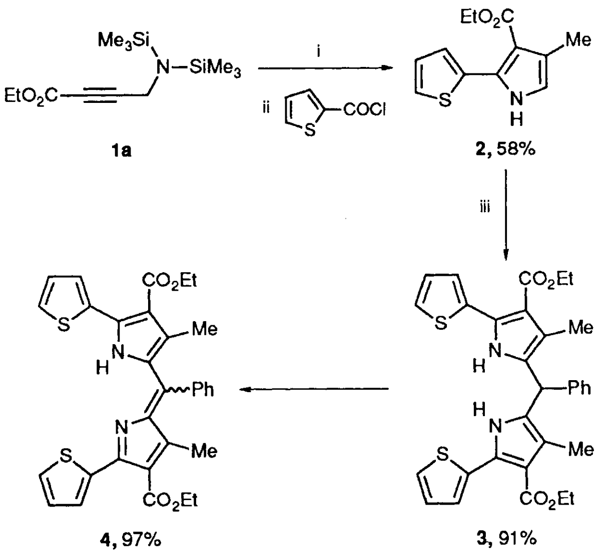
According to Scheme 1, the reaction of thienyl chloride led to 2-thienyl pyrrole **2** (Scheme 2). Treatment of **2** with benzaldehyde in acetic acid afforded a high yield of the dipyrrolylmethane derivative **3**. The latter was oxidized readily upon treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to give the conjugated red derivative **4** (λ_{max} 314 nm, ε 28680; 534 nm, ε 29580). The ^1H and ^{13}C NMR spectra of **4** are consistent with the formation of a single isomer, the stereochemistry of which was not assigned.

In order to obtain dipyrrolylmethane derivatives, which could cyclise to tetrapyrrole macrocycles, we examined the reaction of diacid dichlorides. The use of phthaloyl dichloride (Scheme 3) led to a mixture of products from which only a low yield of a tricyclic pyrrole **5** was isolated. Compound **5** arises

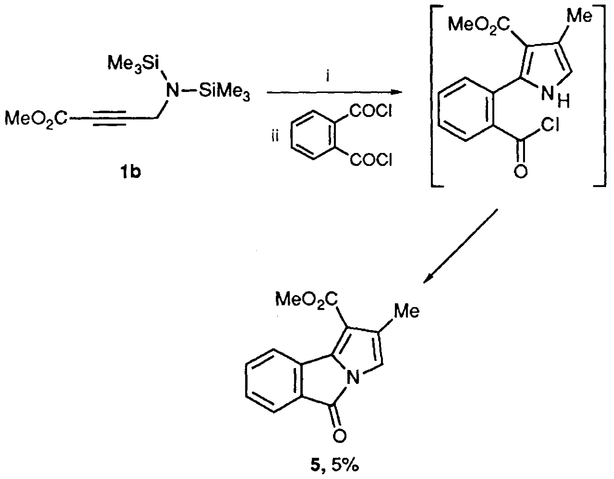


R = Me, Bu
R′ = Me, Ph, EtO₂C
R″ = Me, Et

Scheme 1 *Reagents and conditions*: i, R_2CuLi, Et_2O, −40 °C, 2 h; ii, Et_2O, −40 °C, 2 h, then 20 °C, 10 h



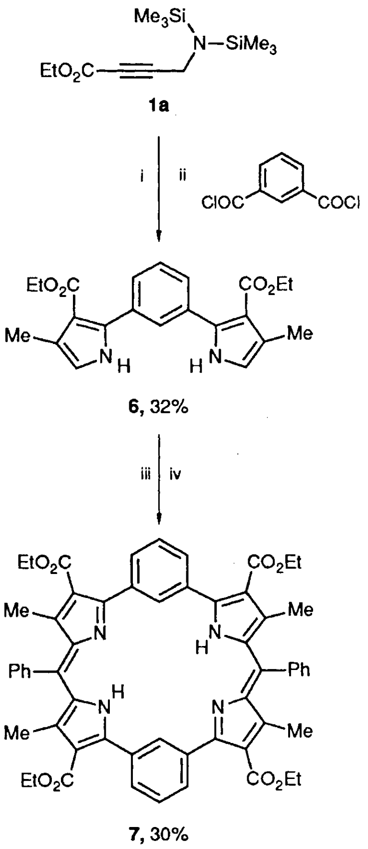
Scheme 2 *Reagents and conditions*: i, Me(Hexynyl)CuLi/Et$_2$O, −50 °C, 2 h; ii, Et$_2$O, −50 to 20 °C, 12 h; iii, PhCHO, AcOH, 70 °C, 3 h; iv, DDQ, toluene, 20 °C, 4 h



