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Amberlyst-15: an efficient and reusable catalyst for the Friedel–Crafts reactions of activated arenes and heteroarenes with α-amido sulfones

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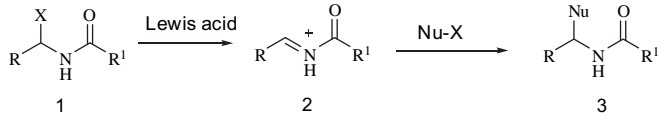
ABSTRACT

The heterogeneous Amberlyst-15 catalyst displays efficient catalytic properties for the Friedel–Crafts reactions between an activated arenes or heteroarenes and α-amido sulfones. Various α-amido sulfones on treatment with 1,2,4-trimethoxy benzene give the Friedel–Crafts reaction products in very good yield. The reactions with heteroarenes show moderate yield of the product. The catalyst can be easily recycled without significant loss of activity.

1. Introduction

The Friedel–Crafts reactions represent a powerful tool to introduce new carbon–carbon bond in aromatic compounds.[1] This reactions can be used for a method to build up polycyclic structure as well.[2] The application of α-amido sulfones has been utilized through the formation of *N*-acyl iminium ions on treatment with Lewis acid (Scheme 1).[3]



Scheme 1. Nucleophilic substitution of α-amido sulfones through *N*-acyl iminium ions.

The poor electrophilic properties of *N*-alkyl and *N*-aryl imines can be augmented by the substitution of electron-attracting group on nitrogen atom. The enhanced electrophilic character of *N*-acyliminium ions allows their reactions with a variety of nucleophiles, which have been utilized to introduce substituent at α-carbon. The reaction of *N*-acyl iminium ions has been utilized for the synthesis of *N*-arylsulfonyl α-amino nitriles,[4a] *N*-homoallylic amines,[4b] α,β-dipeptides,[4c] (1-alkyl-1-aryl)methyl phenyl sulfones,[4d] and α-amino phosphonates.[4e] Mecozzi et al. have reported the reactions of electron-rich aromatic nucleophiles with *N*-acyl iminium ions catalyzed by titanium tetrachloride.[4f] Das et al. have utilized the α-amido sulfones for the synthesis of aza-Morita–Baylis–Hilman adduct using DABCO as an efficient catalyst.[4g] Ballini et al. have demonstrated that the Montmorillonite K-10 could be an efficient catalyst for the Friedel–Crafts reactions of α-amido sulfones with indoles for the synthesis of 3-substituted indoles.[4h]

Development of efficient and practical catalysts for the organic transformation is a considerable interest to both academia and industry.[5] While homogeneous catalysts exhibit the advantage of high activity and selectivity in broad range of synthetic chemistry,[6] their practical application remains limited due to the difficulties associated with their toxicity, disposal of acidic wastes and catalyst/product separation. Heterogeneous catalysis is an another interesting area in organic synthesis as it provides not only an alternative to homogeneous catalysis but also has the advantage of easy catalyst recovery, recycling and mild reaction condition. The introduction of solid acid catalysts such as sulfated zirconia,[7] heteropoly acids,[8] acidic polymers,[9] clays and zeolites[10] has enhanced the development of replacement of liquid acid catalysts for organic transformations. In this regard, acidic cation-exchange polymer resin represents a suitable solid acid material. Amberlyst-15 is one of the polymeric cation-exchange resin with sulfonic acid functionality used as heterogeneous catalysis in non-aqueous as well as aqueous media. Amberlyst-15 retains various advantages such as nontoxic, reusability, non-corrosive, chemical and physical stability and environmental compatibility. The unique properties have lead to the application of Amberlyst-15 as a powerful catalyst for various organic transformations such as Michael addition of pyrroles to α,β-unsaturated ketones.[11a] This can be also utilized for the synthesis of various compounds such as benzodiazepines,[11b] bis and tris

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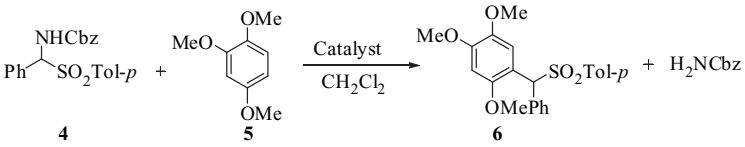
Table 1
Amberlyst-15-catalyzed reactions of *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone with 1,2,4-trimethoxy benzene[a]



4 **5** **6**

Cbz: benzyloxycarbonyl H_2NCbz: aminobenzyloxycarbonyl

Entry	Catalyst	Temp (°C)	Reaction time (h)	Yield[b] (%)
1	Nafion-SAC-13	rt	18	16
2	Nafion-NR50	rt	18	NR
3	$HClO_4$-SiO_2	rt	13	43
4	Amberlyst-15	rt	18	58
5	Amberlyst-15	Reflux	6	86
6	PMA–SiO_2	rt	18	39

[a] Reagent and conditions: 1 mmol of α-amido sulfons, 1 mmol of 1,2,4-trimethoxy benzene and 50 mg of catalyst in CH_2Cl_2 were employed for the reaction.
[b] Isolated yield.

(1*H*-indole-3-yl)methanes,[11c] allyl amides,[11d] xanthenes,[11e,f] α-hydroxy phosphonates,[11g] α-aminophosphate,[11h] and 2,3-unsaturated glycodides.[11i]

2. Results and discussions

In light of the success in developing several catalytic systems for carbon–carbon bond formation reactions,[12] we extend our studies to the Amberlyst-15-catalyzed Friedel–Crafts reactions of α-amido sulfones with electron-rich aromatic compounds and heteroarenes. This could be the first example of Amberlyst-15-catalyzed synthesis of diaryl sulfones.

Various heterogeneous catalysts have been tested for reactions of *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone with 1,2,4-trimethoxy benzene in CH_2Cl_2 (Table 1).

