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<https://hdl.handle.net/2324/7174425>

出版情報 : Journal of Oleo Science. 67 (11), pp.1473-1481, 2018-11-07. 日本油化学会
バージョン :

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A Scandium Arylsulfonate-based Coordination Polymer as a Heterogeneous Catalyst for the Friedel–Crafts Reaction of Indoles with Aldehydes

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Abstract: The scandium sulfonate-based coordination polymer $\text{Sc}_2(\text{BPDS})_3$, which is easily prepared by mixing scandium triisopropoxides and biphenyl-4,4'-disulfonic acid (BPDSA), is an air-stable and storable solid that effectively catalyzes the Friedel–Crafts reaction of indoles with aromatic aldehydes under heterogeneous conditions to afford various aryl(diindolyl)methanes. The catalyst can be reused without significant loss of activity after separation from the reaction mixture by simple centrifugation followed by drying.

Key words: scandium arylsulfonate, coordination polymer, heterogeneous catalysis, reusable catalyst, Friedel–Crafts reaction

1 INTRODUCTION

Heterogeneous catalysts are generally advantageous in terms of recovery and reuse as they can be recovered from reaction mixtures easily by simple separation methods, such as filtration, decantation, or centrifugation, and then reused^{1–3}. Consequently, interest in the development of heterogeneous metal complex catalysts has increased owing to environmental and practical considerations although heterogeneous catalysts are generally less active than the homogeneous counterparts. Coordination polymer-type complex catalysts, including metal organic frameworks (MOFs), have attracted particular attention in organic synthesis as well as materials science^{4–13}. Coordination polymers are typically prepared by simply mixing metal ions, multidirectional ligands, and other components, thus allowing the catalytic centers to be regularly dispersed and well accumulated in a controlled manner by the choice of spacer used.

Trivalent rare earth metal ions have strong Lewis acidity, large ionic radii, and high coordination numbers (usually 6 to 9). Furthermore, some of their complexes, particularly their salts of strong acids, can work as Lewis acid catalysts, even in the presence of Lewis bases such as water and amines. We have focused on these characteristics of rare earth metal ions and developed chiral and achiral rare

earth metal complexes that work as reusable Lewis acid or Lewis acid–base catalysts^{14–16}. In addition, we have synthesized novel polymeric rare earth arylsulfonates, i.e., $\text{RE}_2(\text{BPDS})_3$ (where RE = rare earth and BPDS = biphenyl-4,4'-disulfonate), which bear biphenyl moieties as unbending spacers (Scheme 1)^{17–19}. The scandium complex $\text{Sc}_2(\text{BPDS})_3$ effectively catalyzed the hetero-Diels–Alder reaction of aldehydes with the Danishefsky's diene and the ring-opening reaction of epoxides with amines under solvent-free conditions (Schemes 2 and 3). After the reaction, the catalyst could be separated from the reaction mixture by simple centrifugation and then successfully reused for another reaction without any loss of activity.

We report here the $\text{Sc}_2(\text{BPDS})_3$ -catalyzed Friedel–Crafts reaction of indoles with aromatic aldehydes as a further application of our scandium sulfonate-based coordination polymer. This reaction effectively provided aryl(diindolyl)methanes, which have previously been isolated from terrestrial and marine natural sources, and exhibit several interesting physiological effects, such as antihyperlipidemic²⁰, β -glucuronidase inhibitory²¹, and antimicrobial activities^{22–24}. Aryl(diindolyl)methanes are also utilized as synthetic intermediates for functional materials such as chromogenic sensing agents^{25, 26}. While many types of metal salt or complex catalysts^{27–35}, including scandium

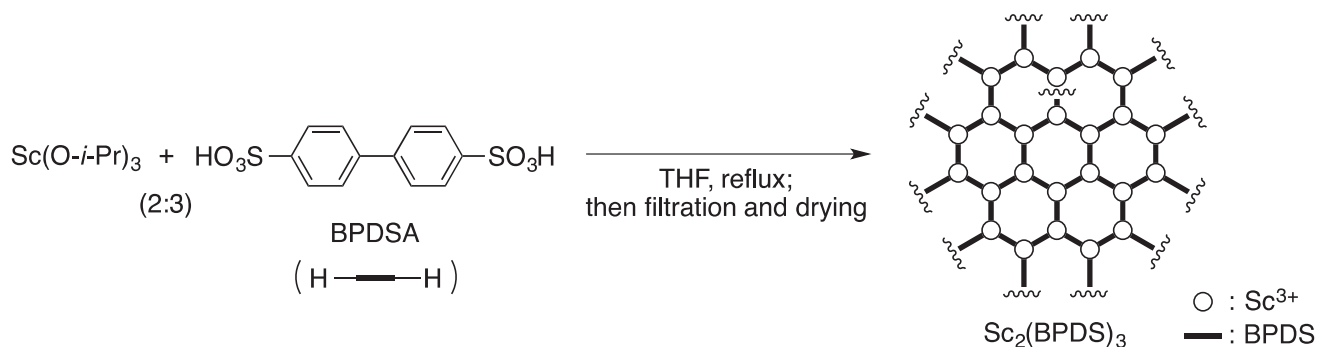
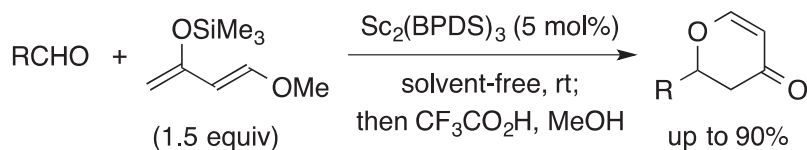
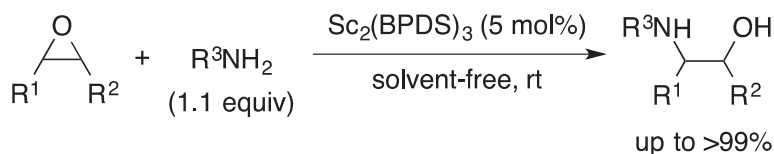
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Accepted July 19, 2018 (received for review April 28, 2018)

