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Magnetic nanoparticle immobilized *N*-propylsulfamic acid: The efficient, green and reusable nanocatalyst for the synthesis of 3,3-Arylidene bis(4-Hydroxycoumarin) derivatives

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Abstract

N-Propylsulfamic acid supported onto magnetic Fe_3O_4 nanoparticles (MNPs-PSA) was investigated as an efficient and magnetically recoverable catalyst for the one-pot synthesis of 3,3-Arylidene bis(4-Hydroxycoumarin) derivatives from the reaction of coumarin with variety aromatic aldehydes in high to excellent yield at room temperature under solvent-free conditions. The magnetic nanocatalyst (MNPs) can be readily recovered by applying an external magnet device and reused for at least 10 reaction runs without considerable loss of its activity. The advantages of this protocol are the mild reaction conditions, operational simplicity, practicability, short reaction times, and high to excellent product yields.

Keywords: *N*-Propylsulfamic acid; substituted coumarins; solvent-free conditions; recoverable catalyst.

Introduction

Magnetic nanoparticles are efficient, readily available, and high surface area resulting in high catalyst loading capacity and outstanding stability support for catalysts. They show identical and sometimes even higher activity than their corresponding homogeneous analogues [1-3]. More important, magnetic separation of the magnetic nanoparticles is more effective than filtration or centrifugation [4], simple, economical and promising for industrial applications [5]. Among the various magnetic nanoparticles as the core magnetic support, Fe_3O_4 nanoparticles are arguably the most extensively studied [6-8].

Sulfamic acid (SA) is environmentally compatible, stable and commercially available catalyst. More important, its water resistance and incapability for the formation of complexes make it an outstanding alternative to metal catalysts, in different areas of organic synthesis, as an efficient and green catalyst [9,10]. However the major disadvantage of this catalyst is its separation from the products, which needs solid-liquid or liquid-liquid techniques in many reactions. This drawback which can be overcome by immobilizing this catalyst

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on magnetic nanoparticles can be easily removed from the reaction mixture by magnetic separation.

Coumarins (2*H*-1-benzopyran-2-ones) are important oxygen containing fused heterocycles used in drugs and dyes [11]. Because of the great structural diversity of biologically active coumarins, it is not surprising that the coumarin ring system has become an important structural component in many pharmaceutical compounds [12,13]. The synthesis of 3-substituted coumarins derivatives is currently of much interest, and various methods have been reported [14-17].

Experimental

General

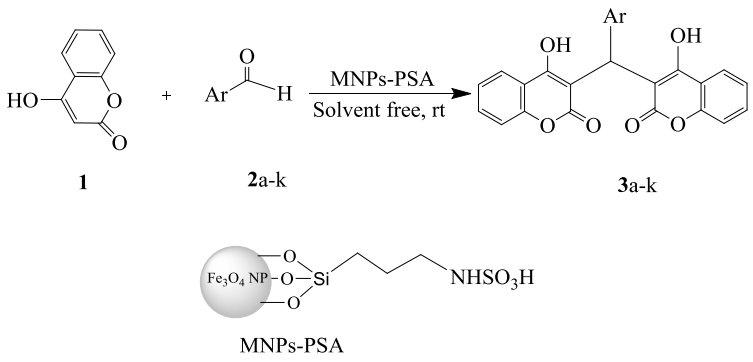
Chemicals were obtained from Merck and Fluka chemical companies. The IR spectra were recorded on a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and NMR spectra were obtained in $CDCl_3$ using a 400 MHz JEOL FT NMR spectrometer. All melting points were determined on an Electro Thermal 9100 melting point apparatus.