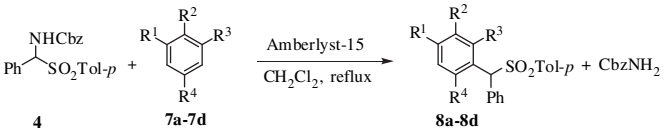
Nafion-NR 50 shows no reactivity towards the Friedel–Crafts reactions while other heterogeneous catalysts such as Nafion-SAC-13, $HClO_4$–SiO_2 and PMA–SiO_2 indicate the moderate reactivity (16–43% yield and 13–18 h). Fortunately Amberlyst-15 has exhibited the higher yield of product (58%) within 18 h reaction time. The result promotes us to increase the reaction temperature up to reflux that gives the highest yield of diaryl sulfones (86%). Accordingly, 50 mg of Amberlyst-15 is sufficient enough for the Friedel–Crafts reactions of α-amido sulfones with 1,2,4-trimethoxy benzene.

The reactivity of various activated benzenes with *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone is investigated for the production of diaryl sulfone. 1,2,4-trimethoxy benzene shows the best result in terms of reaction time and yield (Table 2).

A variety of *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfones were prepared from aromatic and aliphatic aldehydes. They are able to produce the corresponding diaryl sulfones in excellent yield (Table 3). *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone containing electron donating MeO- and Me- groups in the phenyl ring is successfully converted to the corresponding diaryl sulfones with quite high yield (entries 2–3 and 6–8). α-Amido sulfones with aromatic ring substituted with deactivating NO_2– and CN– groups require quite longer reaction time for the reaction to take place (entries 4 and 5). The use of α-amido phenyl sulfone demonstrates similar effect on reactivity relative to α-amido *p*-tolylsulfone (entry 7). α-Amido sulfones derived from acid-sensitive heterocyclic 2-thiophenaldehyde and 2-furaldehyde undergo smoothly for the formation of the products (entries 9 and 10). The electronic and steric effects of chlorine substituted α-amido sulfones have been assessed for the Friedel–Crafts reactions. It was observed that *o*- and *m*-chloro benzenes take longer reaction time relative to *p*- substituted benzene but with comparable yields (entries 11–13). When R in **9** is hydrocinnamyl group, the reaction time is prolonged to 10 h (entry 14). The heterogeneous catalytic protocol is also able to produce diaryl sulfones from corresponding aliphatic compounds (entries 15 and 18). Relative to the cyclic compound, acyclic aliphatic compounds require longer reaction time with lower yield (6 h and 59%).

The reactions of heteroarenes like indole, 2-methyl indole, *N*-methyl indole and methyl indole-6-caboxylate give the moderate yield of corresponding products (Table 4). Reactions of α-amido sulfone with less activated, deactivated and non-activated arenes are examined (Table 5). Less activated arenes such as aniline and anisole as well as non-activated arenes such as benzene show no product formation under the reaction condition. Similarly deactivated arenes of chlorobenzene, nitrobenzene and bromobenzene are again unable to give the corresponding Friedel–Crafts products at all. Relative to activated arenes heteroarenes takes longer reaction time with lower yield. A similar work has been reported by Reutrakul et al.[4d] Our result includes that R of **9** corresponds to variously substituted phenyl (entries 1–8, Table 3) and heteroaromatics (entries 9 and 10, Table 3). Only *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone, that is R in **9** is phenyl is shown in Reutrakul's work with lower yield (76%) than ours (87–91%). Heterogeneous catalyst (Amberlyst-15) allows reusability, which homogeneous one [$Yb(OTf)_3$] could hardly achieve. Reutrakul et al. carried out the reactions at rt while our reactions require reflux temperature. Anisole could not be alkylated under

Table 2
Amberlyst-15-catalyzed reactions of *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone with electron-rich arenes[a]



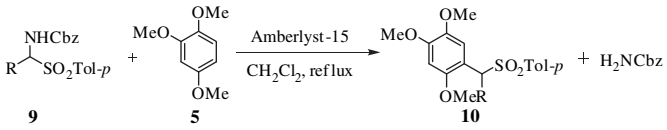
4 **7a-7d** **8a-8d**

7a: R^1,R^2, R^3 = OMe, R^4,R^5, R^6= H
7b: R^1, R^3, R^5 = OMe, R^2,R^4,R^6= H
7c: R^1,R^2,R^4 = OMe, R^3, R^5, R^6= H
7d: R^1, R^3 = OMe, R^2, R^4,R^5,R^6= H

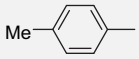
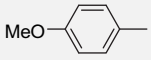
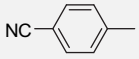
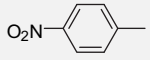
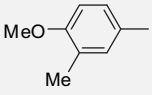
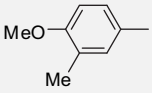
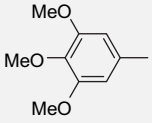
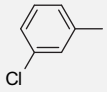
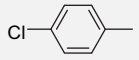
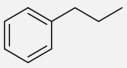
Entry	Arenes (7)	Products	Time (h)	Yield[b] (%)
1	1,2,3-trimethoxy benzene (7a)	8a	6.5	83
2	1,3,5-trimethoxy benzene (7b)	8b	6.5	81
3	1,2,4-trimethoxy benzene (7c)	8c	6	88
4	1, 3-dimethoxy benzene (7d)	8d	10	72

[a] Reagent and conditions: 1 mmol of *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone, 1 mmol of arenes and 50 mg of Amberlyst-15 were used at reflux temperature.
[b] Isolated yield.