Journal of Oleo Science ISSN 1345-8957 print / ISSN 1347-3352 online

<http://www.jstage.jst.go.jp/browse/jos/> <http://mc.manuscriptcentral.com/jjocs>

Scheme 1 Preparation of $\text{Sc}_2(\text{BPDS})_3$.Scheme 2 The $\text{Sc}_2(\text{BPDS})_3$ -catalyzed hetero-Diels-Alder reaction of aldehydes with the Danishefsky's diene under solvent-free conditions.Scheme 3 The $\text{Sc}_2(\text{BPDS})_3$ -catalyzed ring-opening reaction of epoxides with amines under solvent-free conditions.

organosulfonates^{36–38}, have been successfully used for this Friedel–Crafts reaction under homogeneous or heterogeneous conditions, effective catalysis with scandium-based coordination polymers has not been reported^{39,40}.

2 EXPERIMENTAL PROCEDURES

2.1 General

Melting points were measured on a Yanako MP-500D micro melting point apparatus and reported uncorrected. IR spectra were recorded on a JASCO FT/IR-550 spectrometer. ^1H and ^{13}C NMR spectra in solution were measured on a JEOL JMN-LA400 FT NMR system at 400 and 100 MHz, respectively. Chemical shifts are given in terms of δ relative to that of tetramethylsilane (internal standard) or the solvent signal. Solid-state ^{13}C NMR spectra were recorded on a JEOL JNM-ECA 400 system at 100 MHz; the chemical shifts are expressed in δ relative to that of hexamethylbenzene (methyl, 17.36 ppm). Thermogravimetry (TG) and differential thermal analysis (DTA) were performed using Seiko Instruments SII-TG/DTA 6200. X-ray diffraction (XRD) measurements were conducted with a Rigaku RINT2000-TTR III system. Elemental analysis was performed using a Perkin Elmer 2400II/CHN analyzer. Thin-layer chromatography (TLC) was performed on a silica gel plates (Merck Kieselgel 60 F-254, 20 cm \times 20 cm \times 0.25

mm). Column chromatography was carried out with silica gel as an absorbent (Kanto Chemical, silica gel 60N 70–230 mesh). Scandium triisopropoxide was purchased from Sigma–Aldrich Co. Dehydrated solvents were purchased from Kanto Chemical Co. and used without further purification.

2.2 Preparation of $\text{Sc}_2(\text{BPDS})_3$

The $\text{Sc}_2(\text{BPDS})_3$ complex was prepared according to a reported method (Scheme 1)¹⁹: To a solution of scandium triisopropoxide (472 mg, 1.50 mmol) in dry THF (6 mL) was added a solution of biphenyl-4,4'-disulfonic acid (BPDSA) (222 mg, 0.999 mmol) under argon, and the mixture was stirred at 80°C for 18 h. The obtained precipitate was collected by filtration, and washed with THF. After drying in vacuo at 300°C for 24 h, the complex (870 mg, 85%) was obtained as a colorless solid. IR (ATR): 3467, 1599, 1391, 1284 ($-\text{SO}_3^-$, antisymmetric stretch), 1157, 1109, 1039 ($-\text{SO}_3^-$, symmetric stretch), 997 cm^{-1} . Anal. Calcd for $\text{C}_{36}\text{H}_{30}\text{O}_{21}\text{S}_6\text{Sc}_2[\text{Sc}_2(\text{BPDS})_3 \cdot 3\text{H}_2\text{O}]$: C, 40.00; H, 2.80. Found: C, 39.88; H, 2.54. ^{13}C NMR (solid state, CP/MAS, δ): 141.8 (*ipso* for SO_3^-), 139.1 (*para*), 127.6 (*ortho*), 127.3 (*meta*).

2.3 Friedel–Crafts Reaction of Indoles with Aldehydes

A general experimental procedure for the Friedel–Crafts reaction of indoles with aromatic aldehydes is as follows: To a suspension of $\text{Sc}_2(\text{BPDS})_3$ (5.1 mg, 0.0050 mmol) and

an indole (0.41 mmol) in a dry solvent (0.5 mL) was added an aldehyde (0.20 mmol), and the mixture was stirred at the assigned temperature under argon. The reaction mixture was cooled to room temperature and allowed to pass through a Celite pad to remove the catalyst, which was then washed with methanol. The combined organic layer was evaporated, and the chemical yield was determined by ^1H NMR in dimethyl sulfoxide- d_6 . The product was purified by silica gel column chromatography. When the catalyst was reused, the reaction mixture was centrifuged to separate the catalyst from the substrates and the product without the above filtration step, and the catalyst was washed with methanol and dried in vacuo at 200°C.

