Synthesis and Photoisomerization of Diarylcyclobutenes

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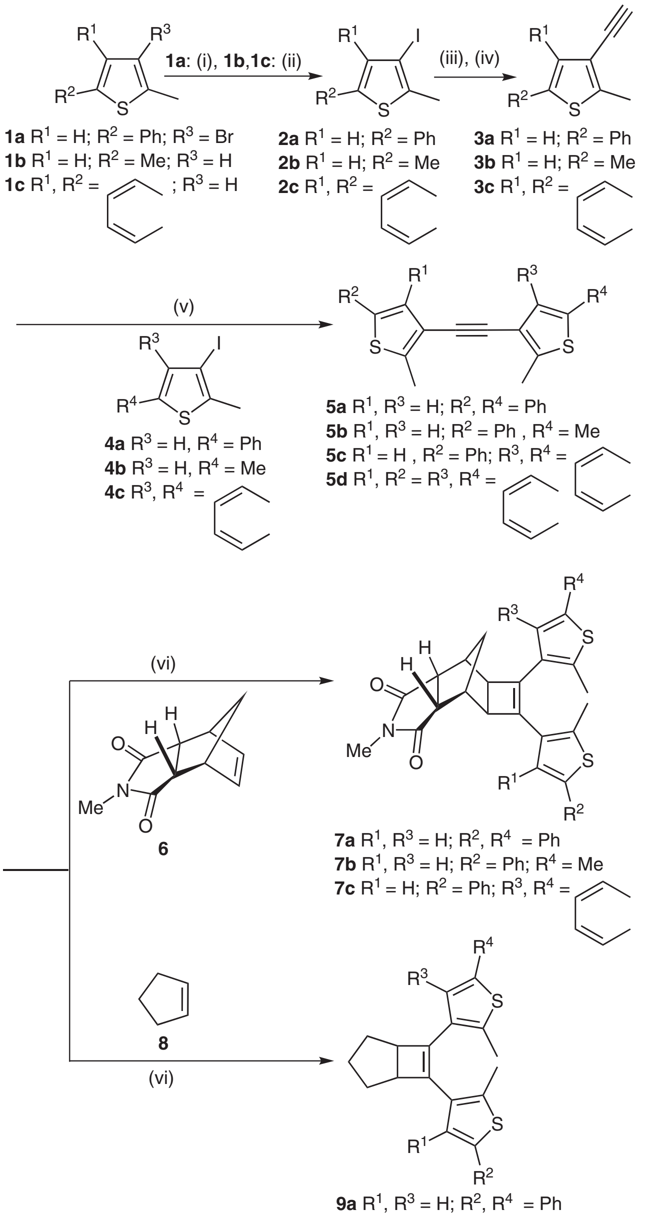
Abstract: Symmetrically and unsymmetrically substituted diarylcyclobutenes are synthesized in 20–70% yields from alkyne precursors via cobalt-catalyzed [2+2] cycloadditions. The reactions proceed under mild conditions and provide access to differently substituted diarylethene derivatives. All the diarylcyclobutene products undergo reversible photoisomerization upon irradiation with UV/Vis light. The ring-closed isomers show different thermal stabilities towards reisomerization with half-lives ranging from 9 to 300 hours.

Key words: diarylethene, photoswitchable, cyclobutene, photochromic reactions, [2+2] cycloaddition

Reversible photoswitchable compounds are interesting for applications in optoelectronic data storage, as active parts of organic polymers with switchable refractive indices,[1] or as photochromic moieties used to control biological processes.[2] One recent example is a diarylethene-based photoswitchable inhibitor for the enzyme, human carboanhydrase.[3] With some diarylethenes both isomers show high fatigue resistance and good thermal stability, which is important for a variety of applications. However, the synthesis of derivatives of higher complexity is challenging, as known routes are either not versatile enough, or the required starting materials are difficult to handle.[4] The most convenient routes for diarylethene synthesis were reported by Feringa[5] and Irie.[6] The key step in the Feringa route is a McMurry[7]coupling reaction using the corresponding diarylketone precursors to afford a five-membered ring system. However, the synthesis of unsymmetric diarylethenes via this approach is limited, as suitable diarylketone precursors are difficult to obtain. The Irie route uses octafluorocyclopentene as the starting material, which is substituted with the appropriate lithiated aryl compounds giving fluorinated cyclopentenes. Octafluorocyclopentene is volatile and therefore difficult to handle; another disadvantage is the formation of monosubstituted side products.[8] Our goal was to establish a new route for the synthesis of symmetrically and unsymmetrically substituted diarylethenes. The described approach uses diarylalkynes, obtained via Sonogashira coupling, and a cobalt-catalyzed [2+2]-cycloaddition reaction to give the photochromic diarylethenes. This reaction sequence leads to diarylethenes bearing a cyclobutene moiety,[9–16] a group of compounds not widely studied so far, and allows the simple preparation of symmetrically and unsymmetrically substituted derivatives. The photochromic properties of the new compounds were investigated.