General procedure for the synthesis of 3,3'-arylidine bis(4-hydroxycoumarin)

A mixture of 4-hydroxycoumarin (2 mmol), aldehydes (1 mmol), and MNPs-PSA (4.5 mg) was stirred at room temperature for the time specified (Table 2). The reaction progress was monitored by TLC (EtOAc/hexane, 1:1). After completion of the reaction, the reaction mixture was diluted with Et_2O (5 mL) and the catalyst was e separated from the product by an external magnet. The remaining magnetic nanocatalyst was further washed with Et_2O (5 mL) to remove residual product. The combined organics were washed with brine (5 mL) and dried over anhydrous Na_2SO_4. The resulting solution was concentrated under reduced pressure to afford the essentially pure products in most cases. Further purification was achieved by short-column chromatography on silica gel with EtOAc/*n*-hexane as eluent. All the products are known and were characterized by IR, ^{1}H NMR, ^{13}C-NMR and melting point comparisons with those authentic samples [26,27].

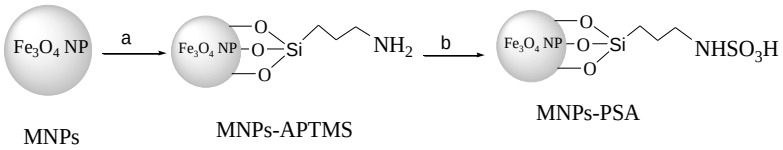
Results and discussion

In continuation of our research program and in order to develop selective, efficient and green methods and catalysts in organic synthesis [18-24], we report the catalytic application of MNPs–PSA as a magnetically heterogeneous nanocatalyst for the synthesis of 3,3′-arylidene bis(4-hydroxycoumarin) (**3**a-k) from the reaction of coumarin (**1**) with variety of aromatic aldehydes (**2**a-k) under solvent-free conditions at room temperature with excellent yields (Scheme 1).



Scheme 1. MNPs-PSA catalyzes the preparation of 3,3'-arylidene bis(4-hydroxycoumarins)

First, the MNPs-PSA was prepared according to the reported method [25] with some modifications as shown in scheme 2.



Scheme 2. Synthesis of supported *N*-propylsulfamic acid on magnetic nanoparticles; (a) (3-aminopropyl)-triethoxysilane (99%, 2.5 mL), ethanol/water, rt, 8 h; (b) chlorosulfuric acid (0.8 mL), dichloromethane, 2 h, rt.

Next, we examined the synthesis of 3,3′-(phenyl methylene) bis(4-hydroxycoumarin) (**3**e) as a model compound using MNPs-MSA under various reaction conditions in terms of time and product yield (Table 1). As shown in Table 1, the reaction was incomplete in the absence of MNPs-PSA even after 12 h (Entry 1). The optimized amount of catalyst for synthesis of 3,3′-arylidene bis(4-hydroxycoumarin) was 4.5 mg under solvent-free conditions at room temperature.

Table 1. Optimization of the reaction conditions for synthesis of 3,3′-(phenyl methylene) bis(4-hydroxycoumarin) (3e).

Entry	Catalyst, [amount, mg]	Solvent	Time	Yields, %
1	Catalyst-Free [0 mg]	Solvent-Free	12 h	0
2	Fe_3O_4 NP [5 mg]	Solvent-Free	2 h	15
3	MNPs-PSA [3 mg]	Solvent-Free	20 min	65
4	MNPs-PSA [4.5 mg]	Solvent-Free	9 min	93
5	MNPs- PSA [7 mg]	Solvent-Free	9 min	93
6	MNPs- PSA [4.5 mg]	CH_3CN	1 h	82
7	MNPs- PSA [4.5 mg]	CH_2Cl_2	1h	60
8	MNPs- PSA [4.5 mg]	EtOH	2 h	50
9	MNPs- PSA [4.5 mg]	H_2O	2 h	45