3,3'-Phenylmethylenedi(1*H*-indole) (3aa): A red solid. Mp 123–125°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.38. IR (ATR): 3410, 3056, 3022, 2853, 1600, 1455, 1330, 1090, 740 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.82 (s, 2H, NH), 7.38–7.34 (m, 4H), 7.29–7.24 (m, 4H), 7.16 (dt, J = 7.7, 1.9 Hz, 1H), 7.03 (ddd, J = 7.7, 6.8, 1.9 Hz, 2H), 6.86 (ddd, J = 7.7, 6.8, 1.9 Hz, 2H), 6.83 (s, 2H), 5.83 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 144.95, 136.56, 128.27, 127.99, 126.61, 125.74, 123.50, 120.83, 119.07, 118.13, 118.04, 111.40, 39.68. CAS Registry number: 35173-74-1.

3,3'-Phenylmethylenebis(1-methyl-1*H*-indole) (3ba): A pink solid. Mp 182–184°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.29. IR (ATR): 3055, 3022, 2935, 1610, 1460, 1330, 1110, 710 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 7.38–7.35 (m, 4H), 7.31–7.35 (m, 4H), 7.17 (dd, J = 8.7, 6.8 Hz, 1H), 7.10 (dd, J = 8.7, 6.8 Hz, 2H), 6.90 (dd, J = 7.7, 7.7 Hz, 2H), 6.82 (s, 2H), 5.83 (s, 1H), 3.69 (s, 6H). ^{13}C NMR (DMSO- d_6 , δ): 144.75, 136.92, 128.19, 128.06, 127.82, 126.86, 125.81, 121.00, 119.17, 118.28, 117.29, 109.54, 39.33, 32.22. CAS Registry number: 29670-54-0.

3,3'-Phenylmethylenebis(5-methyl-1*H*-indole) (3ca): An orange-pink solid. Mp 191–194°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.40. IR (ATR): 3410, 3022, 2920, 2856, 1570, 1455, 1330, 1028, 742 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.65 (s, 2H, NH), 7.33 (d, J = 8.7 Hz, 2H), 7.28–7.22 (m, 4H), 7.16 (dt, J = 7.7, 1.9 Hz, 1H), 7.07 (s, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.70 (d, J = 1.9 Hz, 2H), 5.75 (s, 1H), 2.26 (s, 6H). ^{13}C NMR (DMSO- d_6 , δ): 145.04, 134.93, 128.23, 127.96, 126.82, 126.42, 125.69, 123.63, 122.46, 118.52, 117.61, 111.13, 39.93, 21.27. CAS Registry number: 878796-71-5.

3,3'-Phenylmethylenebis(5-methoxy-1*H*-indole) (3da): A red-brown solid. Mp 219–221°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.22. IR (ATR): 3399, 3314, 3010, 2949, 2922, 1623, 1584, 1484, 1455, 1022, 720 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.66 (s, 2H, NH), 7.37 (d, J = 7.7 Hz, 2H), 7.29–7.23 (m, 4H), 7.17 (t, J = 7.7 Hz, 1H), 6.83 (d, J = 1.9 Hz, 2H), 6.74 (d, J = 1.9 Hz, 2H), 6.70 (dd, J = 8.7, 1.9 Hz, 2H), 5.75 (s, 1H), 3.59 (s, 6H). ^{13}C NMR (DMSO- d_6 , δ): 152.63, 144.99, 131.77, 128.27, 127.94, 126.98, 125.66, 124.24, 117.64, 111.95, 110.51, 101.45, 55.22, 39.61. CAS Registry number: 588719-23-7.

3,3'-Phenylmethylenebis(5-bromo-1*H*-indole) (3ea): Orange oil. R_f (*n*-hexane/ethyl acetate 7:3): 0.30. IR (ATR): 3420, 3020, 2925, 2850, 1570, 1433, 1327, 1092, 725 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 11.07 (s, 2H, NH), 7.43 (s, 2H), 7.34–7.32 (m, 4H), 7.29 (dd, J = 7.7, 6.8 Hz, 2H), 7.19 (t, J = 6.8 Hz, 1H), 7.15 (dd, J = 8.7, 1.9 Hz, 2H), 6.88 (d, J = 1.9 Hz, 2H), 5.86 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 144.29, 135.22, 128.34, 128.19, 128.17, 126.02, 125.20, 123.41, 121.16, 117.62, 113.56, 110.87, 39.98. CAS Registry number: 457057-78-2.