Scheme 1 (i) *n*-BuLi, Et_2O, I_2; (ii) I_2, HIO_3, H_2O, AcOH, CCl_4; (iii) $Me_3SiC{\equiv}CH$, $Pd(PPh_3)_2Cl_2$, Ph_3P, CuI, Et_3N, THF; (iv) K_2CO_3, MeOH; (v) $Pd(PPh_3)_2Cl_2$, Ph_3P, CuI, Et_3N, THF; (vi) $Co(dppp)Br_2$, ZnI_2, Zn, CH_2Cl_2.

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Symmetrically and unsymmetrically substituted diarylethenes **7a**–**c**, **9a** and **9b**, with a central cyclobutene moiety, were prepared as shown in Scheme 1. Thiophene derivatives **1a**–**c** were converted into iodoarenes **2a**–**c** by bromine–iodine exchange using *n*-butyllithium and iodine (for **1a**), or aromatic substitution with iodine and iodic acid (for **1b** and **1c**). Both reactions yielded the desired products in about 70% yield. Palladium-catalyzed Sonogashira coupling of compounds **2** with ethynyltrimethylsilane, followed by cleavage of the trimethylsilyl protecting group with potassium carbonate gave alkynes **3** in good yields. Using a second Sonogashira cross-coupling reaction, terminal alkynes **3** were reacted with thiophenes **4** to yield diarylalkynes **5** as precursors for the subsequent cobalt-catalyzed [2+2] cycloaddition. This reaction was carried out under very mild conditions using the cobalt catalyst previously reported by Hilt.[17,18] At room temperature, zinc was used as the reducing agent to generate the active catalytic cobalt(I) species. Maleimide derivative **6** and cyclopentene (**8**) were used as the alkene components in the cycloaddition reaction. The yield of the reaction strongly depends on the nature of the diarylalkyne and its aryl substitution pattern. Cycloaddition reactions of alkenes **6** and **8** with diarylalkynes **5a** and **5b** gave the corresponding products **7a**, **7b**, **9a** and **9b** in yields of 65–70%, while benzothienyl substituted diarylalkynes **5c** and **5d** each reacted sluggishly, and only product **7c** was isolated in a poor 20% yield.

All the synthesized diarylethenes underwent reversible photochromic ring-closing reactions in dichloromethane on irradiation with UV light (320 nm), and ring-opening in the presence of visible light. The absorption properties and thermal stabilities of the ring-closed forms of compounds **7a**–**c**, **9a** and **9b** are summarized in Table 1.

Table 1 Photophysical Data of Compounds **7a**–**c**, **9a** and **9b**

Compd	λ_{max} (nm) ($\varepsilon \cdot 10^4$) (open form)	λ_{max} (nm) (closed form)	Thermal stability at r.t. [$t_{1/2}$ (h)]
7a	287 (4.1)	534	8.9
7b	288 (3.3)	495	301.3
7c	265 (1.5)	490	133.0
9a	287 (4.1)	534	8.9
9b	288 (3.3)	495	300.1

The ring-closed diarylethenes **7** and **9** can switch back to the ring-open isomers in the presence of visible light, and undergo a slow thermal cycloreversion reaction in the dark. The thermal ring-opening of related four-membered ring systems has been described in the literature.[9] The half-lives of the ring-closed isomers depend on the aromatic stabilization energies gained upon conversion into the ring-open isomer, and therefore on the thiophene substitution pattern.[19] The thermal stabilities range from $t_{1/2}$ = 8.9 hours for compound **7a** to $t_{1/2}$ = 300 hours for the unsymmetrically substituted derivative **7b**. The photoisomerization reactions were performed several times and a loss of about 50% of the initial absorption intensity due to photodecomposition was observed after 10 irradiation cycles. Figure 1 shows the changes in the absorption intensity of compound **7a**, at 312 nm, over 10 photoisomerization cycles.

