Microwave-assisted solvent-free synthesis of (*E*)-stilbenes

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An efficient synthesis of a series of stilbenes is reported using 4-nitrotoluene and substituted arylaldehydes as starting materials in the presence of Cs_2CO_3 and polyethylene glycol under solvent-free microwave irradiation. Compared with conventional method, this strategy exhibited higher stereoselectivity, shorter reaction times and has a lower environmental impact.

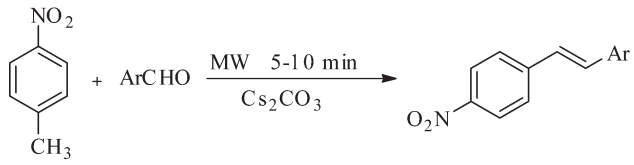
Keywords: stilbene derivatives, Cs_2CO_3, microwave irradiation, arylaldehydes, 4-nitrotoluene

Stilbene-based compounds exist in a variety of plant species and dietary sources[1,2] and are important intermediates in agrochemical[3,4], polymer and pharmaceutical industries.[5,6] Investigations on stilbenes have attracted the attention by biologists and chemists due to their excellent biological activity[7,8] and photophysical properties.[9,10] Applications of stilbenes have extended to anti-fungal, cytotoxic, anti-inflammatory and anti-viral products in the pharmaceutical field.[11] Some hydroxyl substituted (*E*)-stilbenes, such as resveratrol, piceatannol (3,4,3′,5′-tetrahydroxy-*trans*-stilbene),[12] and combretastatin A-4[13] (Fig. 1), have exhibited superior anti-proliferative and pro-apoptotic activity in a number of human cancer cell lines. These compounds have been suggested as potential cancer chemopreventive/chemoprotective agents based on interfering with the dynamics of tubulin polymerization, depolymerization and arresting mitosis.[14] The photochemical and photophysical properties of substituted *trans*-stilbenes which have been fundamental to the understanding of the excited-state behavior of arylalkenes[15] provide a fertile field of investigation, in electroluminescence and light-emitting diodes.[16,17]

There are several strategies for the synthesis of stilbene derivatives, including Wittig reactions,[18] Pd-catalyzed Heck[19,20] and Negishi cross-couplings[21]. However, these procedures have some disadvantages including anhydrous requirement, the use of noble metals and toxic organic solvent, and low stereoselectivity for the *Z*/*E* configuration of C=C bonds. It is of importance to develop simple and green methods for the synthesis of stilbenes. In recent years, microwave (MW) irradiation technology has been widely used to accelerate chemical reactions because of its molecular-level heating.[22,23] Compared with conventional heating method, MW has significant advantages giving shortened reaction times and increased yields.[24] In the present work, we report a novel MW assisted strategy to prepare the stilbene skeleton using the Knoevenagel condensation of 4-nitrotoluene and arylaldehydes in the absence of solvent (Scheme 1).

Results and discussion

The Knoevenagel condensation has been widely used for the preparation of substituted alkenes. Harjani and co-workers reported the use of 1-butyl-3-methylimidazolium chloroaluminate and 1-butylpyridinium chloroaluminate ionic liquids as Lewis acid catalysts in the Knoevenagel condensation for the synthesis of electrophilic mono-aryl alkenes.[25] Although Chidambaram's group used tetrabutylammonium bromide or crown-ether as a phase transfer catalyst in a condensation reaction for the preparation of substituted stilbenes,[26] noxious organic solvents and a long reaction time were required for the process. Herein we present an investigation of the solvent-free synthesis of stilbenes by the Knoevenagel condensation under microwave irradiation with a microwave-induced synthesis/extraction apparatus. The preparation of 3,4,5-trimethoxy-4′-nitrostilbene from 4-nitrotoluene and 3,4,5-trimethoxybenzaldehyde was used as a model reaction in the absence of a solvent to explore the MW promoted effect. A mixture of 15.0 mmol 3,4,5-trimethoxybenzaldehyde, 18.0 mmol 4-nitrotoluene, 30.0 mmol anhydrous K_2CO_3 and 1.7 g polyethylene glycol 400 (PEG-400) as a phase transfer catalyst[27] was introduced into a 50 mL flask. Then the mixture was subjected to MW irradiation at 600 W instead of the conventional heating method reported in our previous work.[28] Unfortunately, it was found that 3,4,5-trimethoxybenzaldehyde was not completely converted to a stilbene even with an extended MW irradiation time of 30 min or increased working power to 850 W. Low yield (18.4%, entry 1 in Table 1) and an unknown by-product in a high ratio were detected by GC/GC-MS. However a better yield (50.4%) was observed (entry 2 in Table 1) when using equivalent Cs_2CO_3 instead of K_2CO_3 under MW irradiation at 600 W, 100 °C for 30 min. In order to adequately mix the reactants, keeping the above condition unchanged, two liquid