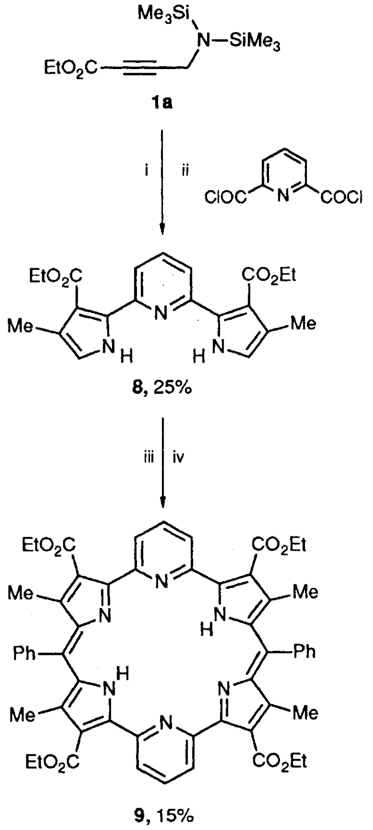
Scheme 3 *Reagents and conditions*: i, Me(Hexenyl)CuLi/Et$_2$O, −50 °C, 2 h; ii, Et$_2$O, −50 to 20 °C, 12 h

from an intramolecular cyclisation reaction of the initially formed monopyrrolyl derivative.[4] The ring closure reaction was avoided by using isophthalic acid dichloride which led to the expected *meta*-dipyrrolylbenzene **6** although in a moderate yield (Scheme 4). Compound **6** was then heated with benzaldehyde in AcOH and the crude reddish mixture was heated with DDQ to give the tetrapyrrole macrocycle **7**. Analytical and spectroscopic results are fully consistent with the proposed structure.† The reactions in Scheme 4, thus, offer a very easy access to a structural analogue of porphyrin in 9% overall yield from **1a**.

Interestingly, 2,6-dipyrrolylpyridine **8** was obtained in a similar way from the reaction of pyridine dicarboxylic acid dichloride (Scheme 5). The dipyrrolylmethane formation with benzaldehyde followed by oxidation allowed isolation of the



Scheme 4 *Reagents and conditions*: i, Me(Hexenyl)CuLi/Et$_2$O, −50 °C, 1 h; ii, Et$_2$O, −50 to 20 °C, 12 h; iii, PhCHO/AcOH, 80 °C, 20 h; iv, toluene, 20 °C, 6 h



Scheme 5 *Reagents and conditions*: i, Me(Hexenyl)CuLi, Et$_2$O, −50, 2 h; ii, Et$_2$O, −50 to 20 °C, 12 h; iii, PhCHO/AcOH, 80 °C, 3 h; iv, toluene, 20 °C, 4 h