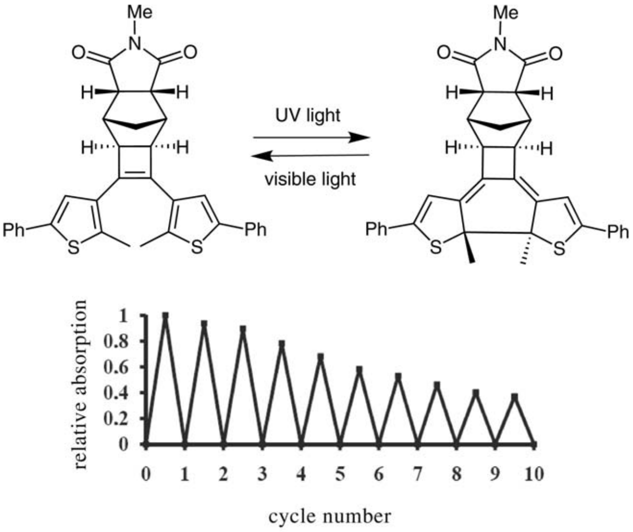

Figure 1 Photoisomerization and bleaching of compound **7a** as monitored by changes in the absorption at 312 nm

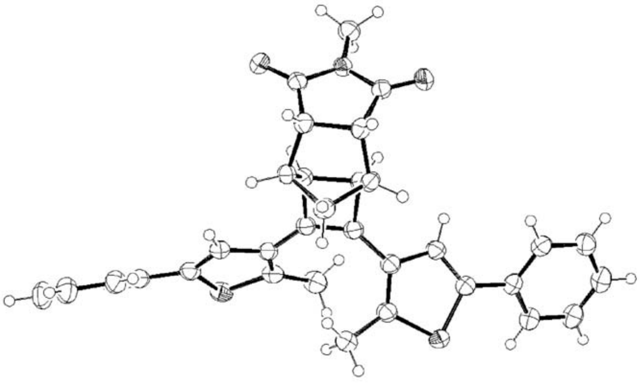

Figure 2 ORTEP representation of the X-ray crystal structure of compound **7a**

The structure of compound **7a** was determined by X-ray crystal structure analysis (Figure 2). The conjugated thiophene rings are twisted due to steric interactions between the methyl substituents. The cyclobutene ring of the [2.2.1]bicycloheptene unit is *exo* configured, while the imide group adopts an *endo* orientation.

In summary, photoisomerizable diarylcyclobutenes were obtained from diarylalkynes via a cobalt-catalyzed [2+2]-cycloaddition reaction. The efficiency of the ring-closing reaction depends on the structure of the diarylalkyne precursor, and product yields of up to 70% were obtained. The products undergo reversible photochromic reactions in dichloromethane by alternating irradiation with UV light and visible light. A specific advantage of the presented synthetic route is the simpler access to diarylethenes bearing two different aryl substituents.

Table 2 Physical Properties, IR and MS Data for Compounds **3c**, **5b**–**d**, **7a**–**c**, **9a** and **9b**

Compd	Mp (°C)	IR (CHCl$_3$) cm^{-1}	Formula	Mass (found)	Mass (calcd)
3c	174–176	2925, 2854, 1458, 1377, 1122, 933, 815	$C_{11}H_8S$	172.0342	172.0347
5b	161–163	2337, 1605, 1301, 748, 539, 496	$C_{19}H_{16}S_2$	308.0690	308.0693
5c	168–170	2911, 2336, 2197, 1595, 837, 681	$C_{22}H_{16}S_2$	344.0695	344.0693
5d	155–157	3053, 2360, 1740, 720, 620, 557	$C_{20}H_{14}S_2$	318.0539	318.0537
7a	223–225	2353, 2132, 1533, 1442, 1291, 1030, 883, 773, 631, 537, 498	$C_{34}H_{29}NO_2S_2$	547.1638	547.1640
7b	[a]	2927, 2361, 2253, 2168, 1769, 1695, 1598, 1434, 1136, 997, 631	$C_{29}H_{27}NO_2S_2$	485.1489	485.1483
7c	[a]	3061, 2933, 2360, 2169, 1942, 1697, 1596, 1433, 1229, 1032, 831, 686, 420	$C_{32}H_{27}NO_2S_2$	521.1490	521.1483
9a	[a]	2361, 2170, 1740, 1369, 1218, 631, 540	$C_{29}H_{26}S_2$	438.1474	438.1476
9b	[a]	2360, 2339, 2207, 2171, 2116, 2032, 1740, 1669, 1437, 1374, 1220, 834	$C_{24}H_{24}S_2$	376.1327	376.1319

[a] Product obtained as a sticky oil.