Scheme 1 Synthesis of stilbenes from the condensation of 4-nitrotoluene and arylaldehydes

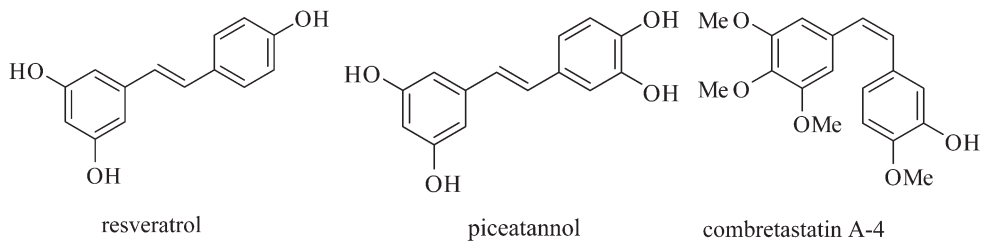


Fig. 1 Structures of resveratrol, piceatannol and combretastatin A-4.

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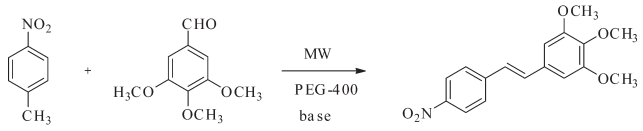
Table 1 Effect of bases on the condensation of 3,4,5-trimethoxybenzaldehyde and 4-nitrotoluene with MW assistance[a]



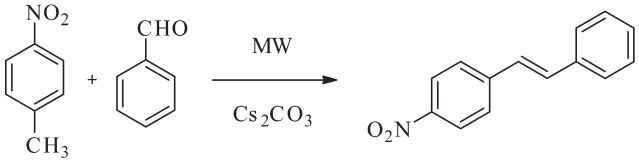
Entry	Base	Additive	PEG-400	Yield/%[b]
1	K_2CO_3	no	1.7 g	18.4
2	Cs_2CO_3	no	1.7 g	50.4
3	Piperidine	no	no	No reaction
4	Pyrrolidine	no	no	No reaction
5	K_2CO_3	Pyrrolidine (1.1 g)	1.7 g	17.5
6	Cs_2CO_3	Pyrrolidine (1.1 g)	1.7 g	41.9
7	K_2CO_3	no	1.7 g	38.4[c]
8	Cs_2CO_3	no	1.7 g	81.7[c]

[a] Conditions: the mixture of 15.0 mmol 3,4,5-trimethoxybenzaldehyde, 18.0 mmol 4-nitrotoluene, 30.0 mmol base was heated at 100 °C for 30 min by MW irradiation with power at 600 W.
[b] Yields determined by GC analysis.
[c] Pre-mixing before MW irradiation and the reaction time was 10 min.