Table 3
Amberlyst-15-catalyzed reactions of α-amido sulfons with 1,2,4-trimethoxy benzene[a]

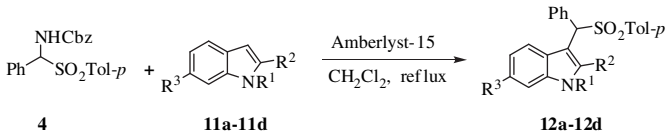


9 **5** **10**

Entry	R in 9	10	Time (h)	Yield[b] (%)
1		10a	6	87
2		10b	4	88
3		10c	4	87
4		10d	8	86
5		10e	7	78
6		10f	4	90
7		10g	4	90[c]
8		10h	4	91
9		10i	10	79
10		10j	3	90
11		10k	8	86
12		10l	7	88
13		10m	5	88
14		10n	10	83
15		10o	4	91
16		10p	4	84
17		10q	6	59
18		10r	8	55

[a] Reagent and conditions: 1 mmol of α-amido sulfons, 1 mmol of 1,2,4-trimethoxy benzene and 50 mg of Amberlyst-15 were employed at reflux.
[b] Isolated yield.
[c] Instead of -SO_2-Tol-*p*, -SO_2-Ph was used.

Table 4
Amberlyst-15-catalyzed reactions of *N*-benzyloxycarbonylamino phenyl *p*-tolylsulfone with heteroarenes[a]



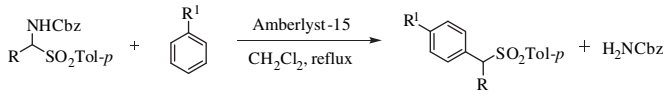
4 **11a-11d** **12a-12d**

11a: R^1 = H, R^2 = H
11b: R^1 = H, R^2 = Me
11c: R^1 = Me, R^2 = H
11d: R^1, R^2 = H, R^3 = CO_2Me

Entry	11	Products	Time (h)	Yield[b] (%)
1	Indole	12a	6	51
2	2-methyl indole	12b	6	45
3	*N*-methyl indole	12c	5	48
4	Methyl indole-6-carboxylate	12d	6	45

[a] Reagent and conditions: 1 mmol of α-amido sulfons, 1 mmol indole and 50 mg of Amberlyst-15 were employed at reflux.
[b] Isolated yield.

Table 5
Amberlyst-15-catalyzed reaction of *N*-benzyloxycarbonylamino phenyl tolylsulfone with non-activated and deactivated arenes[a]



4 **17** **18a-18f**

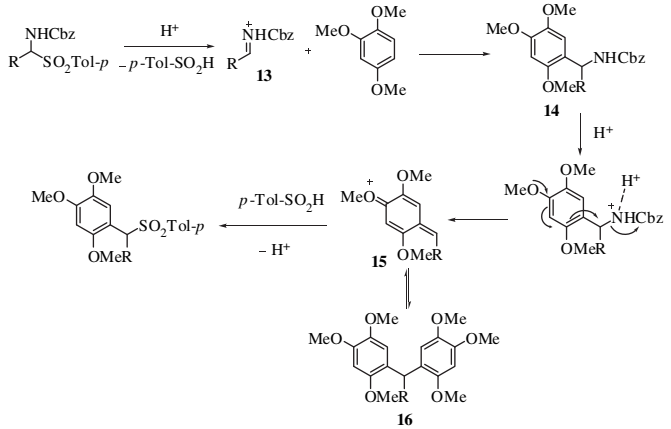
17a = OMe, 17b = NH_2, 73c = Br,
17d = Cl, 17e = NO_2 17f = H

Entry	17	Yield
1	Anisole	NR
2	Aniline	NR
3	Bromobenzene	NR
4	Chlorobenzene	NR
5	Nitrobenzene	NR
6	Benzene	NR

[a] Reagent and conditions: 1 mmol of α-amido sulfons, 1 mmol arenes (**17**) and 50 mg of Amberlyst-1were reflux for 8 h.

our reaction condition but Reutrakul managed the alkylation of anisole with low yield (11%). Heteroarenes demonstrates comparable outcome with similar reaction time on both works. (Table 3 of Ref. 4d and Table 4 from ours).

A plausible mechanism for the formation of Friedel–Crafts products is shown in Scheme 2. α-Amido sulfones on treatment with Amberlyst-15 give the *N*-acyliminium ions **13** through elimination of arenesulfinic acid. The reaction of strong



Scheme 2. Mechanism for the Amberlyst-15-catalyzed Friedel–Crafts reactions of α-amido sulfone with 1,2,4-trimethoxy benzene.

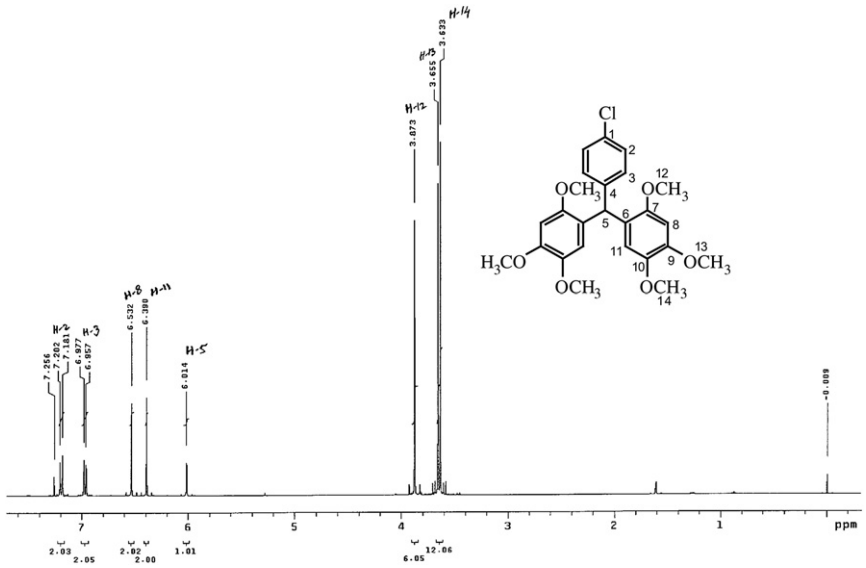


Figure 1. ^{1}H NMR of 5,5′-((4-chlorophenyl)methylene)-bis-(1,2,4-trimethoxy benzene) **16**.