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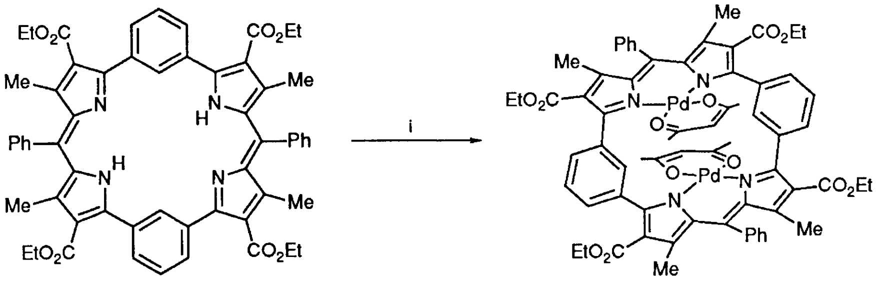
† *Selected spectroscopic data* for compound **7**: MS: *m/z* 932(M$^+$). Visible spectra (C$_6$H$_6$) λ_{max} 450 nm, ε 6.3 × 10^4; ^{1}H NMR (CDCl$_3$): δ 1.1(12H, t), 1.5(12H, s), 4.1(8H, q), 7.2–7.7(16H, m), 7.9(2H, s), 14.1(2H, br s). ^{13}C NMR (CDCl$_3$): δ 13.80, 14.27, 60.34, 123.28, 126.99, 127.34, 129.15, 129.66, 130.83, 135.02, 137.24, 138.55, 144.94, 145.80, 155.20, 158.06, 165.62.



7

10, 95%

Scheme 6 *Reagents and conditions*: i, Pd(acac)$_2$, PhOH, 130 °C, 12 h

macrocycle **9**‡ with six nitrogen atoms in the ring. The reaction of diacid dichloride, therefore, offers an easy route to enlarged tetrapyrrolic macrocycles as well as macrocycles with more than four heterocycles. It seems that various new macrocycles, which could allow the complexation of one or two metal atoms, could be envisaged.

Finally we studied some complexation properties of the tetrapyrrole **7**. We first examined the reaction of palladium salts which are known to form very stable metalloporphyrins.[5] Upon treatment of **7** with Pd(acac)$_2$ a stable, red complex **10** was isolated (Scheme 6). The analytical results§ are consistent with the formation of a bimetallic species containing two palladium atoms, one macrocyclic and two acetylacetonate (acac) ligands. No crystals suitable for X-ray analysis could be obtained. We propose that the two palladium atoms in complex **10** are located above and below the macrocyclic plane, the coordination of each metal being square planar. A similar structure has been determined in the case of a related octaethylporphyrin (oep) tetracarbonyl dirhodium complex: Rh$_2$(oep)(CO)$_4$.[6] While the square planar coordination of palladium is retained, strain within the molecule is probably relieved by a folding of the ligand.[7] The macrocyle **7** seems too large for the coordination of a single metal atom and the two dipyrrolylmethane units of the symmetrical ligand formed independent palladium(II) complexes. A bimetallic dinickel complex with identical spectroscopic properties was similarly obtained upon treatment of **7** with Ni(acac)$_2$.

The synthesis of bis-pyrrole derivatives from diacid dichloride offers a simple route to new macrocycles that can be converted to new analogues of metalloporphyrins.

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‡ *Selected spectroscopic data* for compound **9**: MS: *m/z* 934(M$^+$); ^{1}H NMR (CDCl$_3$): δ 1.0 (12H, t), 1.7(12H, s), 4.05(8H, d), 7.1–7.75(16H, m); ^{13}C NMR (CDCl$_3$) δ 11.13, 14.28, 60.14, 119.87, 123.74, 127.30, 127.66, 128.40, 129.22, 129.90, 133.78, 139.90, 149.30, 150.11, 166.22.

§ *Selected spectroscopic data* for compound **10**: MS: *m/z* 1342(M$^+$). IR (CCl$_4$, cm^{-1}): 1700s, 1580s, 1518s, 1495s, 1470s, 1395s, 1288s, 1253m, 1182m, 1120s. Visible spectra (C$_6$H$_6$): λ_{max} 502 nm, ε 1.2 × 10^5; ^{1}H NMR (CDCl$_3$): δ 1.1(12H, t); 1.4(12H, s), 1.5(12H, s), 4.1(8H,q), 4.7(2H, s), 7.2–7.7(16H, m), 8.5(2H, s); ^{13}C NMR (CDCl$_3$): δ 14.28, 14.51, 25.03, 60.43, 100.05, 115.67, 124.89, 126.46, 128.45, 129.38, 129.99, 130.95, 135.71, 136.21, 137.90, 146.18, 150.65, 161.82, 166.01, 185.11.