Table 3 Yields and NMR Spectroscopic Data for Compounds **3c**, **5b**–**d**, **7a**–**c**, **9a** and **9b**

Compd	Yield (%)	^{1}H NMR (ppm)	^{13}C NMR (ppm)
3c	70	2.72 (s, 3 H), 3.48 (s, 1 H), 7.30–7.41 (m, 2 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H)	15.4, 82.3, 111.5, 114.8, 122.0, 122.4, 124.5, 124.7, 137.4, 140.0, 146.6
5b	75	2.41 (s, 3 H), 2.52 (s, 3 H), 2.58 (s, 3 H), 6.68 (s, 1 H), 7.22 (s, 1 H), 7.24–7.30 (m, 2 H), 7.34–7.40 (m, 2 H), 7.52–7.57 (m, 1 H)	14.5, 14.7, 15.2, 85.6, 86.7, 119.4, 121.1, 125.2, 125.6, 127.1, 127.5, 128.9, 134.0, 135.9, 140.2, 140.9, 142.2
5c	72	2.64 (s, 3 H), 2.71 (s, 3 H), 7.23–7.42 (m, 5 H), 7.54–7.58 (m, 2 H), 7.73 (d, *J* = 7.7 Hz, 1 H), 7.86 (d, *J* = 7.4 Hz, 2 H)	14.8, 15.4, 84.8, 89.1, 116.0, 120.9, 122.1, 122.4, 124.5, 124.7, 125.2, 125.6, 127.6, 129.0, 133.9, 137.5, 139.9, 140.4, 142.6, 144.4
5d	74	2.77 (s, 6 H), 7.30–7.48 (m, 4 H), 7.93 (d, *J* = 7.6 Hz, 2 H), 7.75 (d, *J* = 7.9 Hz, 2 H)	15.5, 87.7, 116.0, 122.1, 122.4, 124.5, 124.8, 137.6, 139.8, 144.5
7a	70	1.50 (d, *J* = 10.7 Hz, 1 H), 2.11 (d, *J* = 10.7 Hz, 1 H), 2.27 (s, 6 H), 2.80–2.85 (m, 2 H), 2.96 (s, 2 H), 3.01 (s, 3 H), 3.27–3.30 (m, 2 H), 7.09 (s, 2 H), 7.20–7.28 (m, 2 H), 7.30–7.38 (m, 4 H), 7.48–7.53 (m, 4 H)	14.9, 24.4, 34.7, 37.5, 44.0, 48.1, 122.8, 125.4, 127.4, 128.9, 133.7, 134.0, 134.2, 136.7, 140.4, 177.8
7b	65	1.42 (d, *J* = 10.6 Hz, 1 H), 2.02 (d, *J* = 10.6 Hz, 1 H), 2.12 (s, 3 H), 2.21 (s, 3 H), 2.32 (s, 3 H), 2.74 (s, 2 H), 2.82–2.90 (m, 2 H), 2.94 (s, 3 H), 3.22–3.30 (m, 2 H), 6.50 (s, 1 H), 7.01 (s, 1 H), 7.16–7.20 (m, 1 H), 7.25–7.30 (m, 2 H), 7.43–7.47 (m, 2 H)	14.6, 14.8, 15.1, 24.4, 34.6, 37.5, 43.9, 48.2, 77.3, 122.9, 125.1, 125.4, 127.3, 128.9, 132.5, 133.3, 133.9, 134.1, 134.7, 134.9, 136.0, 136.5, 140.2, 177.8
7c	20	1.28 (d, *J* = 10.7 Hz, 1 H), 1.54 (d, *J* = 10.7 Hz, 1 H), 2.10 (s, 3 H), 2.42 (s, 3 H), 2.66 (d, *J* = 5.3 Hz, 1 H), 3.01 (d, *J* = 5.4 Hz, 1 H), 3.03–3.05 (m, 4 H), 3.20–3.21 (m, 1 H), 3.25 (dd, *J* = 5.4, 9.2 Hz, 1 H), 3.34 (dd, *J* = 5.4, 9.2 Hz, 1 H), 6.99 (s, 1 H), 7.21–7.32 (m, 5 H), 7.39–7.40 (m, 2 H), 7.51–7.56 (m, 1 H), 7.73–7.76 (m, 1 H)	14.7, 15.5, 24.4, 34.9, 37.3, 37.8, 43.8, 45.3, 47.9, 48.3, 122.0, 122.5, 123.8, 124.3, 125.4, 127.3, 128.0, 128.8, 132.6, 133.6, 133.9, 137.1, 137.8, 137.9, 138.8, 139.3, 140.3, 177.6, 177.8
9a	65	1.35–1.47 (m, 2 H), 1.74–1.88 (m, 4 H), 2.29 (s, 6 H), 3.94 (d, *J* = 6.5 Hz, 2 H), 7.18 (s, 2 H), 7.21–7.26 (m, 2 H), 7.32–7.37 (m, 4 H), 7.51–7.54 (m, 4 H)	14.8, 23.4, 26.8, 46.9, 123.2, 125.4, 127.1, 128.8, 134.3, 134.9, 135.6, 135.8, 139.9
9b	70	1.30–1.42 (m, 2 H), 1.68–1.84 (m, 4 H), 2.20 (s, 3 H), 2.26 (s, 3 H), 2.38 (s, 3 H), 3.40–3.47 (m, 2 H), 6.59 (s, 1 H), 7.13 (s, 1 H), 7.20–7.37 (m, 3 H), 7.49–7.53 (m, 2 H)	14.5, 14.7, 15.2, 23.3, 26.8, 30.3, 46.8, 77.0, 123.3, 125.3, 125.4, 127.1, 128.8, 133.6, 133.9, 134.4, 134.8, 135.3, 135.5, 135.7, 136.0, 139.7