organic bases piperidine[29] and pyrrolidine were selected instead of Cs_2CO_3. Unfortunately, the reaction did not proceed at all (entry 3, 4 in Table 1). We believed that the basicity of piperidine and pyrrolidine were not strong enough to remove the proton of the activated methyl of 4-nitrotoluene to yield the carbanion for the nucleophilic addition to the carbonyl of 3,4,5-trimethoxybenzaldehyde. An improved result was not obtained with K_2CO_3 or Cs_2CO_3 as base in the reaction in the presence of pyrrolidine as additive (entry 5, 6 in Table 1). In further research, an interesting result was observed through the following pre-mixing process. Firstly, a mixture of 4-nitrotoluene, 3,4,5-trimethoxybenzaldehyde and PEG-400 was heated at 60 °C without adding any base (m.p. of 4-nitrotoluene is 51.9 °C), and the mixture completely turned into a liquid. Then K_2CO_3 or Cs_2CO_3 was introduced into the above liquid. Subsequently, the system was irradiated with MW at 600 W and 100 °C. This pre-mixing strategy led to the starting materials being completely consumed in a very short time (10 min) and gave a much higher yield (entry 7, 8 in Table 1). The experiments suggested that higher yield (81.7%) can be obtained with Cs_2CO_3 as base rather than K_2CO_3 (38.4%). These results indicated that pre-mixing step and the use of Cs_2CO_3 are the most important parameters in the MW irradiation process.

In order to further increase the yield in the condensation reaction, benzaldehyde was selected as a model substrate due to its low cost for optimising the MW conditions including working power, temperature and irradiation time. Firstly the starting materials benzaldehyde, 4-nitrotoluene and PEG-400 were heated for pre-mixing. Then the reaction was carried out in the presence of Cs_2CO_3 under MW irradiation at 600 W, 100 °C, 20 min. Unfortunately, significant over-reaction occurred in the experiment. We found that lower power and temperature (500 W, 90 °C) gave a higher yield of 64.2% than that of 52.0% under 600 W, 100 °C in 5 min (entry 2, 3 in Table 2). However, incomplete conversion of benzaldehyde was detected by GC after MW irradiated for 5 min (500 W, 90 °C). When the irradiation time was prolonged to 10 min, benzaldehyde was totally consumed, and the yield was up to 75.4% (entry 4 in Table 2). A longer irradiation time than 10 min gave undesired complex products in the reaction system. Therefore we concluded that the optimised MW condition was as follows: 500 W, 90 °C for 10 min.

Table 2 Effect of microwave conditions on the yields of 4-nitrostilbene[a]

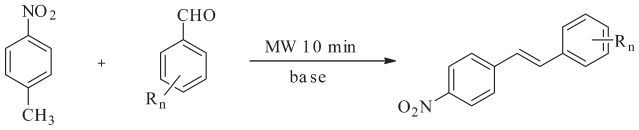


Entry	MW conditions			Yield/%[b]
	Power/W	Temperature/°C	Time/min	
1	600	100 °C	20	39.4
2	600	100 °C	5	52.0
3	500	90 °C	5	64.2
4	500	90 °C	10	75.4

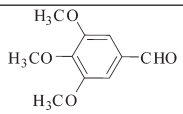
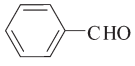
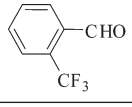
[a] Conditions: to pre-mixure of 15.0 mmol benzaldehyde, 18.0 mmol 4-nitrotoluene and 1.7 g PEG-400, 30.0 mmol Cs_2CO_3 was added. Subsequently, the mixture was irradiated with MW.
[b] Yields were determined by GC/GC-MS.

On the basis of the above optimised MW condition, we further investigated the important role of Cs_2CO_3 in the improvement of yield and stereoselectivity. 3,4,5-Trimethoxybenzaldehyde, benzaldehyde and 2-(trifluoromethyl)benzalde hyde were selected as substrates, and K_2CO_3 was used in the control experiment instead of Cs_2CO_3. The results indicated that a lower yield (38.4%), lower *E*/*Z* ratio (72: 28) and a mass of by-product were detected by GC/GC-MS in the synthesis of 3,4,5-trimethoxy-4′-nitrostilbene in the presence of K_2CO_3, while higher yield of 81.7% with an excellent stereoselectivity (*E*/*Z* ratio=96: 4) were obtained when Cs_2CO_3 was used as a base (entry 1 in Table 3). Both satisfactory yields and high *E*/*Z* ratios were also achieved from other two substrates in the presence of Cs_2CO_3 under MW irradiation. The above results

Table 3 Comparisons of yield and stereoselectivity for the condensation reaction in the presence of K_2CO_3 or Cs_2CO_3 under MW irradiation[a]