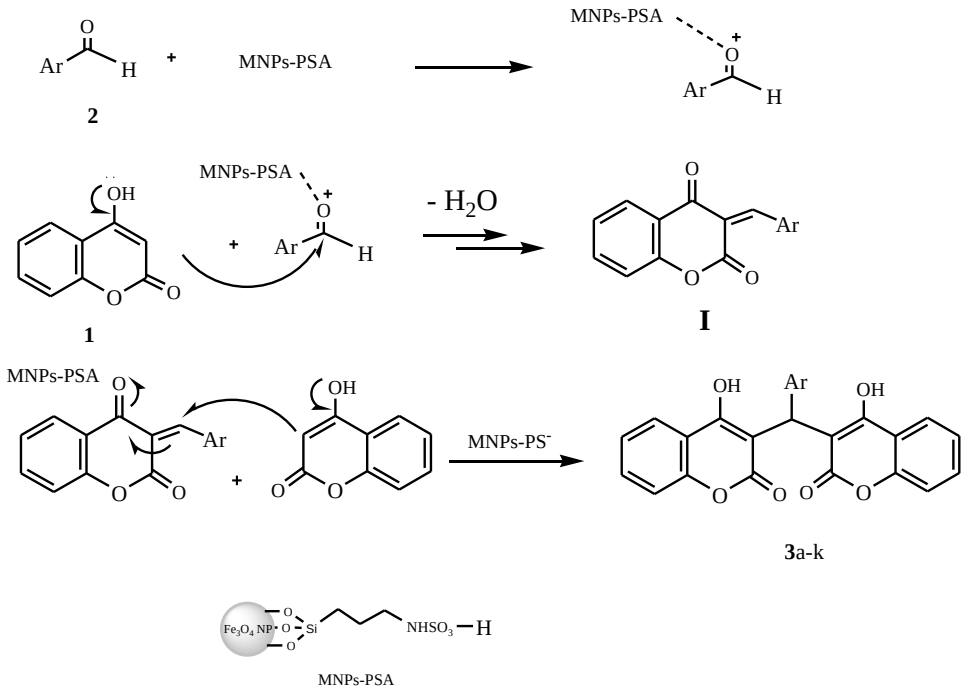
With the optimal conditions in hand, the generality and the applicability of this method were further examined for the synthesis of 3,3′-arylidene bis(4-hydroxycoumarin) (Table 2).

Table 2. Synthesis of 3,3′-arylidene bis(4-hydroxycoumarin) (**3**) using MNPs-PSA (4.5 mg) under optimized conditions

Entry	Product	Ar	Time/ min	Yield[a], %	M.P., ºC	M.P., ºC [lit.]
1	3a	C_6H_5	6	94	226-228	228-230 [26]
2	3b	2-FC_6H_4	7	93	213-215	--
3	3c	4-FC_6H_4	5	96	257-259	258-260[27]
4	3d	4-ClC_6H_4	5	95	253-256	252-254 [26]
4	3e	2-MeC_6H_4	9	93	237-238	237-238
5	3f	2-$NO_2C_6H_4$	8	92	106-108	104-106 [27]
6	3g	4-$NO_2C_6H_4$	5	95	240-242	232-234 [26]
7	3h	3-$NO_2C_6H_4$	6	94	235-237	234-236[27]
8	3i	3-$OMeC_6H_4$	8	92	199-201	---
9	3j	2-$OMeC_6H_4$	10	92	234-236	236-238 [27]
10	3k	2-BrC_6H_4	7	93	253-255	256-258 [27]