The following compounds were prepared according to literature methods: 3-bromo-2-methyl-5-phenylthiophene (**1a**),[20] 2-methylbenzo[*b*]thiophene (**1c**),[21] 3-iodo-2-methyl-5-phenylthiophene (**2a**),[19] 3-iodo-2-methylbenzo[*b*]thiophene (**2c**)[20] and 1,2-bis(2-methyl-5-phenylthiophene-3-yl)ethyne (**5a**).[21] All other reagents were obtained from commercial sources. Unless otherwise noted, solvents (analytical grade) were purchased from commercial suppliers and used without further purification. Melting points were obtained using a Lambda Photometrics Optimelt MPA100 apparatus (Lambda Photometrics, Harpenden, UK), and are not corrected. IR spectra were obtained using a Varian Biorad FT-IR Excalibur FTS 3000 spectrometer. ^{1}H NMR spectra were recorded at 300 MHz on a Bruker Avance 300 spectrometer, or at 600 MHz on a Bruker Avance III Br600 with a cryogenic probe head (Bruker, Karlsruhe, Germany). ^{13}C NMR spectra were recorded at 75 MHz on a Bruker Avance 300 spectrometer. The NMR spectra were recorded in $CDCl_3$ as solvent and chemical shifts are reported in ppm. UV/Vis spectra were recorded using a Varian Cary BIO 50 UV/Vis/NIR spectrophotometer (Varian Inc., CA, USA). Mass spectra were obtained using Finnigan SSQ 710A (EI), Finnigan MAT 95 (CI) or Finnigan MAT TSQ 7000 (Thermo FINNIGAN, USA) (ES/LC–MS)] instrumentation. Thin layer chromatography (TLC) was performed on alumina plates coated with silica gel (Merck silica gel 60 F_{245}, thickness 0.2 mm). Column chromatography was accomplished with Merck Geduran SI 60 silica gel as the stationary phase. Petroleum ether (PE) refers to the fraction boiling in the 70–90 °C range.