3,3'-Phenylmethylenebis(5-nitro-1*H*-indole) (3fa): A yellowish orange solid. Mp 298–299°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.22. IR (ATR): 3399, 3314, 1624, 1515, 1470, 1333, 1090, 715 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 11.68 (s, 2H, NH), 8.33 (d, J = 1.9 Hz, 2H), 7.99 (dd, J = 8.7, 1.9 Hz, 2H), 7.56 (d, J = 8.7, 2H), 7.41 (d, J = 7.7 Hz, 2H), 7.34 (dd, J = 7.7, 7.7 Hz, 2H), 7.24 (t, J = 7.7 Hz, 1H), 7.15 (d, J = 1.9 Hz, 2H), 6.21 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 143.73, 140.19, 139.77, 128.43, 128.17, 127.57, 126.37, 125.76, 120.50, 116.59, 116.18, 112.09, 38.47. CAS Registry number: 1173883-99-2.

3,3'-(4-Nitrophenyl)methylenedi(1*H*-indole) (3ab): An orange solid. Mp 220–222°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.22. IR (ATR): 3450, 3425, 3385, 1590, 1425, 1330, 1090, 743 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.93 (s, 2H, NH), 8.15 (d, J = 8.7 Hz, 2H), 7.61 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 7.29 (d, J = 7.7 Hz, 2H), 7.06 (dd, J = 8.7, 6.8 Hz, 2H), 6.90–6.87 (m, 4H), 6.03 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 153.10, 145.73, 136.55, 126.40, 126.32, 123.81, 123.37, 121.05, 118.86, 118.38, 116.64, 111.54, 39.43. CAS Registry number: 7501-91-9.

3,3'-(4-Fluorophenyl)methylenedi(1*H*-indole) (3ac): Red oil. R_f (*n*-hexane/ethyl acetate 7:3): 0.35. IR (ATR): 3441, 3055, 1599, 1509, 1455, 1035, 741 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.83 (s, 2H, NH), 7.38–7.34 (m, 4H), 7.27 (d, J = 7.7 Hz, 2H), 7.08 (dd, J = 8.7, 8.7 Hz, 2H), 7.03 (dd, J = 7.7, 6.8 Hz, 2H), 6.86 (dd, J = 7.7, 6.8 Hz, 2H), 6.81 (s, 2H), 5.85 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 159.25, 141.05 (d, J_{CF} = 2.5 Hz), 136.58, 129.92 (d, J_{CF} = 8.2 Hz), 126.49, 123.51, 120.88, 119.02, 118.18, 117.92, 114.63 (d, J_{CF} = 21.3 Hz), 111.45, 38.87. CAS Registry number: 698376-88-4.

3,3'-(4-Bromophenyl)methylenedi(1*H*-indole) (3ad): A red solid. Mp 100–103°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.38. IR (ATR): 3415, 3055, 1487, 1455, 1335, 1089, 740 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.85 (s, 2H, NH), 7.45 (d, J = 8.7 Hz, 2H), 7.35 (d, J = 7.7 Hz, 2H), 7.30 (d, J = 8.7 Hz, 2H), 7.27 (d, J = 7.7 Hz, 2H), 7.04 (dd, J = 8.7, 6.8 Hz, 2H), 6.87 (dd, J = 7.7, 6.8 Hz, 2H), 6.83 (d, J = 1.9 Hz, 2H), 5.83 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 144.41, 136.56, 130.87, 130.50, 126.43, 123.58, 120.92, 118.98, 118.71, 118.23, 117.44, 111.46, 39.01. CAS Registry number: 540729-21-3.

4-[Di(1*H*-indol-3-yl)methyl]benzonitrile (3ae): An orange solid. Mp 204–205°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.25. IR (ATR): 3395, 3170, 2940, 2250, 1600, 1410,

755 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.91 (s, 2H, NH), 7.72 (d, $J=7.7$ Hz, 2H), 7.53 (d, $J=8.7$ Hz, 2H), 7.36 (d, $J=7.7$ Hz, 2H), 7.27 (d, $J=8.7$ Hz, 2H), 7.05 (dd, $J=7.7, 7.7$ Hz, 2H), 6.89–6.85 (m, 4H), 5.96 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 150.90, 136.57, 132.11, 129.31, 126.39, 123.79, 121.07, 119.08, 118.92, 118.39, 116.81, 111.57, 108.63, 39.66. CAS Registry number: 698377-27-4.

3,3'-(4-Methoxyphenyl)methylenedi(1*H*-indole) (**3af**): An orange solid. Mp 185–187°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.30. IR (ATR): 3390, 3050, 2945, 2920, 2830, 1510, 1455, 1022, 740 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.78 (s, 2H, NH), 7.34 (d, $J=8.7$ Hz, 2H), 7.27 (d, $J=7.7$ Hz, 2H), 7.25 (d, $J=8.7$ Hz, 2H), 7.02 (dd, $J=7.7, 7.7$ Hz, 2H), 6.87–6.79 (m, 6H), 5.76 (s, 1H), 3.69 (s, 3H). ^{13}C NMR (DMSO- d_6 , δ): 157.33, 136.97, 136.62, 129.21, 126.64, 123.44, 120.86, 119.17, 118.47, 118.15, 113.41, 111.44, 54.94, 38.87. CAS Registry number: 33985-68-1.