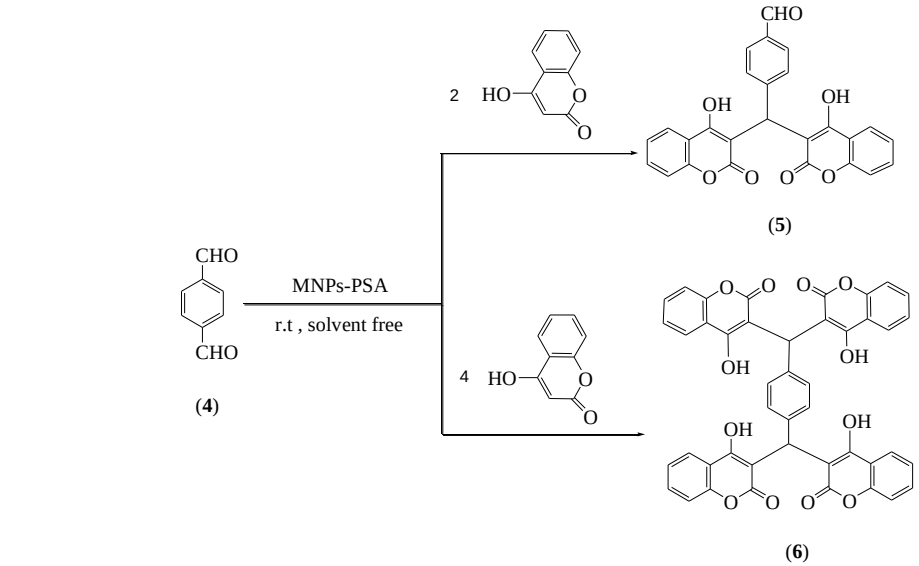
[a]Isolated Yield

Mechanistically, a reasonable pathway for the synthesis of bis-4-hydroxycoumarins **3**a-k using MNPs-PSA is described in Scheme 3. We presume that the aldehydes act as acceptors and the coumarin as the nucleophile resulting in a Michael adduct which, under the influence of MNPs-PSA, forms an intermediate **I** which undergoes nuclophilic reactions with 4-hydroxycoumarin to afford 3,3′-arylidene bis(4-hydroxycoumarin) **3**.

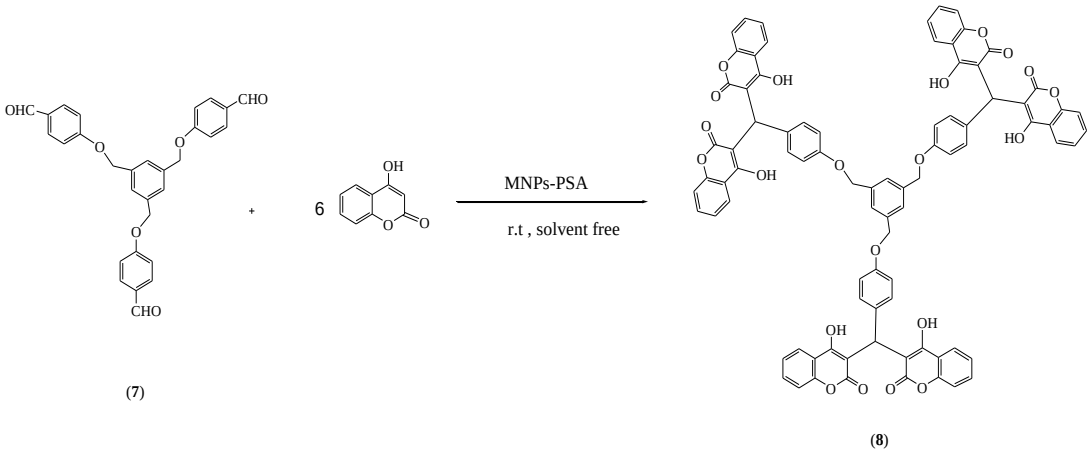


Scheme 3. The suggested mechanism for the formation of 3,3′-arylidene bis(4-hydroxycoumarin) catalyzed by MNPs-PSA

