A New Efficient Synthesis of the Stilbenoid Laser Dyes BPS and Stilbene I by Palladium-Catalyzed Coupling of Ethene with Bromoarenes

Jörg Rümper, Viktor V. Sokolov, Karsten Rauch, and Armin de Meijere*

Institut für Organische Chemie der Georg-August-Universität Göttingen
Tammannstraße 2, D-37077 Göttingen, Germany
Fax: (internat.) +49(0)551/39-9475
E-mail: ameijer1@uni-goettingen.de

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The palladium-catalyzed coupling of ethene with 4-bromobiphenyl and 4'-bromo-4-biphenylsulfonic acid permits a facile one-pot preparation of the laser dyes (*E*)-4,4'-diphenylstilbene (BPS, **3**) and bis(triethylammonium) (*E*)-4,4'-diphenylstilbene-4'',4'''-disulfonate (**6**) in diastereomerically pure form on a multigram scale, with yields of 69 and 64%, repectively. The latter can easily be transformed to its dipotassium salt **7**, the Stilbene I dye.

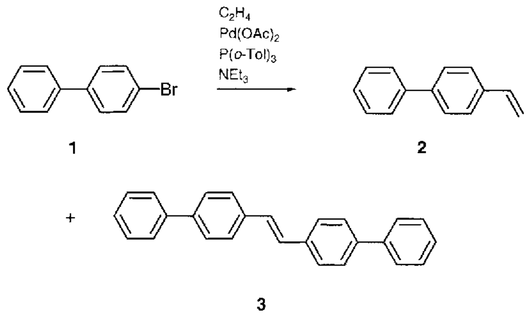
Stilbene and stilbene derivatives have been the subject of many photophysical investigations over the past two decades. Accordingly, methods for the preparation of configurationally pure *trans*-stilbenes have gained considerable importance[1]. Well-established methods for the preparation of alkenes, like the Wittig reaction[2] and the McMurry coupling[3], generally yield mixtures of *cis* and *trans* isomers when applied to the synthesis of stilbenes. The published procedures for the synthesis of 4,4'-diphenylstilbene (BPS, **3**)[4] and dipotassium (*E*)-4,4'-diphenylstilbene-4'',4'''-disulfonate (Stilbene I, **7**)[5] have significant experimental drawbacks with respect to the number of steps and the isolation of pure products. The palladium-catalyzed coupling of bromoarenes with alkenes, the so-called Heck reaction, has proved to be an efficient method for the facile and stereoselective assembly of alkenylarenes[7]. Even multiple alkenylations of di-, tri- and oligohaloarenes have been carried out with good success[8]. Although the twofold coupling of ethene with bromoarenes to yield symmetrical stilbenes was published as early as 1978[9a], it has only rarely been applied[9b]. We here report on the straightforward coupling of ethene with two molecules of 4-bromobiphenyl and 4'-bromobiphenyl-4-sulfonic acid to yield diastereomerically pure *trans*-4,4'-diphenylstilbene (BPS, **3**) and bis(triethylammonium) *trans*-4,4'-diphenylstilbene-4'',4'''-disulfonate (**6**). The latter is readily transformed to its dipotassium salt, which is the frequently used laser dye Stilbene I[6a].

Results and Discussion

The first investigation of the palladium-catalyzed coupling of bromoarenes with ethene by Heck et al. focussed on the product distribution as a function of the ethene pressure. At high ethene pressure, its concentration in the reaction mixture increases, and this in turn leads to an increase of the fraction of monocoupling product (styrene) formed. The highest yields of the monocoupling product were obtained at 13.8 bar. The type of bromoarene used also had a significant influence on the product composition. A combination of 1 mol% palladium acetate, 2 mol% tri-*o*-tolylphosphane and triethylamine as a base was found to be the best catalyst system for this coupling[9a].

Using this catalyst system, the coupling of ethene with 4-bromobiphenyl (**1**) gave vastly differing ratios of 4-ethenylbiphenyl (4-phenylstyrene) (**2**) and 4,4'-diphenylstilbene (biphenylstilbene, BPS, **3**) depending on solvent, the ethene pressure and the bromoarene concentration (see Scheme 1 and Table 1).