4-[Di(1*H*-indol-3-yl)methyl]phenol (**3ag**): An orange-red solid. Mp 119–121°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.12. IR (ATR): 3470, 3375, 3030, 2995, 1635, 1584, 1365, 748 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.75 (s, 2H, NH), 9.14 (s, 1H, OH), 7.33 (d, $J=7.7$ Hz, 2H), 7.27–7.13 (m, 4H), 7.02 (dd, $J=8.7, 6.8$ Hz, 2H), 6.85 (dd, $J=8.7, 6.8$ Hz, 2H), 6.78 (s, 2H), 6.66 (dd, $J=7.7, 1.9$ Hz, 2H), 5.71 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 155.26, 136.60, 135.20, 129.11, 126.67, 123.36, 120.77, 119.17, 118.68, 118.05, 114.76, 111.36, 38.88. CAS Registry number: 151358-47-3.

2-[Di(1*H*-indol-3-yl)methyl]phenol (**3ah**): A red-brown solid. Mp 298–299°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.25. IR (ATR): 3410, 3056, 1700, 1590, 1486, 1456, 1330, 1092, 745 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.71 (s, 2H, NH), 9.39 (s, 1H, OH), 7.33 (d, $J=7.7$ Hz, 2H), 7.26 (d, $J=7.7$ Hz, 2H), 7.07–6.97 (m, 4H), 6.87–6.83 (m, 3H), 6.73 (s, 2H), 6.65 (dd, $J=7.7, 6.8$ Hz, 1H), 6.18 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 154.24, 136.58, 130.95, 129.34, 126.88, 126.55, 123.48, 120.76, 119.01, 118.60, 118.14, 118.03, 115.01, 111.36, 31.49. CAS Registry number: 33948-97-9.

5-Bromo-2-[di(1*H*-indol-3-yl)methyl]phenol (**3ai**): Orange-brown oil. R_f (*n*-hexane/ethyl acetate 7:3): 0.25. IR (ATR): 3410, 3055, 1485, 1456, 1338, 1090, 742 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.76 (s, 2H, NH), 9.95 (s, 1H, OH), 7.34 (d, $J=7.7$ Hz, 2H), 7.24 (d, $J=8.7$ Hz, 2H), 7.05–7.01 (m, 3H), 6.97 (d, $J=8.7$ Hz, 1H), 6.88–6.83 (m, 3H), 6.73 (d, $J=1.9$ Hz, 2H), 6.11 (s, 1H). ^{13}C NMR (DMSO- d_6 , δ): 155.54, 136.61, 131.08, 130.75, 126.69, 123.58, 121.40, 120.86, 118.86, 118.57, 118.15, 117.55, 117.41, 111.44, 31.42.

2,2'-Phenylmethylenebis(3-methyl-1*H*-indole) (**4**): A yellowish green solid. Mp 160–162°C. R_f (*n*-hexane/ethyl acetate 7:3): 0.60. IR (ATR): 3429, 3380, 3022, 2930, 1599, 1485, 1455, 1330, 1022, 745 cm^{-1} . ^1H NMR (DMSO- d_6 , δ): 10.45 (s, 2H, NH), 7.44 (d, $J=8.7$ Hz, 2H), 7.35–7.30 (m, 4H), 7.25 (t, $J=7.7$ Hz, 1H), 7.16 (d, $J=7.7$ Hz, 2H), 7.03 (dd, $J=6.8, 6.8$ Hz, 2H), 6.97 (dd, $J=6.8, 6.8$ Hz, 2H), 6.06 (s, 1H), 2.17 (s, 6H). ^{13}C NMR (DMSO- d_6 , δ): 141.17,

135.57, 134.25, 128.46, 128.43, 128.20, 126.54, 120.68, 118.24, 117.87, 110.98, 106.77, 39.94, 8.43. CAS Registry number: 95816-67-4.

3 RESULTS and DISCUSSION

The IR spectrum of the prepared complex $\text{Sc}_2(\text{BPDS})_3$ shows that the sulfonic acid of BPSDA is almost completely converted to the corresponding sulfonate (Fig. 1). The TG-DTA curves of the complex indicated that the complex showed 1.66% weight loss in the temperature 30 to 355°C and additional 3.33% weight loss upon heating to ca. 400°C (Fig. 2). The first and second weight losses corresponded

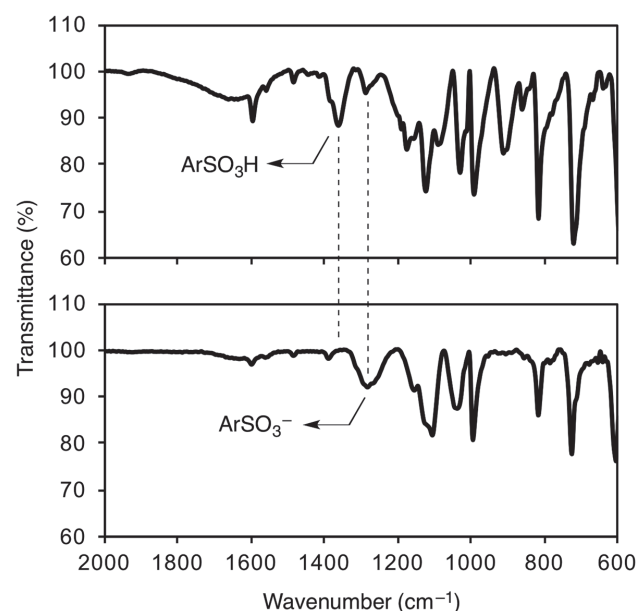


Fig. 1 IR spectra of BPDSA (above) and $\text{Sc}_2(\text{BPDS})_3 \cdot 3\text{H}_2\text{O}$ (below). The measurement was performed by an attenuated total reflection (ATR) method.