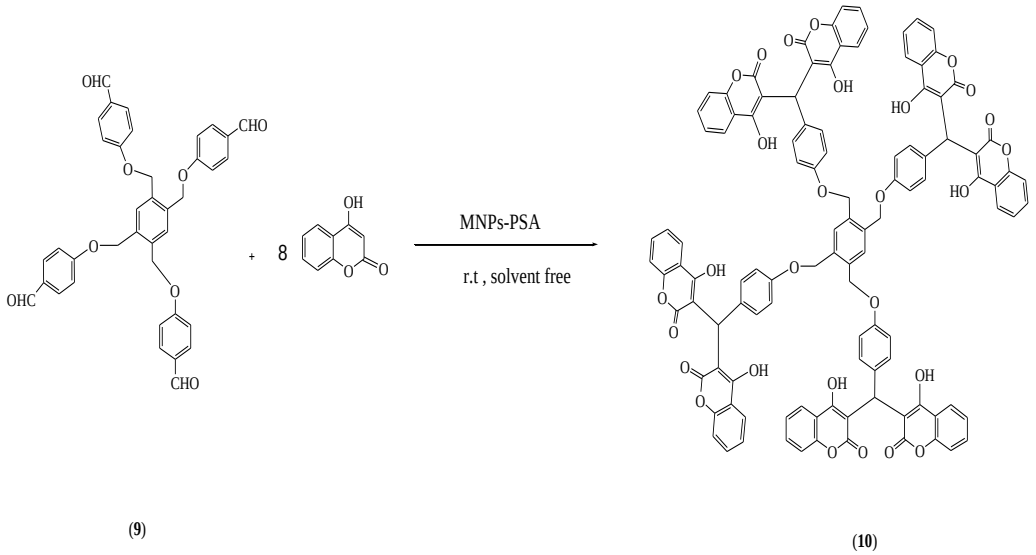
Following the synthesis of coumarin derivatives, Selective condensation of a dialdehyde **4**, that is, terephthaldialdehyde to the corresponding bis-phenyl coumarin was achieved by controlling the molar ratio of coumarin (Scheme 4). The results showed that the addition of 2 equivalents of coumarin to terephthaldialdehyde, gives **5** in good yield (Scheme 4). Treatment of 4 equivalents of coumarin with terephthaldialdehyde gives the corresponding di-(3,3′-arylidene bis(4-hydroxycoumarin)), **6** in excellent yield at room temperature under same conditions. This reaction was further explored for the synthesis of tri-(bis -phenyl) coumarin **8** and tetra-(3,3′-arylidene bis(4-hydroxycoumarin) **10** as new triarylcoumarins, by the condensation of aldehyde **7** with **6** equivalents coumarin and aldehydes **9** with 8 equivalents coumarin under similar condition (solvent-free and grinding) in high yields (Schemes 5 and 6).



Scheme 4.



Scheme 5.



(**9**) (**10**)

Scheme 6.

For practical purposes, the ability to easily recycle the catalyst is highly desirable. To investigate this issue, the recyclability of the catalyst was examined for the synthesis of substituted coumarins. We found that this catalyst demonstrated remarkably excellent reusability; after the completion of the reaction, the reaction mixture was diluted with diethyl ether and the catalyst was easily and rapidly separated from the product by exposure to an external magnet and decantation of the reaction solution (Figure 1). The remaining magnetic nanocatalyst was further washed with diethylether to remove residual product. Then, the reaction vessel was charged with fresh substrate and subjected to the next. The catalyst can be recycled up to 10 runs without any significant loss of activity. In addition, one of the attractive features of this novel catalyst system which is the rapid (within 5 s) and efficient separation of the catalyst (100%) by using an appropriate external magnet minimizes the loss of catalyst during the separation.

Figure 1. Image showing MNPs-PSA can be separated by applied magnetic field. A reaction mixture in the absence (left) or presence of a magnetic field (right)

A comparison of MNPs-PSA with SA for the synthesis of 3,3′-arylidene bis(4-hydroxycoumarin) is shown in Table 3. We have found that SA requires harsh reaction conditions for the synthesis of 3,3′-arylidene bis(4-hydroxycoumarin). In adition to, the number of catalyst recycles is increased when MNPs-PSA is used as catalyst.