Scheme 1. For details see Table 1



Thus, the best conditions for the formation of the twofold coupling product BPS **3** were those given in entry 6, with *N*-methylpyrrolidone (NMP) as solvent, a rather high concentration of 4-bromobiphenyl, and an ethene pressure of only 1 bar. Because of the low solubility of **1**, it precipitated from the solution as it formed. Afterwards, it had to be separated from the other solids formed during the reaction, especially triethylammonium bromide, by recrystallization from xylene. The 4'-bromobiphenyl-4-sulfonic acid (**4**) required for the preparation of dipotassium (*E*)-4,4'-diphenylstilbene-4'',4'''-disulfonate (Stilbene I, **7**) was synthesized in 95% yield following the procedure of Schultz et

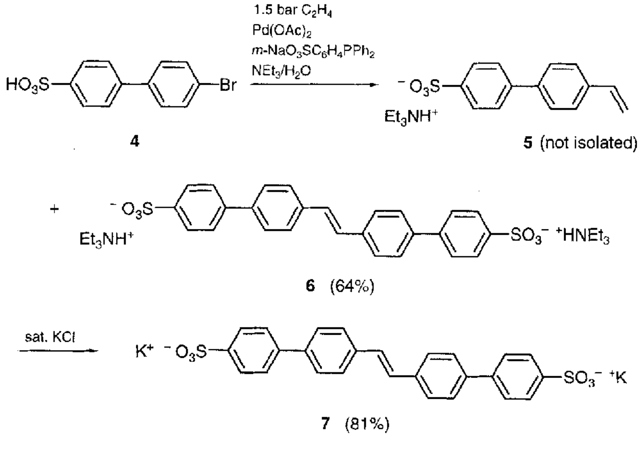
Table 1. Palladium-catalyzed coupling of 4-bromobiphenyl (**1**) with ethene under various conditions

Entry	Conditions	Styrene **2** (%)	Stilbene **3** (%)
1	MeCN (10 ml), 1 mmol **1**, 10 bar C_2H_4	78	trace
2	MeCN (10 ml), 10 mmol **1**, 8 bar C_2H_4	66	< 5
3	MeCN (10 ml), 1 mmol **1**, 6 bar C_2H_4	61	25
4	MeCN (10 ml), 10 mmol **1**, 6 bar C_2H_4	43	14
5	DMF (10 ml), 20 mmol **1**, 2 bar C_2H_4	11	54
6	NMP (13 ml), 42.9 mmol **1**, 1 bar C_2H_4	trace	69

al.[10] The reaction conditions for the coupling of **4** with ethene were first chosen according to our experience with the preparation of BPS **3**; i.e. the first coupling reactions were carried out in NMP with the catalyst system $Pd(OAc)_2/P(o\text{-}Tol)_3$ and an ethene pressure of 0.5–1.5 bar.

Although the yield of the salt **6** under these conditions was probably high enough, it was impossible to isolate it in pure form from the reaction mixture. Therefore the corresponding free acid was prepared by acidification of **6**, then partly purified and again transformed into **6**. The dipotassium salt **7** was obtained from **6** as described below, but its purity was insufficient for use as a laser dye. Better results were achieved by alkenylation of **4** in a concentrated water/triethylamine mixture at an ethene pressure of 1.5 bar. According to reports by Beletskaya et al.[11], palladium-catalyzed alkenylations of haloarenes with alkenes can favorably be carried out in water. Genet et al. reported Heck reactions of substituted iodoarenes with various alkenes in good yields in aqueous acetonitrile using the water-soluble phosphane ligand trisodium triphenylphosphane-3,3′,3″-trisulfonate (TPPTS) and palladium acetate as a catalyst[12]. Applying this ligand as the sodium salt in an aqueous solvent system to the coupling of **4** with ethene led to the problem of separating mixtures of salts with different cations. The best conditions with respect to coupling yield and ease of purification were eventually found to be the use of sodium 3-(diphenylphosphanyl)benzenesulfonate[13] in a mixture of water and triethylamine (Scheme 2).

Scheme 2



The bis(triethylammonium) salt **6** thus obtained (64% yield) was purified by crystallization from methanol/acetone/triethylamine (3:3:2) and finally transformed to the dipotassium salt **7** by adding a saturated solution of potassium chloride to an aqueous solution of **6** (overall yield 52%, based on consumed starting material **4**). The bis(triethylammonium) salt **6** can also be applied as a laser dye, with similar results to those with the dipotassium salt **7**. However, salt **6** is rather hygroscopic and may be contaminated with small amounts of triethylammonium bromide, and therefore it cannot be handled as conveniently as the dipotassium salt **7**. The salt **7** could be obtained on a 100-g scale and was pure enough for use as a laser dye[6a].