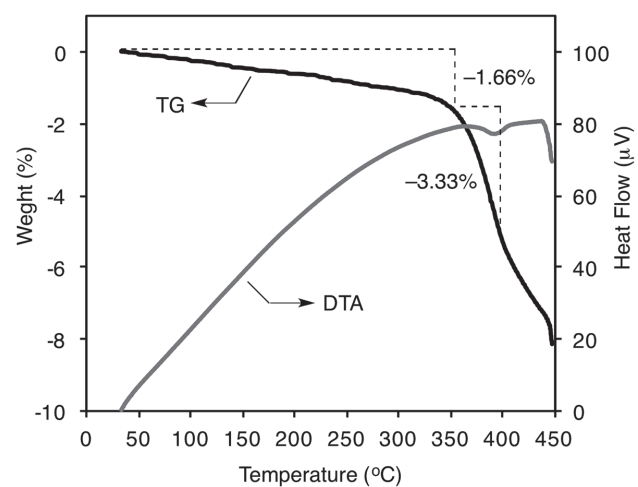


Fig. 2 TG-DTA curves of $\text{Sc}_2(\text{BPDS})_3 \cdot 3\text{H}_2\text{O}$.

to H₂O and 2H₂O in Sc₂(BPDS)₃·3H₂O, respectively. The results were consistent with the composition obtained by the elemental analysis of the complex, as shown in the experimental procedure. The complex might decompose at temperatures beyond 400°C. Powder XRD measurements indicated that the complex may not be amorphous but may show a certain degree of structural regularity; however, the detailed structure is not yet clear.

Sc₂(BPDS)₃ was used as the catalyst [loading: 2.5 mol% (5 mol% with respect to Sc)] for the Friedel–Crafts reaction of indole **1a** (R¹ = R² = H) with benzaldehyde **2a** (Ar = Ph) in 2:1 ratio under heterogeneous conditions (Scheme 4). The reaction performed at 30°C for 2 h proceeded successfully in several solvents, and the corresponding condensation product **3aa** was obtained in high yields (Table 1).

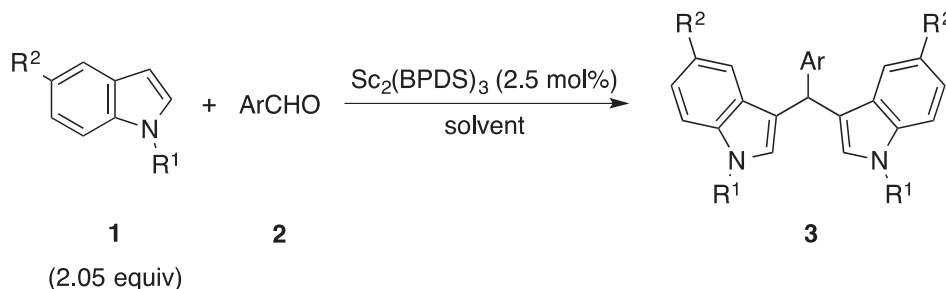
Reactions of 1(*N*)- or 5-substituted indoles **1b–f** with benzaldehyde **2a** (Ar = Ph) were carried out in toluene to explore the substrate scope of the reaction (Table 2). In the case of 1-methylindoles **1b**, the corresponding products **1ba** was obtained in only moderate yields, even at a higher reaction temperature of 60°C (entries 2 and 3). The unsatisfactory result may be attributed to the steric hindrance by the methyl group at the 1-position. The reactions of

Table 1 The Sc₂(BPDS)₃-catalyzed Friedel–Crafts reaction of **1a** (R¹ = R² = H) with **2a** (Ar = Ph) in various solvents (Scheme 4).

Entry	Solvent	Yield (%) ^a
1	<i>n</i> -Hexane	95
2	Toluene	>99
3	CH ₂ Cl ₂	99
4	CHCl ₃	92
5	Et ₂ O	>99
6	THF	98
7	MeCN	>99
8	EtOH	>99
9	MeOH	>99

^a Determined by ¹H NMR using mesitylene as an internal standard

indoles having a methyl, methoxy, or bromo group at the 5-position (**1c–e**) proceeded smoothly (entries 4–8). 5-Nitroindole **1f** did not undergo the Friedel–Crafts reaction with **2a** at 30°C for 24 h, presumably because of the strong electron-withdrawing ability of the nitro group (entry 9).



Scheme 4 The Sc₂(BPDS)₃-catalyzed Friedel–Crafts reaction of indoles **1** with aromatic aldehydes **2**.

Table 2 The Sc₂(BPDS)₃-catalyzed Friedel–Crafts reaction of indoles **1** with **2a** (Ar = Ph) in toluene (Scheme 4).