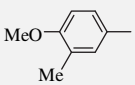
electrophilic *N*-acyliminium ions **13** with 1,2,4-trimethoxy benzene gives rise to the alkylation products **14**, which are converted to oxonium ions **15** with the elimination of carbamate. The oxonium ion **15** then reacts with 1,2,4-trimethoxy benzene in a second Friedel–Crafts reactions giving rise to bis-arene through reversible reaction **16**. The spot of bis-arene **16** has been detected (3 h) just above the mark of the desired product by TLC analysis that completely disappeared at the end of reaction (5 h). 5,5′-((4-Chlorophenyl)methylene)-bis-(1,2,4-trimethoxy benzene) **16** was isolated from reaction mixture after 3 h reaction time and characterized by NMR analysis (Fig. 1). The formation of **16** indicates that the reaction proceed through oxonium ion **15**. The oxonium ions 15 undergo the reaction with *p*-Tol–SO_2H to produce the desired diaryl sulfones. [4h]

We have turned our attention to the reusability of Amberlyst-15. The recycling of the solid acid is an important factor in heterogeneous reaction. The major advantage of heterogeneous catalyst is easy recovery by filtration or centrifugation. Amberlyst-15 is consecutively reused by simple filtration without any special treatment and the results are shown in Table 6.

3. Summary

A novel and efficient catalytic method has been developed for the synthesis of diaryl sulfones through Friedel–Crafts reactions of α-amido sulfones with the activated arenes and heteroarenes. α-Amido sulfones derived from various types of aldehydes are coupled with activated benzenes using Amberlyst-15 as a heterogeneous catalyst. Amberlyst-15 is inexpensive, non-corrosive solid acid and can be recycled.

Table 6
Recycling of Amberlyst-15 for Friedel–Crafts reactions of α-amido sulfones with 1,2,4-trimethoxy benzene

Entry	α-amido sulfone	Cycle	Yield[a] (%)
1		1	90
		2	90
		3	88
		4	85

[a] Isolated yield.

4. Experimental section

4.1. General

In all cases the ^{1}H NMR (400 MHz) spectra were recorded with Varian Gemini 2000 spectrometer. Chemical shifts were reported in ppm in $CDCl_3$ with tetramethylsilane as an internal standard. ^{13}C NMR data were collected on a Varian Gemini 2000 spectrometer (50 MHz). All products were identified by HRMS (EI) with Jeol DMX 303.

4.2. General procedure for the synthesis of diaryl sulfones

To a mixture of α-amido sulfones (1 mmol) and 1,2,4-trimethoxy benzene or heteroarenes (1.0 mmol), Amberlyst-15 (50 mg) were added in CH_2Cl_2 and the mixture was stirred at reflux condition. The completion of the reaction was monitored with TLC. After the completion of reaction, the reaction mixture was filtered and concentrated. The viscous mass was subjected to silica gel flash column chromatography to obtain the pure compound.

^{1}H, ^{13}C NMR data and HRMS values for all products are given below.

4.2.1. Compound ***8a***. White solid, mp 88–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, J=8.2 Hz, 1H), 7.53–7.49 (m, 4H), 7.29–7.27 (m, 3H), 7.14 (d, J=8.5 Hz, 2H), 6.74 (d, J=8.2 Hz, 1H), 5.88 (s, 1H), 3.84 (s, 3H), 3.71 (s, 3H), 3.58 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 153.9, 152.0, 144.2, 135.8, 133.6, 130.1, 129.2, 129.0, 128.6, 128.4, 124.4, 119.5, 107.3, 67.2, 61.0, 60.6, 55.9, 21.6; HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{24}O_5S$: 412.1344, found: 412.1342.

4.2.2. Compound ***8b***. White solid, mp 128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, J=8.4 Hz, 2H), 7.50 (d, J=8.5 Hz, 2H), 7.25–7.39 (m, 3H), 7.17 (d, J=8.4 Hz, 2H), 6.15 (s, 1H), 6.06 (s, 2H), 3.77 (s, 3H), 3.64 (s, 6H), 2.37 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 161.6, 143.3, 138.2, 134.4, 130.2, 128.8, 128.7, 127.8, 127.5, 104.3, 91.0, 67.7, 55.6, 55.2, 21.5; HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{24}O_5S$: 412.1344, found: 412.1316.

4.2.3. Compound ***8c***. Light yellow solid, mp 171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (s, 1H), 7.57 (d, J=8.4 Hz, 2H), 7.50 (d, J=8.0 Hz, 2H), 7.31–7.29 (m, 3H), 7.14 (d, J=8.4 Hz, 2H), 6.23 (s, 1H),

5.98 (s, 1H), 3.91 (s, 3H), 3.82 (s, 3H), 3.51 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.6, 149.8, 144.0, 143.0, 135.9, 133.5, 129.9, 128.9, 128.8, 128.5, 128.2, 113.1, 112.9, 96.8, 66.3, 56.5, 56.3, 55.9, 21.5; HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{24}O_5S$: 412.1344, found: 412.1343.

4.2.4. Compound ***8d***. White solid, mp 110–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, J=8.0 Hz, 1H), 7.64 (d, J=8.5 Hz, 2H), 7.56 (d, J=8.5 Hz, 2H), 7.36–7.33 (m, 3H), 7.19 (d, J=8.0 Hz, 2H), 6.62 (d, J=8.5 Hz, 1H), 6.32 (s, 1H), 6.03 (s, 1H), 3.82 (s, 3H), 3.54 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 160.9, 157.9, 144.1, 136.0, 133.7, 130.8, 130.2, 129.0, 128.5, 128.2, 114.3, 104.7, 98.3, 66.4, 55.4, 55.3, 21.6; HRMS-EI (m/z): $[M]^+$ calcd for $C_{22}H_{22}O_4S$: 382.1239, found: 382.1263.