Table 3. Comparison of SA and MNPs-PSA for the synthesis of 3,3′-arylidene bis(4-hydroxycoumarin)

Catalyst	Reaction Conditions	Time (min)	Yield (%)	No. recycle
MNPs-SA	Solvent-free, rt	6-10	92-95	10
SA	H_2O, MWI, 150 ºC	6-8	75-96	-

Conclusion

The MNPs- PSA was used as a recyclable nanocatalyst for the green synthesis of 3,3′-arylidene bis(4-hydroxycoumarin) in short reaction times with high to excellent yields under solvent-free conditions at room temprature. Besides that, the system couples the advantages of heterogeneous (easy separation, and excellent reusability of up to 10 runs) and homogeneous SA-based (high activity and reproducibility), which make it as a promising material for practical and large-scale applications.

Characterization data

Compound (3b) Light yellow crystals; mp. 213-215 ºC; IR (KBr): υ 3070, 2925, 1643, 1624, 1579, 1353, 1257, 751 cm^{-1}. ^{1}H NMR (DMSO-*d*6, 400 MHz): *δ* 12.28 (b, 1H), 9.86 (s, 1H), 7.72 (d, 2H, *J*=8.4Hz), 7.61-7.69 (2H, m), 7.48 (t, 2H, *J*=8Hz), 7.26-7.30 (m, 3H), 7.01-7.05 (3H, m), 6.35 (s, 1H). ^{13}CNMR (DMSO-*d*6, 100 MHz): *δ* 166.57, 164.92, 163.17, 158.93, 152.12, 148.08, 132.42, 132.01, 131.88, 131.15, 130.95, 128.56, 123.87, 123.51, 123.06, 116.86, 116.29, 115.39, 103.50, 103.21, 36.89; ESI-MS: m/z [M+, 430]. Anal. calcd. For $C_{25}H_{15}FO_6$; C: 69.77, H: 4.41, Found: C: 70.03, H: 4.39%.

Compound (3i) Milk-white crystals, mp 199–201 ºC; IR (KBr): υ 3049, 2927, 1681, 1647, 1527, 1316, 1210, 1071, 748 cm^{-1}; ^{1}H NMR (DMSO-*d*6, 400 MHz): *δ* 11.34 (b, 1H), 10.22 (s, 1H), 7.70 (dd, 2H, *J*=8.4 Hz), 7.48 (d, 2H, *J*=8 Hz), 7.39-7.44 (2H, m), 7.22 (dd, 4H, *J*=8.4 Hz), 6.85-6.93 (m, 2H), 6.19 (s, 1H), 3.65 (s, 3H). ^{13}CNMR (DMSO-*d*6, 100 MHz): *δ* 165.44, 163.57, 160.11, 158.93, 152.12, 148.08, 146.21, 153.63, 140.08, 137.06, 112.02, 117.12, 118.97, 119.30, 116.86, 116.11, 115.73, 103.66, 103.08, 58.34, 38.49; ESI-MS: m/z [M+, 457]. Anal. calcd. For $C_{26}H_{18}O_7$; C: 70.59, H: 4.10, Found: C: 71.21, H: 4.05%.

Compound (5) White crystals, mp 230–232 ºC; IR (KBr): υ 3049, 1810, 1681, 1622, 1547, 1332, 1216, 1085, 757 cm^{-1}; ^{1}H NMR (DMSO-*d*6, 400 MHz): *δ* 11.35 (b, 1H), 11.01 (s, 1H), 10.09 (s, 1H), 7.73 (d, 2H, *J*=8 Hz), 7.55-7.61 (m, 2H), 7.51 (t, 2H, *J*=8 Hz), 7.35-7.38 (2H, m), 7.19 (dd, 4H, *J*=8.4 Hz), 6.43 (s, 1H); ^{13}CNMR (DMSO-*d*6, 100 MHz): *δ* 173.54, 167.21, 165.49, 160.15, 158.57, 148.39,

142.50, 136.70, 131.75, 131.08, 128.17, 126.83, 123.64, 121.18, 120.95, 119.21, 118.24, 118.03, 111.89, 111.07, 103.55, 38.19; ESI-MS: m/z [M+, 440]. Anal. calcd. For $C_{26}H_{16}O_7$, C: 70.91, H: 3.66, Found: C: 71.97, H: 3.58%.