Entry	R ¹	R ²	1/3	Temperature (°C)	Time (h)	Yield (%) ^a
1	H	H	1a/3aa	30	2	>99
2	Me	H	1b/3ba	30	24	25
3	Me	H	1b/3ba	60	2	39
4	H	Me	1c/3ca	30	24	88
5	H	Me	1c/3ca	60	0.5	>99
6	H	MeO	1d/3da	30	24	63
7	H	MeO	1d/3da	60	0.5	>99
8	H	Br	1e/3ea	30	12	>99
9	H	NO ₂	1f/3fa	30	24	NR ^b
10	H	NO ₂	1f/3fa	100	48	50

^a Determined by ¹H NMR using mesitylene (entries 1–3) or 3,4,5-trichloropyridine (entries 4–13) as an internal standard. ^bNo reaction.

Table 3 The $\text{Sc}_2(\text{BPDS})_3$ -catalyzed Friedel–Crafts reaction of **1a** ($\text{R}^1=\text{R}^2=\text{H}$) with aromatic aldehydes **2** in toluene at 30°C for 24 h (Scheme 4).

Entry	Ar	2/3	Yield (%) ^a
1	Ph	2a/3aa	>99
2	4- NO_2 - C_6H_4	2b/3ab	40
3	4-F- C_6H_4	2c/3ac	62
4	4-Br- C_6H_4	2d/3ad	55
5	4-NC- C_6H_4	2e/3ae	94
6	4-MeO- C_6H_4	2f/3af	99
7	4-HO- C_6H_4	2g/3ag	>99
8	2-HO- C_6H_4	2h/3ah	72
9	2-HO-4-Br- C_6H_3	2i/3ai	>99

^a Determined by ^1H NMR using 3,4,5-trichloropyridine as an internal standard

However, when the reaction temperature was raised to 100°C , the corresponding products **3fa** was obtained in moderate yield for 48 h (entry 10).

The Friedel–Crafts reaction of indole **1a** with aromatic aldehydes **2a–i** was also carried out in toluene at 30°C for 24 h (Table 3). Benzaldehydes bearing an electron-withdrawing group (nitro, fluoro, bromo, or cyano), an electron-donating group (methoxy), or a hydroxyl group at the 4-position successfully underwent the reaction, and the corresponding products were obtained in moderate to high yields (entries 1–7). The reaction with 2-hydroxybenzaldehyde **2h** and 4-bromo-2-hydroxybenzaldehyde **2i** also successfully proceeded (entries 8 and 9). It is noteworthy that Sc_2BPDS_3 could also catalyze the reaction with aldehydes having a free hydroxyl group (entries 7–9). In addition, the Friedel–Crafts reaction of 3-methylindole **1h** with **2a** proceeded well in methanol rather than in toluene, and substitution occurred at the 2-position of the indole ring instead of the 3-position (Scheme 5).

A plausible mechanism of the Friedel–Crafts reaction is illustrated in Fig. 3. $\text{Sc}_2(\text{BPDS})_3$ can accelerate not only the reaction between indoles and aldehydes by enhancing electrophilicity of the aldehydes as a Lewis acid (A to B), but also the benzylic C–O bond cleavage (C to D and C' to

D') and the reaction between indoles and conjugated imine intermediates (D to E), to afford aryl(diindolyl) methanes.

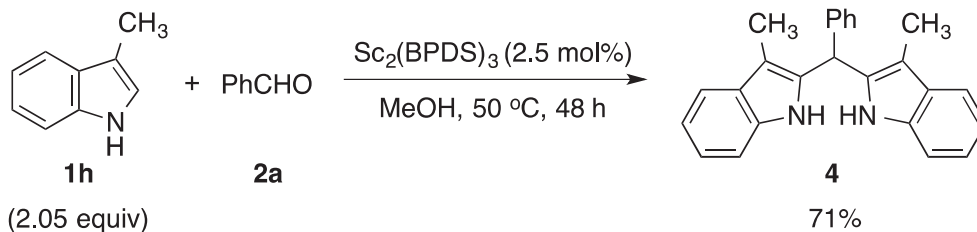
Finally, we assessed the reusability of $\text{Sc}_2(\text{BPDS})_3$ in the Friedel–Crafts reaction. After the reaction of **1d** with **2a** in toluene at 60°C for 30 min, the catalyst was separated from the reaction mixture by simple centrifugation. The recovered catalyst was dried in vacuo at around 300°C and reused in a subsequent reaction. $\text{Sc}_2(\text{BPDS})_3$ successfully catalyzed the reaction again, even up to the fifth run, without notable loss of the original activity (yields of **3da**: >99% in the 1st and 2nd runs, 99% in the 3rd and 4th runs, and 97% in the 5th run).

4 CONCLUSION

The air-stable and storable scandium sulfonate-based coordination polymer $\text{Sc}_2(\text{BPDS})_3$ was successfully applied as a heterogeneous catalyst for the Friedel–Crafts reaction of indoles with aromatic aldehydes, and the corresponding aryl(diindolyl) methanes were obtained. The catalyst could be separated from the reaction mixture by simple centrifugation, and reused without significant loss of activity.