4.2.5. Compound ***10b***. White solid, mp 122–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (s, 1H), 7.51 (d, J=8.4 Hz, 2H), 7.45 (d, J=8.0 Hz, 2H), 7.14 (d, J=8.0 Hz, 2H), 7.12 (d, J=8.4 Hz, 2H), 6.31 (s, 1H), 5.95 (s, 1H), 3.91 (s, 3H), 3.82 (s, 3H), 3.50 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.6, 149.8, 143.9, 143.1, 138.2, 136.1, 129.9, 129.3, 129.0, 128.9, 113.3, 113.2, 96.9, 66.1, 56.6, 56.4, 56.0, 21.6, 21.1; HRMS-EI (m/z): $[M]^+$ calcd for $C_{24}H_{26}O_5S$: 426.1501, found: 426.1511.

4.2.6. Compound ***10c***. White solid, mp 143.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (s, 1H), 7.52–7.48 (m, 4H), 7.14 (d, J=8.0 Hz, 2H), 6.84 (d, J=8.6 Hz, 2H), 6.32 (s, 1H), 5.93 (s, 1H), 3.92 (s, 3H), 3.82 (s, 3H), 3.76 (s, 3H), 3.51 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 159.6, 151.6, 149.8, 144.0, 143.1, 136.0, 131.3, 129.0, 128.8, 125.3, 114.0, 113.3, 113.1, 97.0, 65.8, 56.6, 56.5, 56.0, 55.2, 21.5; HRMS-EI (m/z): $[M]^+$ calcd for $C_{24}H_{26}O_6S$: 442.1450, found: 442.1460.

4.2.7. Compound ***10d***. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, J=8.4 Hz, 2H), 7.56 (d, J=8.4 Hz, 2H), 7.46 (d, J=8.0 Hz, 2H), 7.44 (s, 1H), 7.13 (d, J=8.4 Hz, 2H), 6.27 (s, 1H), 5.96 (s, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.46 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.6, 150.3, 144.5, 143.1, 138.9, 135.3, 132.1, 130.6, 129.1, 128.7, 118.3, 112.8, 111.9, 111.5, 96.7, 66.9, 56.6, 56.1, 55.9, 21.5; EI (m/z): $[M]^+$ 437, 283, 282, 266.

4.2.8. Compound ***10e***. Yellow solid, mp 148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, J=8.6 Hz, 2H), 7.73 (d, J=8.2 Hz, 2H), 7.46 (d, J=8.6 Hz, 2H), 7.43 (s, 1H), 7.11 (d, J=8.2 Hz, 2H), 6.28 (s, 1H), 6.04 (s, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 3.44 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.5, 150.2, 147.2, 144.5, 142.9, 140.8, 135.0, 130.7, 129.0, 128.5, 123.3, 112.6, 111.2, 96.5, 65.5, 56.4, 56.0, 55.7, 21.3; HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{23}NO_7S$: 457.1195, found: 457.1189.

4.2.9. Compound ***10f***. White solid, mp 146–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (s, 1H), 7.47 (d, J=8.2 Hz, 2H), 7.37 (d, J=8.0 Hz, 1H), 7.22 (s, 1H), 7.08 (d, J=8.2 Hz, 2H), 6.71 (d, J=8.0 Hz, 1H), 6.26 (s, 1H), 5.86 (s, 1H), 3.87 (s, 3H), 3.76 (s, 3H), 3.73 (s, 3H), 3.44 (s, 3H), 2.29 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 157.6, 151.4, 149.6, 143.7, 142.9, 135.9, 132.3, 128. 8, 128.7, 128.3, 126.5, 124.5, 113.2, 113.1, 109.7, 96.8, 65.6, 56.5, 56.2, 55.8, 55.1, 21.3, 16.1; HRMS-EI (m/z): $[M]^+$ calcd for $C_{25}H_{28}O_6S$: 456.1607, found: 456.1597.

4.2.10. Compound ***10g***. White solid, mp 131–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, J=8.4 Hz, 2H), 7.57 (s, 1H), 7.49–7.42 (m, 2H), 7.33 (t, J=7.6 Hz, 2H), 7.27 (s, 1H), 6.76 (d, J=8.4 Hz, 1H), 6.27 (s, 1H), 5.92 (s, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 3.77 (s, 3H), 3.45 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 157.8, 151.5, 149.8, 143.0, 138.9, 132.9, 128.7, 128.4, 128.2, 126.7, 124.3, 113.3, 113.1, 109.8, 96.8, 65.7, 56.5, 56.2, 55.8, 55.1, 16.1; HRMS-EI (m/z): $[M]^+$ calcd for $C_{24}H_{26}O_6S$: 442.1450, found: 442.1460.

4.2.11. Compound ***10h***. White solid, mp 156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (s, 1H), 7.49 (d, J=8.0 Hz, 2H), 7.13 (d, J=8.4 Hz, 2H), 6.77 (s, 1H), 6.29 (s, 1H), 5.87 (s, 1H), 3.88 (s, 3H), 3.80 (s, 3H), 3.78 (s, 9H), 3.47 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 153.0, 151.7, 150.0, 144.1, 143.1, 135.9, 129.0, 128.9, 128.8, 113.2, 112.7, 107.3, 96.9, 66.2, 60.8, 56.6, 56.3, 56.0, 56.0, 21.5; HRMS-EI (m/z): $[M]^+$ calcd for $C_{26}H_{30}O_8S$: 502.1661, found: 502.1661.