R = H, OCH_3, CF_3; n=1~3

Entry	Aromatic aldehyde	K_2CO_3		Cs_2CO_3	
		E/*Z*[b]	Yield/%[c]	*E*/*Z*[b]	Yield/%[c]
1[d]		72: 28	38.4	96: 4	81.7
2[e]		62: 38	45.0	90: 10	75.4
3[f]		62: 38	83.8	88: 12	94.8

[a] Conditions: to pre-mixture of 15.0 mmol aromatic aldehyde, 18.0 mmol 4-nitrotoluene and 1.7 g PEG-400, 30.0 mmol Cs_2CO_3 was added. Subsequently, the mixture was irradiated with MW.
[b] *E*/*Z* ratios determined by GC-MS.
[c] Combined yield of both *E*/*Z* isomers.
[d] Power = 600 W, temperature = 100 °C, t = 10 min.
[e] Power = 500 W, temperature = 90 °C, t = 10 min.
[f] Power = 500 W, temperature = 80 °C, t = 5 min.

demonstrated that Cs_2CO_3 was crucial for the enhanced yield and stereoselectivity during the microwave-assisted synthesis of stilbenes.

As highlighted in Table 4, the method proved to be successful for a wide range of substituted aromatic aldehydes. We maintained the molar ratio of aromatic aldehydes or heteroaryl aldehyde and 4-nitrotoluene at 1: 1.2 in the presence of Cs_2CO_3 and PEG-400 under solvent-free MW irradiation. All arylaldehydes with both electron withdrawing group (EWG) and electron donating group (EDG) completely condensed with 4-nitrotoluene within 10 minutes under the above optimised MW reaction conditions and provided a series of new stilbene derivatives (entry 6–14 Table 4). It was found that the yield of stilbenes was very sensitive to electronic effects.[30,31] Substrates with EDG such as OCH_3 had higher yields, while replacement of EDG with EWG such as F, Cl and Br led to decreased yields. The position of the substitutent also affected the condensation reaction. For instance, arylaldehyde bearing CF_3 group at position-2 gave a higher yield with a lower reaction temperature and shorter time than those with a CF_3 group at position-3 and position-4 (entries 6-8 in Table 4). The results in Table 4 also revealed that excellent stereoselectivity for the *E*/*Z* configuration of C=C bonds (*E*/*Z* ratio = 75–98%) were obtained.

In summary, we have demonstrated a facile microwave-assisted strategy for the preparation of a series of stilbenes under solvent-free condition. When the mixture of substituted arylaldehydes and 4-nitrotoluene (molar ratio at 1:1.2) was heated with microwave irradiation in the presence of Cs_2CO_3 and polyethylene glycol 400, stilbenes with high E/Z ratio for the configuration of C=C bonds can be obtained in short time by Knoevenagel condensation reaction. This novel solvent-free microwave-assisted strategy provided a green and clean process for the synthesis of stilbene derivatives.

Experimental

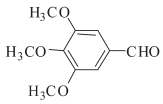
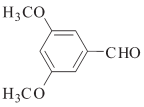
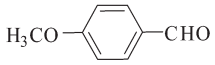
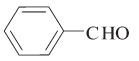
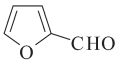
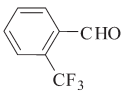
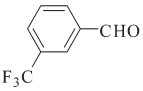
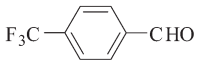
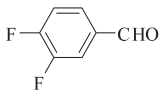
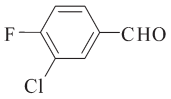
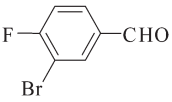
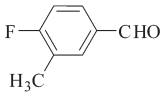
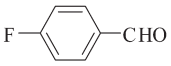
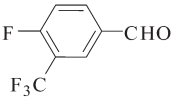
Unless otherwise stated, all chemicals were purchased from commercial sources and used without purification. ^{1}H NMR (300MHz) and ^{13}C NMR (75 MHz) spectra which were recorded using $CDCl_3$ as a solvent on a Bruker Avance 300 MHz spectrometer. Chemical shifts (δ) are reported in parts per million, and coupling constants (J) are in hertz, using TMS as an internal standard. Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The IR spectra were recorded with a Nicolet Avatar 360E.S.P. FT-IR spectrometer using KBr pellets. GC-MS/GC analysis were performed on Shimadzu GCMS-QP2010 apparatus with RTX-5MS capillary column (30 m × 0.25 mm × 0.25 μm). The melting points were determined using X-5 micro melting point instrument (the thermometer was not corrected). High resolution mass spectra were performed on a MaXis UHR-TOF with direct injection of the sample. All reactions were performed in a Xianghu microwave-induced synthesis/extraction apparatus (XH-100B), produced by Beijing Xianghu Science and Technology Development Co., Ltd, Beijing, P. R. China.