ACKNOWLEDGMENT

We are deeply grateful to Professor Dr. Hideo Nagashima (Institute for Materials Chemistry and Engineering (IMCE), Kyushu University) and Professor Emeritus Dr. Junji Inanaga (Kyushu University) for their helpful support and discussion. We give a special thanks to Dr. Atsushi Tahara (IMCE, Kyushu University) for his technical support regarding elemental analysis. We also express our heartfelt gratitude to Prof. Dr. Andy M. Spring (Faculty of Engineering Sciences, Kyushu University), Ms. Keiko Ideta (IMCE, Kyushu University), and Mr. Yasumasa Matsumoto (IMCE, Kyushu University) for measuring TG-DTA, solid-state NMR, and XRD, respectively. This work was supported by JSPS KAKENHI (Grant-in-Aid for Scientific Research) Grant Numbers 23750176 (to H.F.), and also by the Kyushu University Program for Leading Graduate Schools “Advanced Graduate Program in Global Strategy for Green Asia”.



Scheme 5 The $\text{Sc}_2(\text{BPDS})_3$ -catalyzed Friedel–Crafts reaction of **1h** with **2a**.

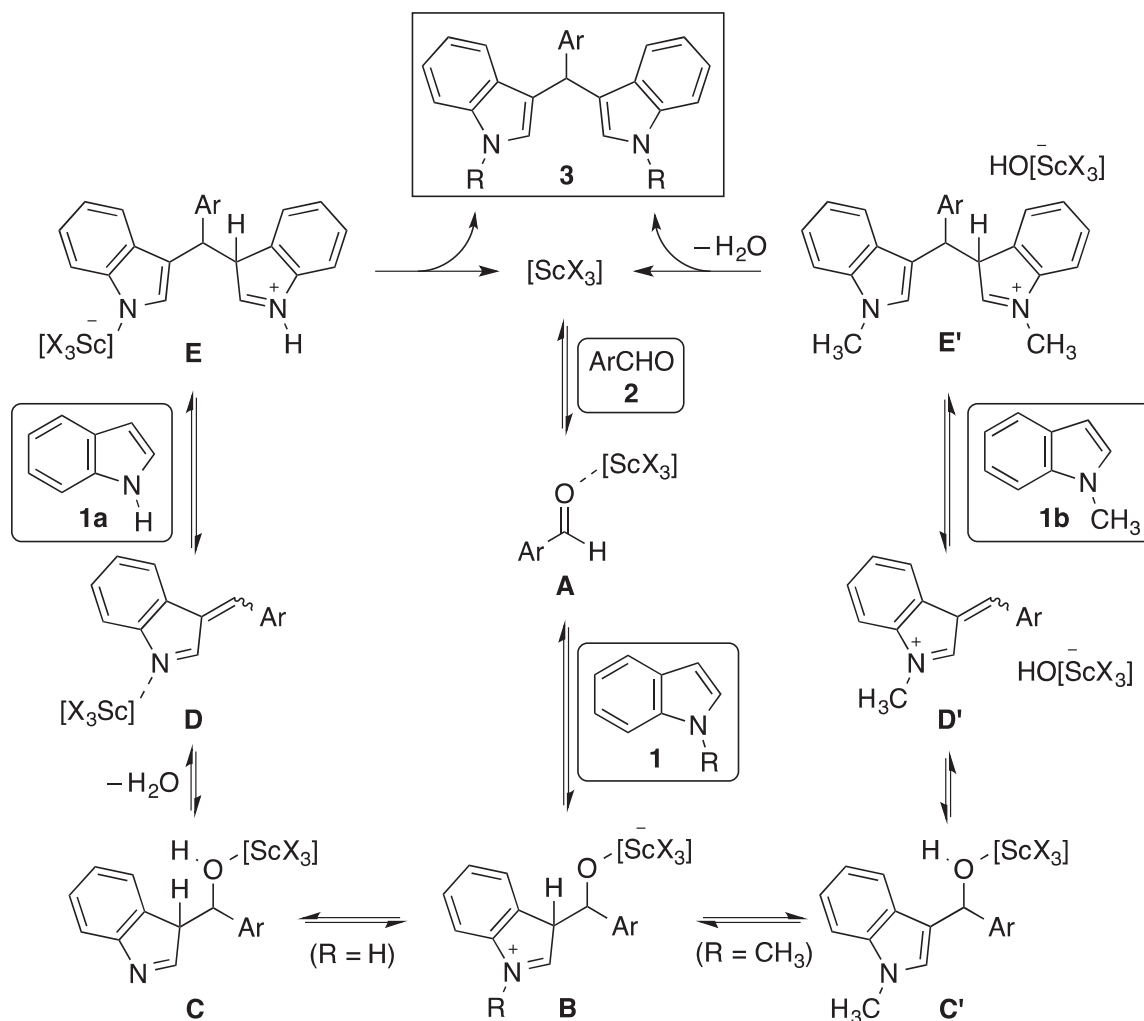


Fig. 3 A plausible mechanism of the $Sc_2(BPDS)_3$ -catalyzed Friedel-Crafts reaction of indoles **1** with aromatic aldehydes **2**. X = OSO_2Ar in BPDS.

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