4.2.12. Compound ***10i***. White solid, mp 147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 (d, J=8.0 Hz, 2H), 7.44 (s, 1H), 7.26 (d, J=5.1 Hz, 1H), 7.20 (d, J=4.4 Hz, 1H), 7.11 (d, J=8.0 Hz, 2H), 6.95 (dd, J=5.1, 4.4 Hz, 1H), 6.28 (s, 1H), 6.23 (s, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.49 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.6, 150.1, 144.1, 142.9, 134.9, 134.4, 129.4, 128.9, 128.8, 126.6, 124.5, 113.1, 112.1, 96.6, 62.2, 56.8, 56.3, 55.8, 21.3; HRMS-EI (m/z): $[M]^+$ calcd for $C_{21}H_{22}O_5S_2$: 418.0909, found: 418.0915.

4.2.13. Compound ***10j***. White solid, mp 173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48 (d, J=8.0 Hz, 2H), 7.42 (s, 1H), 7.17 (d, J=8.0 Hz, 2H), 6.53 (d, J=3.4 Hz, 1H), 6.37–6.36 (m, 1H), 6.34 (s, 1H), 6.12 (s, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.55 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.9, 150.4, 146.2, 144.2, 143.4, 143.3, 135.2, 129.1, 129.0, 114.0, 111.8, 110.8, 110.4, 96.7, 61.3, 56.5, 56.4, 56.0, 21.6; HRMS-EI (m/z): $[M]^+$ calcd for $C_{21}H_{22}O_6S$: 402.1137, found: 402.1141.

4.2.14. Compound ***10k***. White solid, mp 146–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.36 (d, J=8.6 Hz, 1H), 7.64 (d, J=8.2 Hz, 2H), 7.62 (s, 1H), 7.46 (t, J=8.6 Hz, 1H), 7.41 (d, J=7.6 Hz, 1H), 7.33 (t, J=8.6 Hz, 1H), 7.29 (d, J=8.2 Hz, 2H), 6.73 (s, 1H), 6.47 (s, 1H), 4.02 (s, 3H), 3.95 (s, 3H), 3.62 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 152.1, 150.0, 144.2, 142.8, 135.7, 135.1, 131.9, 130.4, 129.5, 129.2, 128.9, 128.8, 126.7, 113.4, 111.9, 96.6, 61.9, 56.4, 56.1, 55.7, 21.3; HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{23}ClO_5S$: 446.0955, found: 446.0955.

4.2.15. Compound ***10l***. White solid, mp 157–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57–7.54 (m, 5H), 7.32 (s, 2H), 7.22 (d, J=8.5 Hz, 2H), 6.37 (s, 1H), 5.99 (s, 1H), 3.97 (s, 3H), 3.88 (s, 3H), 3.56 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.6, 150.1, 144.3, 143.1, 135.6, 135.5, 134.3, 130.1, 129.7, 129.1, 128.8, 128.4, 128.0, 112.9, 112.2, 96.7, 65.7, 56.6, 56.3, 55.9, 21.5; HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{23}ClO_5S$: 446.0955, found: 446.0949.

4.2.16. Compound ***10m***. White solid, mp 137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50–7.47 (m, 5H), 7.25 (d, J=8.5 Hz, 2H), 7.17 (d, J=8.5 Hz, 2H), 6.29 (s, 1H), 5.93 (s, 1H), 3.88 (s, 3H), 3.79 (s, 3H), 3.46 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.5, 149.9, 144.1, 143.0, 135.5, 134.1, 132.0, 131.2, 128.9, 128.6, 128.5, 112.9, 112.3, 96.7, 65.5, 56.5, 56.1, 55.8, 21.3; HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{23}ClO_5S$: 446.0955, found: 446.0955.

4.2.17. Compound ***10n***. White solid, mp 123–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (d, J=8.5 Hz, 2H), 7.36 (s, 1H), 7.28–7.23 (m, 2H), 7.20–7.13 (m, 3H), 7.07 (d, J=8.5 Hz, 2H), 6.99 (s, 1H), 6.30 (s, 1H), 4.79 (d, J=6.5 Hz, 1H), 3.87 (s, 6H), 3.37 (s, 3H), 2.80–2.77 (m, 1H), 2.68–2.43 (m, 1H), 2.42–2.38 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.9, 149.1, 143.0, 142.3, 139.6, 134.3, 128.0, 127.8, 127.5, 127.5, 127.4, 127.2, 127.1, 125.2, 110.5, 95.5, 65.7, 55.6, 55.0, 54.9, 31.7, 27.9, 20.6; HRMS-EI (m/z): $[M]^+$ calcd for $C_{25}H_{28}O_5S$: 440.1657, found: 440.1656.

4.2.18. Compound ***10o***. White solid, mp 117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (d, J=8.4 Hz, 2H), 7.32 (s, 1H), 7.31 (s, 1H),

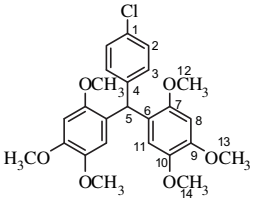
7.30–7.25 (m, 2H), 7.10 (d, *J*=14.0 Hz, 2H), 7.01 (d, *J*=8.0 Hz, 2H), 6.09 (d, *J*=5.6 Hz, 1H), 5.06–5.00 (m, 4H), 4.74 (t, *J*=8.0 Hz, 1H), 3.85 (s, 3H), 3.75 (s, 3H), 3.33 (s, 3H), 2.79–2.56 (m, 2H), 2.27 (s, 3H), 2.04–1.89 (m, 3H), 1.72–1.57 (m, 2H), 1.29–1.20 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 156.8, 152.1, 151.9, 149.5, 143.0, 142.8, 136.3, 136.0, 128.1, 127.7, 111.9, 96.0, 66.3, 56.3, 55.5, 33.8, 29.3, 24.5, 24.4, 21.0; HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{23}H_{28}O_5S$: 416.1657, found: 416.1665.