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Experimental Section

All palladium-catalyzed coupling reactions were performed in degassed solvents under an ethene atmosphere in 250-ml- and 1000-ml glass autoclaves. – ^1H NMR: Bruker AM 250 (250 MHz), VXR 500 (500 MHz); $\delta = 0$ for TMS, and $\delta = 4.78$ for $[D_3]$methanol. Abbreviations for some groups of protons are Ar-H = aromatic, Olef-H = olefinic. – FT-IR: Bruker IFS 66. – MS: Finnigan MAT 95. – UV/VIS spectra: Cary 219, evaluation and implement steering by HP 9845 B and MPF219 program developed by Dr. B. Knieriem, Universität Göttingen.

(E)-4,4′-Diphenylstilbene (**3**). – *Method 1:* Under a stream of nitrogen, a 250-ml glass autoclave equipped with a magnetic stirring bar was charged with 2.33 g (10.0 mmol) of 4-bromobiphenyl (**1**), 10 ml of DMF, 2.1 ml (15.0 mmol) of triethylamine, 61 mg (0.20 mmol) of tri-*o*-toluylphosphane[9c] and 22 mg (0.10 mmol) of palladium acetate. The autoclave was closed and ethene was added with stirring until a pressure of 2 bar was reached. The reaction mixture was heated to 125°C for 3.5 d. The ethene pressure had to be recharged every 2 h during the first 12 h, and once every 12 h thereafter. The volatile components were removed from the reaction mixture under reduced pressure and the residue was washed twice with 200 ml of warm methanol. The collected solids were suspended in 200 ml of chloroform, and 10 g of silica gel was added to the suspension. The solvent was removed in a rotary evaporator under reduced pressure (20 Torr), the residue was ground up in a mortar and extracted with chloroform in a Soxhlet extractor for 3 d. The solvent was evaporated under reduced pressure (20 Torr). After recrystallization from DMF, 0.90 g (54%) of **3** was obtained as a slightly yellow solid, m.p. 303°C. – IR (KBr): $\tilde{\nu} = 3054\ cm^{-1}$ (ν C–H of C=CH), 3032 (ν C–H of Ar), 1596, 1560, 1488, 1410, 1348, 1158, 973 (*trans*-HC=CH), 840, 763, 689. – UV (dioxane): λ_{max} (lg ε) = 343 nm (4.789). – MS (EI, 70 eV), *m/z* (%): 332 (100) $[M^+]$, 315 (6), 241 (20) $[M^+ - C_7H_7]$, 166 (13) $[M^{2+}]$, 152 (5), 138 (4), 91 (8) $[C_7H_7^+]$, 77 (4) $[C_6H_5^+]$. The combined methanolic filtrates were evaporated under reduced pressure (1 Torr). Chromatography of the residue on 60 g of silica gel (25 × 3 cm, light petroleum) gave 0.20 g (11%) of *4-ethenylbiphenyl* (**2**): [14] – ^1H NMR (250 MHz, $CDCl_3$): δ = 5.27 [dd, ^3J = 10.5, ^2J = 0.8 Hz, 1H, (*E*)-HC=CH_2], 5.79 [dd, ^3J = 17.6, ^2J = 0.8 Hz, 1H, (*Z*)-HC=CH_2], 6.76 (dd, ^3J = 10.5 Hz, ^3J = 17.6 Hz, 1H, *H*C=CH_2), 7.27–7.73 (m, 9H, Ar-H).

The reactions compiled in Table 1 (apart from entry 6) were carried out according to method 1 using various solvents, ethene pressures and concentrations of **1**.