Synthesis of stilbene compounds under MW irradiation; general procedure

A mixture of the aromatic aldehyde (15.0 mmol), 4-nitrotoluene (18.0 mmol) and PEG-400 (1.7 g) in a 50 mL three neck flask was heated to melt with magnetic stirring. Then Cs_2CO_3 (30.0 mmol) was introduced into the above mixture. The flask was fixed in a microwave-induced synthesis/extraction apparatus and irradiated for 5–10 min with output power of 500 W or 600 W. The MW reaction was programmed under a constant temperature (80–100 °C). Then the reaction mixtures were washed with water for several times to obtain the crude products. The crude products were analysed by GC and GC-MS. Isolation of products was carried out by recrystallisation from ethanol or silica column chromatography.

All products were characterised by m.p., ^{1}H NMR, ^{13}C NMR, IR, and MS analysis. Selected spectral data for new compounds (entries 6–14) are given as follows.

Table 4 Synthesis of stilbene derivatives with microwave-assistance under optimised conditions[a]

Entry	Substrate	MW irradiation		
		Time/min	E/Z[b]	Yield/%[c]
1		10	96: 4	81.7[d]
2		10	83: 17	83.1[e]
3		10	92: 8	52.2[f]
4		10	90: 10	75.4[f]
5		5	98: 2	98.5[e]
6		5	88: 12	94.8[f]
7		10	82: 18	72.8[e]
8		10	83: 17	72.1
9		10	93: 7	30.5
10		10	93: 7	69.1
11		10	83: 17	26.7
12		10	75: 25	11.0
13		10	94: 6	60.9
14		10	92: 8	18.5

[a] The reaction conditions: to pre-mixture of 15.0 mmol aromatic aldehyde, 18.0 mmol 4-nitrotoluene and 1.7 g PEG-400, 30.0 mmol Cs_2CO_3 was added, then the mixture was irradiated with MW at 500 W, 100 °C.
[b] *E*/*Z* ratios were determined by GC-MS analysis.
[c] Yields were obtained by GC analysis.
[d] Power = 600 W, temperature = 100 °C.
[e] Power = 500 W, temperature = 90 °C.
[f] Power = 500 W, temperature = 80 °C.

trans-3,4,5-Trimethoxy-4'-nitrostilbene (entry 1 Table 4): Yellow solid; m.p. 193.2–194.8 °C (lit.[32], m.p. 192–193 °C).

trans-3,5-Dimethoxy-4'-nitrostilbene (entry 2 Table 4): Yellow solid; m.p. 134.6–135.3 °C (lit.[32], m.p. 134–135°C).

trans-4-Methoxy-4′-nitrostilbene (entry 3 Table 4): Yellow solid; m.p. 128.1–130.1 °C (lit.[33], m.p. 129–130 °C).

trans-4-Nitrostilbene (entry 4 Table 4): Yellow solid; m.p. 155.4–156.1 °C (lit.[34], m.p. 150–155 °C).

trans-2-(4-Nitrostyryl)furan (entry 5 Table 4): Yellow solid; m.p. 130.9–131.9 °C (lit.[35], m.p. 128–131 °C).