4.2.19. Compound ***10p***. White solid, mp 127–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39–7.30 (m, 3H), 7.16 (s, 1H), 7.04 (d, *J*=8.8 Hz, 2H), 6.12 (s, 1H), 4.69 (d, *J*=6.5 Hz, 1H), 3.89 (s, 3H), 3.78 (s, 3H), 3.35 (s, 3H), 2.52–2.48 (m, 2H), 2.42–2.38 (m, 2H), 2.30 (s, 3H), 1.80–1.76 (m, 2H), 1.70–1.63 (m, 2H), 1.39–1.14 (m, 3H), 1.00–0.95 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 152.3, 149.5, 143.2, 143.0, 136.9, 128.4, 128.3, 128.1, 128.0, 112.6, 112.5, 96.3, 66.8, 66.1, 56.6, 56.0, 55.9, 38.2, 32.0, 30.6, 26.1, 25.9, 21.4; HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{23}H_{30}O_5S$: 418.1814, found: 418.1797.

4.2.20. Compound ***10q***. White solid, mp.85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, *J*=8.0 Hz, 2H), 7.30 (s, 1H), 7.10 (d, *J*=8.0 Hz, 2H), 6.91 (s, 1H), 6.21 (s, 1H), 5.04 (d, *J*=12.0 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.32 (s, 3H), 2.31 (s, 3H), 2.14–1.98 (m, 2H), 1.31–1.11 (m, 2H), 0.83 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 152.4, 149.6, 143.5, 142.8, 135.1, 128.5, 128.1, 127.7, 111.5, 96.3, 66.2, 56.4, 55.7, 55.6, 28.5, 21.1, 19.5, 13.2; HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{20}H_{26}O_5S$: 378.1501, found: 378.1508.

4.2.21. Compound ***10r***. White solid, mp 79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.29 (m, 4H), 7.11 (s, 1H), 7.00 (d, *J*=7.4 Hz, 2H), 6.10 (s, 1H), 4.57 (d, *J*=6.5 Hz, 1H), 3.84 (s, 3H), 3.75 (s, 3H), 3.32 (s, 3H), 2.77–2.74 (m, 1H), 2.27 (s, 3H), 1.26 (d, *J*=6.5 Hz, 1H), 0.89 (d, *J*=6.5 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 152.2, 149.5, 143.2, 142.9, 136.7, 128.4, 128.3, 128.1, 112.5, 96.2, 66.7, 56.5, 55.9, 55.8, 28.7, 21.4, 21.3, 20.9; HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{20}H_{26}O_5S$: 378.1501, found: 378.1508.

4.2.22. Compound ***16***.



5,5′-((4-chlorophenyl)methylene)-bis-(1,2,4-trimethoxy benzene): white solid, mp. 168–169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.19 (d, *J*=8.4 Hz, 2H), 6.97 (d, *J*=8.4 Hz, 2H), 6.53 (s, 2H), 6.39 (s, 2H), 6.01 (s, 1H), 3.87 (s, 6H), 3.65 (s, 6H), 3.63 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.5, 148.1, 142.9, 142.6, 131.3, 130.2, 128.0, 123.7, 114.3, 98.1, 56.8, 56.6, 56.0, 41.9; HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{25}H_{27}ClO_6$: 458.1496, found: 458.1497.

4.2.23. Compound ***12a***. Brown solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.63 (d, *J*=6.5 Hz, 1H), 7.56 (s, 1H), 7.50–7.40 (m, 5H), 7.23–7.19 (m, 4H), 7.06–6.99 (m, 4H), 5.68 (s, 1H), 2.25 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 144.3, 135.4, 135.1, 133.4, 130.0, 129.2, 129.1, 128.8, 128.3, 126.9, 124.9, 122.2, 119.8, 118.1, 111.5, 106.8, 69.0, 21.4.

4.2.24. Compound ***12b***. Brown solid, mp 137–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (br s, 1H), 7.80–7.74 (m, 3H), 7.41 (d, *J*=7.5 Hz, 2H), 7.33–7.30 (m, 3H), 7.21(d, *J*=7.2 Hz, 1H), 7.08 (t, *J*=7.0 Hz, 1H), 7.05 (d, *J*=7.5 Hz, 2H), 5.63 (s, 1H), 2.32 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 144.1, 135.8, 135.5, 133.0, 129.9, 129.0, 128.5, 128.3, 128.0, 127.0, 121.3, 121.0, 119.9, 110.4, 103.8, 69.6, 21.4, 11.67.

4.2.25. Compound ***12c***. Brown solid, mp 137–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (s, 1H), 7.50 (d, *J*=7.6 Hz, 2H), 7.48–7.39 (m, 2H), 7.38 (d, *J*=7.2 Hz, 1H), 7.26–7.22 (m, 4H), 7.17 (t, *J*=7.2 Hz, 1H), 7.08 (d, *J*=7.6 Hz, 2H), 7.02 (t, *J*=7.2 Hz, 1H), 5.65 (s, 1H), 3.77 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 144.2, 136.4, 135.4, 133.9, 130.1, 129.2, 129.0, 128.4, 127.7, 122.0, 119.6, 118.5, 109.4, 105.8, 69.0, 33.1, 21.5; HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{23}H_{21}NO_2S$: 375.1293, found: 375.1297.

4.2.26. Compound ***12d***. Brown solid, mp 189–190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.98 (br s, 1H), 8.00 (s, 1H), 7.87 (s, 1H), 7.70 (d, *J*=7.0 Hz, 1H), 7.50 (d, *J*=7.4 Hz, 2H), 7.46–7.41 (m, 3H), 7.28 (s, 1H), 7.26 (d, *J*=7.4 Hz, 3H), 7.12 (d, *J*=7.0 Hz, 2H), 5.67 (s, 1H), 3.90 (s, 3H); 2.33 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 167.8, 144.5, 134.9, 134.8, 133.2, 130.5, 130.0, 129.3, 128.9, 128.5, 128.3, 124.0, 120.9, 117.8, 113.8, 107.5, 68.8, 51.9, 21.5; HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{24}H_{21}NO_4S$: 419.1191, found: 419.1201.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2009.10.044.