Method 2: A 250-ml glass autoclave equipped with a magnetic stirring bar was charged under a stream of nitrogen with 10.00 g (42.9 mmol) of 4-bromobiphenyl (**1**), 13 ml of anhydrous NMP, 13 ml (93.3 mmol) of triethylamine, 264 mg (0.86 mmol) of tri-*o*-toluylphosphane[9c] and 22 mg (0.43 mmol) of palladium acetate. The autoclave was closed and ethene was added with stirring until a pressure of 1 bar was reached. The reaction mixture was heated with stirring at 100°C for 1 d and at 120°C for a further 2 d. The ethene pressure had to be recharged every 2–3 h during the first 24 h, and thereafter only every 12 h. The nearly solid reaction mixture was suspended in 300 ml of methanol with the aid of ultrasonication; the suspension was heated under reflux and filtered while hot. This procedure was repeated twice with the collected solids. The pale yellow product collected on the filter was dried, suspended in chloroform with 10 g of silica gel, and the solid mixture extracted with chloroform in a Soxhlet extractor for 3 d. The solvent was removed from the extract in a rotary evaporator under reduced pressure (20 Torr). The crude product was sublimed under high vacuum ($p < 10^{-4}$ Torr, 250°C). The sublimate was recrystallized from xylene to yield 4.92 g (69%) of **3** as a pale yellow solid, m.p. 300–302°C. The purity of BPS **3** thus obtained met the standard set for use as a laser dye[6a], with a molar absorption coefficient of $\lg \varepsilon = 4.75$ in the UV spectrum at 343 nm in dioxane.

Dipotassium (E)-4,4'-Diphenylstilbene-4",4'"-disulfonate (Stilbene I) (**7**): A 1-l glass autoclave was charged with a magnetic stirring bar and a mixture of 4'-bromobiphenyl-4-sulfonic acid (**4**; 172 g, 0.55 mol), sodium 3-(diphenylphosphanyl)benzenesulfonate (3.78 g, 10.4 mmol) and demineralized water (174 ml). The autoclave was cooled with ice-water, while triethylamine (189 ml, 1.36 mol) was added slowly with manual stirring until the solids had dissolved. The solution was purged with nitrogen for 10 min under stirring at rt, then Pd(OAc)$_2$ (1.24 g, 5.5 mmol) was added. The autoclave was closed with its nitrogen atmosphere, filled with ethene up to a pressure of 1.4–1.5 bar with intensive magnetic stirring for 10 min, then the ethene pressure was released under a well working hood. This cycle of filling with 1.4–1.5 bar of ethene and releasing was repeated twice, and finally the autoclave was filled with ethene up to a pressure of 1.4–1.5 bar, then heated to 100°C in an oil bath with vigorous stirring. During the first 24 h ethene had to be added every 2–3 h, and later every 12 h. After 72 h the autoclave was cooled to rt, and the remaining ethene was blown off with care. The reaction mixture was transferred into a 1-l flask and the autoclave was washed with small amounts of water and methanol. The solvent was removed under reduced pressure (20 Torr) in a rotary evaporator at 60–80°C, the warm residue was dissolved in 1.5 l of methanol, and 20 g of powdered charcoal was added. After 10 min under reflux the solution was filtered twice through the same filter. Methanol was evaporated under reduced pressure, and the warm residue dissolved again in 300 ml of methanol. To this solution were added carefully 300 ml of acetone and ca. 250 ml of triethylamine, and the clear solution was cooled to between −20 and −30°C. The triethylammonium salt of the stilbene crystallized together with a small amount of triethylammonium hydrobromide; it was filtered off after 30 min and washed with 100 ml of cooled methanol/acetone (1:1, −30°C). The solid was recrystallized twice from methanol/acetone/triethylamine (3:3:2; more triethylamine led to the formation of an oil), and dried in a rotary evaporator at 70°C under reduced pressure (20 Torr) to give 119.9 g of the bis(triethylammonium) salt **6** as a pale yellow hygroscopic powder which contained some triethylammonium bromide.

To a solution of this salt in 500 ml of hot demineralized water, 200 ml of a saturated aqueous solution of potassium chloride was added dropwise with swirling. The mixture was kept at rt for 30 min and filtered. The solid was washed with 20 ml of saturated potassium chloride and twice with 50 ml of water, dried, then treated for 10 min with 400 ml of refluxing water, and filtered again while hot. (At this stage the solid should be slightly yellow or colorless, otherwise this procedure has to be repeated.) The product was washed with 100 ml of cold methanol, 100 ml of acetone and 100 ml of pentane and dried at rt in vacuo (20 Torr), then at 80–100°C (0.01 Torr) to yield 81.5 g (52% based on consumed starting material) of Stilbene I (**7**) as a colorless or slightly yellow powder. Its purity was checked by measuring the extinction at 400 nm of a solution of 12.5 mg of **7** in 25 ml of ethylene glycol in a 1-cm cuvette: $E = 0.15$ (should be $E \leq 0.25$)[6b].

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