trans-2-Trifluoromethyl-4′-nitrostilbene (entry 6 Table 4): Yellow solid; m.p. 124.6–126.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.23 (d, 2H, *J* = 8.8 Hz), 7.78 (d, 1H, *J* = 7.8 Hz), 7.59–7.72 (m, 5H), 7.43 (m, 1H), 7.14 (d, 1H, *J* = 16.1 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 146.3, 142.2, 131.2, 129.5, 129.3, 127.9, 127.4, 126.6, 126.3, 125.3, 123.2, 122.6, 121.5; IR: ν_{max} 3076, 1650, 1592, 1514, 1456, 1336, 1317, 1155, 1103, 1037, 960, 850, 830, 760, 683, 530; HRMS (ESI-TOF) for $C_{15}H_{10}F_3NO_2$ [M+Na]: Calcd: 316.0561, found: 316.0547.

trans-3-Trifluoromethyl-4′-nitrostilbene (entry 7 Table 4): Yellow solid; m.p. 121.5–122.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.23 (d, 2H, *J* = 8.4 Hz), 7.80 (s, 1H), 7.50–7.73 (m, 5H), 7.27 (d, 1H, *J* = 16.4 Hz), 7.24 (d, 1H, *J* = 16.4 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 146.7, 142.6, 136.5, 131.1, 129.6, 128.9, 127.6, 126.6, 124.7, 123.7, 123.1, 121.7; IR: ν_{max} 3035, 1636, 1594, 1509, 1446, 1339, 1191, 1121, 1069, 968, 865, 834, 798, 693; HRMS (ESI-TOF) for $C_{15}H_{10}F_3NO_2$ [M+Na]: Calcd: 316.0561, found: 316.0544.

trans-4-Trifluoromethyl-4′-nitrostilbene (entry 8 Table 4): Yellow solid; m.p. 171.4–172.8°C; ^{1}H NMR(300 MHz, $CDCl_3$) δ: 8.22 (d, 2H, *J* = 8.6 Hz), 7.65–7.67 (m, 6H), 7.26 (d, 1H, *J* = 16.2 Hz), 7.24 (d, 1H, *J* = 16.2 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 146.7, 142.5, 139.1, 131.1, 129.7, 128.3, 126.7, 126.6, 125.4, 125.3, 123.7; IR: ν_{max} 3107, 3039, 1636, 1613, 1593, 1511, 1418, 1325, 1160, 1107, 1065, 1012, 973, 951, 849, 818, 752, 686; HRMS (ESI-TOF) for $C_{15}H_{10}F_3NO_2$ [M+Na]: Calcd: 316.0561, found: 316.0548.

trans-3,4-Difluoro-4′-nitrostilbene (entry 9 Table 4): Yellow solid; m.p. 181.4–182.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.21 (d, 2H, *J* = 8.8 Hz), 7.63 (d, 2H, *J* = 8.8 Hz), 7.36–7.37 (m, 1H), 7.19 (d, 1H, *J* = 16.3 Hz), 7.14 (m, 2H), 7.07 (d, 1H, *J* = 16.3 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 151.2, 147.8, 146.1, 142.2, 132.5, 130.0, 126.4, 126.1, 123.2, 122.6, 116.7, 114.1; IR: ν_{max} 3112, 3051, 1636, 1602, 1591, 1516, 1432, 1339, 1292, 1269, 1107, 965, 863, 835, 748; HRMS (ESI-TOF) for $C_{14}H_9F_2NO_2$ [M+Na]: Calcd: 284.0499, found: 284.0488.

trans-3-Chloro-4-fluoro-4′-nitrostilbene (entry 10 Table 4): Yellow solid; m.p. 159.2–163.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.25 (d, 2H, *J* = 8.3 Hz), 7.64 (bs, 1H), 7.61 (d, 2H, *J* = 8.3 Hz), 7.41 (bs, 1H), 7.20 (m, 1 H), 7.14 (d, 1H, *J* = 16.2 Hz), 7.09 (d, 1H, *J* = 16.2 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 159.3, 155.9, 142.6, 133.1, 130.2, 129.1, 128.3, 126.9, 123.7, 123.3 116.7, 116.4; IR: ν_{max} 3072, 3037, 1695, 1635, 1594, 1509, 1345, 1251, 1108, 1055, 969, 864, 835, 811, 735, 702, 577; HRMS (ESI-TOF) for $C_{14}H_9ClFNO_2$ [M+Na]: Calcd: 300.0204, found: 300.0192.