3-Ethynyl-2-methylbenzo[*b*]thiophene (3c)

A mixture of THF–Et_3N (48 mL, 2:1) was degassed for 10 min and then 3-iodo-2-methylbenzo[*b*]thiophene (**2c**) (5.3 g, 19.3 mmol), $Me_3SiC≡CH$ (5.57 mL, 38.7 mmol), $Pd(PPh_3)_2Cl_2$ (54 mg, 0.4 mol%), Ph_3P (40 mg, 0.8 mol%) and CuI (29 mg, 0.6 mol%) were added under an N_2 atm. The resulting soln was heated at 65 °C for 12 h. The reaction mixture was cooled, Et_2O (40 mL) and H_2O (40 mL) were added and the organic layer was separated. Subsequently, the water layer was extracted with Et_2O (2 × 40 mL). Then the organic layers were combined, dried over $MgSO_4$ and the solvent was removed. The residue was dissolved in MeOH (220 mL), K_2CO_3 (2.97 g, 21.1 mmol) was added and the resulting soln was stirred for 2 h at r.t. The reaction mixture was filtered, the solvent was removed and the residue was purified by silica gel flash chromatography (PE; R_f = 0.6). Physical and analytical data for compound **3c** are given in Tables 2 and 3.

Diarylalkynes 5b–d; General Procedure

A mixture of THF–Et_3N (24 mL, 2:1) was degassed for 10 min and then iodothiophene **4a–c** (10.0 mmol), acetylene **3a–c** (10.0 mmol), $Pd(PPh_3)_2Cl_2$ (27 mg, 0.4 mol%), Ph_3P (20 mg, 0.8 mol%) and CuI (15 mg, 0.6 mol%) were added under an N_2 atm. The resulting soln was heated at 65 °C for 12 hours. The reaction mixture was cooled, Et_2O (20 mL) and H_2O (20 mL) were added and the organic layer was separated. Subsequently, the water layer was extracted with Et_2O (2 × 20 mL) and then the organic layers were combined and dried over $MgSO_4$. The solvent was removed and the residue was purified by silica gel flash chromatography (PE–EtOAc, 9.5:0.5). Physical and analytical data for compounds **5b–d** are given in Tables 2 and 3.

Diarylcyclobutenes 7a-c; General Procedure

In a Schlenk tube, [1,3-bis(diphenylphosphino)propane]cobalt(II) bromide $[Co(dppp)Br_2]$ (64 mg, 0.1 mmol, 20 mol%), anhyd ZnI_2 (64 mg, 0.2 mmol, 40 mol%) and Zn powder (13 mg, 0.2 mmol, 40 mol%) were dissolved in anhyd CH_2Cl_2 (2 mL) under an N_2 atm. The alkyne **5a–c** (0.5 mmol) and alkene **6** (0.5 mmol) were added and the mixture stirred for 24 h at r.t. CH_2Cl_2 (10 mL) and H_2O (10 mL) were then added to the reaction mixture and the organic layer was separated. Subsequently, the water layer was extracted with CH_2Cl_2 (2 × 10 mL) and then the organic layers were combined and dried over $MgSO_4$. The solvent was removed and the residue was purified by silica gel flash chromatography (**7a** and **7b**: PE–EtOAc, 1:1; R_f ~0.5) or by preparative HPLC (**7c**). Physical and analytical data for compounds **7a–c** are given in Tables 2 and 3. The X-ray structure analysis data of compound **7a** have been deposited with the Cambridge Crystallographic Data Centre under the deposition number CCDC 811884.

Diarylcyclobutenes 9a and 9b; General Procedure

In a Schlenk tube, [1,3-bis(diphenylphosphino)propane]cobalt(II) bromide $[Co(dppp)Br_2]$ (64 mg, 0.1 mmol, 20 mol%), anhyd ZnI_2 (64 mg, 0.2 mmol, 40 mol%) and Zn powder (13 mg, 0.2 mmol, 40 mol%) were dissolved in anhyd CH_2Cl_2 (2 mL) under an N_2 atm. The alkyne **5a** or **5b** (0.5 mmol) and cyclopentene (**8**) (0.045 mL, 0.5 mmol) were added and the mixture stirred for 24 h at r.t. CH_2Cl_2 (10 mL) and H_2O (10 mL) were then added to the reaction mixture and the organic layer was separated. Subsequently, the water layer was extracted CH_2Cl_2 (2 × 10 mL) and then the organic layers were combined and dried over $MgSO_4$. The solvent was removed and the residue was purified by preparative HPLC (**9a**) or by silica gel flash chromatography (**9b**: PE–EtOAc, 9.75:0.25). Physical and analytical data for compounds **9a**,**b** are given in Tables 2 and 3.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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