References and notes

1. Friedel, C.; Crafts, J.M.; Compt. Rend., 1877, 84, 1392 and 1450. For reviews see: (a) Sartori, G.; Maggi, R. *Chem. Rev.* **2006**, *106*, 1077–1104; (b) Groves, J. K. *Chem. Soc. Rev.* **1972**, *1*, 73–97.
2. (a) Nagata, T.; Nishida, A.; Nakagawa, M. *Tetrahedron Lett.* **2001**, *42*, 8345–8349; (b) Padwa, A.; Waterson, A. G. *J. Org. Chem.* **2000**, *65*, 235–244; (c) Koseki, Y.; Sato, H.; Watanabe, Y.; Nagasaka, T. *Org. Lett.* **2002**, *4*, 885–888.
3. (a) Speckamp, W. N.; Moolenaar, M. *Tetrahedron* **2000**, *56*, 3817–3856; (b) Petrini, M. *Chem. Rev.* **2005**, *105*, 3949–3977.
4. (a) Ooi, T.; Umatsu, Y.; Fujimoto, J.; Fukumoto, K.; Maruoka, K. *Tetrahedron Lett.* **2007**, *48*, 1337–1340; (b) Das, B.; Damodar, K.; Saritha, D.; Chowdhury, N.; Krishnaiah, M. *Tetrahedron Lett.* **2007**, *48*, 7930–7933; (c) Petrini, M.; Seri, M. *Tetrahedron* **2006**, *62*, 960–967; (d) Kuhakarn, C.; Tangdenpaisal, K.; Kongsaeree, P.; Prabpai, S.; Tuchinda, P.; Pohmakotr, M.; Reutrakul, V. *Tetrahedron Lett.* **2007**, *48*, 2467–2470; (e) Das, B.; Damodar, K.; Bhunia, N. *J. Org. Chem.* **2009**, *74*, 5607–5609; (f) Mecozzi, T.; Petrini, M.; Profeta, T. *Tetrahedron: Asymmetry* **2003**, *14*, 1171–1178; (g) Das, B.; Kongra, D.; Chowdhury, N.; Saritha, D.; Ravikant, B.; Krishnaiah, M. *Tetrahedron* **2008**, *64*, 9396–9400; (h) Ballini, R.; Plamieri, A.; Petrini, A.; Torregiani, E. *Org. Lett.* **2006**, *8*, 4093–4096.
5. (a) *Catalysis from A To Z: A Concise Encyclopedia*; Cornils, B., Herrmann, W. A., Muhler, M., Wong, C.-H., Eds.; Wiley-VCH: Weinheim, 2007; pp 1–3; (b) Sheldon, R.; Arends, I.; Hanefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, 2007.
6. van Leeuwen, P. W. N. M. *Homogeneous Catalysis-Understanding the Art*; Kluwer Academic: Dordrecht, 2004.
7. (a) Arata, K.; Matsuhashi, H.; Hino, M.; Nakamura, H. *Catal. Today* **2003**, *81*, 17–30; (b) Song, X.; Sayari, A. *Catal. Rev. Sci. Eng.* **1996**, *38*, 329–412.
8. Okuhara, T. *Chem. Rev.* **2002**, *102*, 3641–3666.
9. Harmer, M. A.; Sun, Q. *Appl. Catal., A* **2001**, *221*, 45–62.
10. Corma, A. *Adv. Mater.* **1995**, *7*, 137–144.
11. (a) Das, B.; Damodar, K.; Choudhury, N. *J. Mol. Catal. A: Chem.* **2007**, *269*, 81–84; (b) Yadav, J. S.; Reddy, B. V. S.; Eshwaraiah, E.; Anuradha, K. *Green Chem.* **2002**, *4*, 592–594; (c) Ramesh, C.; Banerjee, J.; Pal, R.; Das, B. *Adv. Synth. Catal.* **2003**, *345*, 557–559; (d) Das, B.; Majhi, A.; Banerjee, J.; Chowdhury, N. *J. Mol. Catal. A: Chem.* **2006**, *260*, 32–34; (e) Ko, S.; Yao, C. *Tetrahedron Lett.* **2006**, *47*, 8827–8829; (f) Das, B.; Thirupathi, P.; Mahender, I.; Reddy, V. S.; Rao, Y. K. *J. Mol. Catal. A: Chem.* **2006**, *247*, 233–239; (g) Tajbakhsh, M.; Heydari, A.; Khalizadeh, M. M.; Lakouraj, B.; Zamenian, S. *Synlett* **2007**, 2347–2350; (h) Tajbakhsh, M.; Heydari,

A.; Ghanei, M.; Khaksar, S. *Synthesis* **2008**, 352–354; (i) Tian, Q.; Zhu, X.-M.; Yang, J.-S. *Synth. Commun.* **2007**, *37*, 691–701.

12. (a) Kim, S. S.; Kadam, S. T. *Tetrahedron* **2009**, *65*, 6330–6334; (b) Kim, S. S.; Thirupathi, P. *Tetrahedron* **2009**, *65*, 5168–5173; (c) Kim, S. S.; Rajagopal, G.; Lee, H. *Tetrahedron* **2009**, *65*, 4735–4741; (d) Kim, S. S.; Kadam, S. T. *Appl. Organomet. Chem.* **2009**, *23*, 119–123; (e) Kim, S. S.; Majhi, A.; Kadam, S. T. *Tetrahedron* **2008**, *64*, 5509–5514; (f) Kim, S. S.; Majhi, A.; Kim, H. S. *Appl. Organomet. Chem.* **2008**, *22*, 466–470; (g) Kim, S. S.; Kadam, S. T. *Catal. Commun.* **2008**, *9*, 1342–1345; (h) Kim, S. S.; Lee, S. H.; Kwak, J. M. *Tetrahedron: Asymmetry* **2006**, *17*, 1165–1169; (i) Kim, S. S.; Kwak, J. M. *Tetrahedron* **2006**, *62*, 49–53.