trans-3-Bromo-4-fluoro-4′-nitrostilbene (entry 11 Table 4): Yellow solid; m.p. 172.7–173.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.21 (d, 2H, *J* = 8.5 Hz), 7.76 (d, 1H, J = 6.1 Hz), 7.63 (d, 2H, *J* = 8.5 Hz), 7.43–7.45 (m, 1H), 7.15–7.17 (m, 1H), 7.14 (d, 1H, *J* = 16.3 Hz), 7.08 (d, 1H, *J* = 16.3 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 160.8, 157.5, 147.1, 143.1, 133.9, 131.7, 130.6, 127.6, 126.9, 124.2, 117.0, 116.7; IR: ν_{max} 3070, 3036, 1635, 1592, 1509, 1341, 1248, 1109, 1042, 967, 865, 834, 810, 698; HRMS (ESI-TOF) for $C_{14}H_9BrFNO_2$ [M+Na]: Calcd: 343.9698, found: 343.9687.

trans-4-Fluoro-3-methyl-4′-nitrostilbene (entry 12 Table 4): Yellow solid; m.p. 114.7–115.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.20 (d, 2H, *J* = 8.8 Hz), 7.62 (d, 2H, *J* = 8.8 Hz), 7.32–7.39 (m, 2H), 7.17 (d, 1H, *J* = 16.3 Hz), 7.06 (d, 1H, *J* = 16.3 Hz), 7.02 (d, 1H, *J* = 8.4 Hz), 2.31 (s, 3H); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 163.3, 160.0, 146.7, 143.8, 132.1, 130.1, 126.8, 126.1, 125.7, 124.2, 115.7, 115.4, 14.6; IR: ν_{max} 3068, 3034, 2921, 1634, 1587, 1502, 1457, 1339, 1246, 1216, 1107, 969, 866, 836, 808, 748; HRMS (ESI-TOF) for $C_{15}H_{12}FNO_2$ [M+Na]: Calcd: 280.0750, found: 280.0737.

trans-4-Fluoro-4′-nitrostilbene (entry 13 Table 4): Yellow solid; m.p. 138.0–139.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.21 (d, 2H, *J* = 8.8 Hz), 7.60 (d, 2H, *J* = 8.8 Hz), 7.52 (dd, 2H, *J* = 8.6, 5.5 Hz), 7.20 (d, 1H, *J* = 16.3 Hz), 7.09 (d, 2H, *J* = 8.6 Hz), 7.08 (d, 1H, *J* = 16.3 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 164.7, 161.4, 143.7, 132.4, 128.6, 127.5, 126.8, 126.1, 124.2, 116.0; IR: ν_{max} 3108, 3076, 1631, 1589, 1509, 1420, 1337, 1234, 1157, 1108, 976, 845, 818, 748, 709, 685, 528; HRMS (ESI-TOF) for $C_{14}H_{10}FNO_2$ [M+Na]: Calcd: 266.0593, found: 266.0582.

trans-4-Fluoro-3-trifluoromethyl-4′-nitrostilbene (entry 14 Table 4): Yellow solid; m.p. 174.5–176.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.22 (d, 2H, *J* = 8.3 Hz), 7.78 (d, 1H, *J* = 6.8 Hz), 7.71 (d, 1H, *J* = 6.8 Hz), 7.66 (d, 2H, *J* = 8.3 Hz), 7.21 (d, 1H, *J* = 16.4 Hz), 7.24 (s, 1H), 7.15 (d, 1H, *J* = 16.4 Hz); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 164.7, 158.6, 147.2, 142.9, 132.8, 132.0, 130.4, 127.9, 127.1, 125.5, 124.2, 117.7, 117.4; IR: ν_{max} 3073, 3038, 1638, 1617, 1594, 1506, 1430, 1337, 1243, 1127, 1051, 964, 837, 687, 540; HRMS (ESI-TOF) for $C_{15}H_9F_4NO_2$ [M+Na]: Calcd: 334.0467, found: 334.0453.

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