Compound (6) Pink solid, mp 241–243 ºC; IR (KBr): υ 3049, 1679, 1629, 1455, 1216, 1109, 759 cm^{-1}; ^{1}H NMR (DMSO-*d*6, 400 MHz): *δ* 11.41 (b, 2H), 11.17 (s, 2H), 8.58-8.61 (d, 6H, *J*=8 Hz), 7.60-7.66 (m, 3H), 8.29-8.32 (dd, 4H, *J*=4.3 Hz), 7.80-7.86 (t, 3H, *J*=6 Hz), 7.56-7.72 (dd, 2H, *J*=4.3 Hz), 7.22-7.29 (m, 2H), 6.78 (s, 2H); ^{13}CNMR (DMSO-*d*6, 100 MHz): *δ* 168.11, 163.27, 160.56, 157.14, 149.51, 148.80, 144.06, 135.54, 132.93, 132.19, 131.12, 124.65, 123.72, 123.72, 122.61, 121.28, 119.70, 112.15, 102.15, 37.17; Anal. calcd. For $C_{44}H_{26}O_{12}$, C: 70.78, H: 3.51, Found: C: 69.90, H: 3.59%.

Compound (8) Light red solid, mp 239–241 ºC; IR (KBr): υ 3021, 2950, 1680, 1635, 1516, 1377, 1216, 1173, 742 cm^{-1}; ^{1}H NMR (DMSO-*d*6, 400 MHz): *δ* 12.17 (b, 3H), 11.87 (s, 3H), 7.69 (d, 6H, *J*=8 Hz), 7.60-7.66 (m, 6H), 7.55 (d, 6H, *J*=8 Hz), 7.32-7.37 (m, 3H), 7.18-7.25 (m, 6H), 6.84-7.14 (m, 12H), 6.73 (s, 3H); 5.89 (s, 6H); ^{13}CNMR (DMSO-*d*6, 100 MHz): *δ* 166.51, 163.87, 161.66, 159.11, 155.05, 146.54, 142.94, 138.28, 135.72, 135.51, 131.87, 129.87, 128.22, 128.03, 127.92, 123.28, 121.16, 114.65, 113.57, 110.53, 103.57, 40.27, 38.56; Anal. calcd. For $C_{84}H_{54}O_{21}$, C: 72.10, H: 3.89, Found: C: 73.08, H: 3.78%.

Compound (10) Red solid, mp 226–228 ºC; IR (KBr): υ 3017, 2926, 1677, 1619, 1526, 1338, 1218, 1172, 1127, 1012, 745 cm^{-1}; ^{1}H NMR (DMSO-*d*6, 400 MHz): *δ* 11.32 (b, 4H), 10.90 (s, 4H), 7.65 (d, 8H, *J*=8 Hz), 7.44-7.48 (m, 2H), 7.27-7.31 (m, 16H), 7.12-7.16 (m, 8H), 6.97-7.02 (m, 8H), 6.84-6.62 (m, 8H), 6.07 (s, 4H); 5.70 (s, 8H); ^{13}CNMR (DMSO-*d*6, 100 MHz): *δ* 166.28, 165.72, 164.95, 161.76, 158.64, 154.67, 142.90, 141.52, 136.02, 135.90, 132.53, 131.86, 129.94, 128.97, 128.13, 127.90, 127.72, 127.55, 120.70, 114.53, 113.20, 109.05, 103.65, 40.20, 35.64; Anal. calcd. For $C_{110}H_{70}O_{28}$, C: 71.82, H: 3.83, Found: C: 72.18, H: 3.89%.

Acknowledgments

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