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REMARKABLY FACILE HECK REACTIONS IN AQUEOUS TWO-PHASE SYSTEM CATALYZED BY REUSABLE Pd/C UNDER LIGAND-FREE CONDITIONS

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GRAPHICAL ABSTRACT



Abstract A fast and convenient Heck reaction was achieved catalyzed by Pd/C in aqueous two-phase system. The aqueous two-phase system has been shown to be a highly active solvent for Heck reactions of aryl halides even in the absence of organic ligands.

Keywords Aqueous two-phase system; Heck reaction; Pd/C; trans-cinnamate

INTRODUCTION

The Heck reaction, a palladium-catalyzed cross-coupling of olefins with aryl and vinyl halides,^[1] is widely employed in modern organic synthesis for preparation of alkenes containing virtually any functional groups.^[2] The reaction is usually carried out in organic solvents with prolonged heating in the presence of palladium complexes with phosphine ligands (1–5 mol%) and an appropriate base.^[3] In recent years, catalysts based on phosphorus,^[4] sulfur,^[5] nitrogen-containing^[6] palladacycles,^[7] and nucleophilic *N*-heterocyclic carbenes^[8] have been proposed instead of palladium complexes with phosphine. However, even in the presence of new, more efficient catalysts, the reaction is completed at 100–150 °C in 24–90 h.^[9,10] For this reason, a search for a more active reaction system is still among the most important tasks in the study of Heck reactions.^[10]

Another promising line (from the practical standpoint) in this area is the use of water instead of toxic and difficult to recover organic solvents, because water is the most accessible, safe, and ecologically pure solvent.^[11] Recently, much effort has been directed toward using water as a solvent for organic and organometallic

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reactions,^[12] but the main problem with the application of water in organic synthesis is the long time of reaction and the insolubility of many reagents and catalysts in this medium.

An aqueous two-phase system (ATPS) is widely used in biochemistry and biotechnology for purification of proteins,^[13] enzymes,^[14] amino acids^[15] and so on.^[16] ATPS has great potential for industrial applications because it can be used to obtain a concentrated and purified product in one step by addition of crude broths containing suspended matter (e.g., cells) and offers gentle nontoxic environments for labile biomolecules. To seek new reaction solvents, we found that the ATPS is more effective than pure water or other traditional organic solvents in the Heck reaction, so we now report a new method for the Heck reaction that using ATPS as solvent catalyzed by ligand-free and reusable Pd/C catalysts.

RESULTS AND DISCUSSION

Generally there are two type of aqueous two-phase systems: one is composed of a polymer, a phase-separation salt (which is the key factor because the organic solvent and the salts absorb the water together until it has a dynamic balance to form the two-phase system), and water (e.g., $PEG/Na_2SO_4/H_2O$), and another is composed of an organic solvent, a phase-separation salt, and water (e.g., acetone/ $(NH_4)_2SO_4/H_2O$). As a model, the Heck reaction of PhI with methyl acrylate (MA) catalyzed by $3 \mod^{9} Pd/C$ (5%) without ligand and cocatalyst under reflux condition (about 77-80°C) was examined in different ATPSs such as ethanol/ K_2 HPO₄/H₂O, and the results seen in Table 1. In pure water, only 16% conversion was obtained after 12 h (Table 1, entry 2). While using the base of K_2CO_3 in pure water, the product is a mixture that include the methyl cinnamate and cinnamic acid (Table 1, entry 1). Addition of a phase-transfer catalyst (PTC) (e.g., cetyltrimethylammonium bromide, CTAB) led only to a gradual increase in the conversion rate. In anhydrous ethanol, only 21% conversion was obtained after 12h (Table 1, entry 3); we also scanned other traditional solvents, and both the yields and reaction times are moderate to good (Table 1, entries 4–7). While using the ATPS as solvent, the product conversion increased very quickly. In ethanol/K2HPO4 ATPS, the yield of methyl cinnamate increased dramatically to 96% after 2h (Table 1, entries 9 and 10). This result encouraged us to explore the Heck reaction in a series of ATPSs to find the optimal conditions for the cross-coupling reaction.

To optimize the ATPS and find an efficient protocol for Heck coupling reaction, we studied the effect of various parameters such as solvent, phase-separation salts (they act in a double role: those salts can separate the mixture solvent into two phases, and the basic salt can also promote the Heck reaction, while the acidic salts did not work for the reaction), and catalyst (Scheme 1). The results are summarized in Table 1. We selected three simple ATPSs as reaction solvents to find the best one for the Heck reaction (Scheme 1). The alkalinity of K_2CO_3 is too strong to lead the product to hydrolyze into cinnamic acid (entries 1 and 8), and the Heck reaction (entries 9 and 10) proceeded in 96% yield catalyzed by Pd/C in the EtOH/ K_2HPO_4 ATPS reflux for 2 h. In the acetone/ K_2HPO_4 system, it proceeded in 87% yield (entry 11), and in the PEG2000/ K_2HPO_4 system (entry 14) it gave 89% yield. No reaction occurred in the acid ATPS such as acetone/ $(NH_4)_2SO_4$ or

Entry	Solvent	Phase-separation salts	Catalyst	$T (^{\circ}C/h)$	Yield ^b (%)
1	Water	K ₂ CO ₃	Pd/C	Reflux/12	Mixture
			$Pd(OAc)_2$	Reflux/12	Mixture
2	Water	K ₂ HPO ₄	Pd/C	Reflux/12	$16, 21^c$
		2 .	$Pd(OAc)_2$	Reflux/12	$15, 19^c$
3	EtOH	K ₂ HPO ₄	Pd/C	Reflux/12	21
		2 .	$Pd(OAc)_2$	Reflux/12	23
4	DMF	K ₂ HPO ₄	Pd/C	Reflux/8	82
5	DMSO	K ₂ HPO ₄	Pd/C	Reflux/8	85
6	1,4-Dioxane	K ₃ PO ₄	Pd/C	Reflux/8	73
7	Toluene	K ₃ PO ₄	Pd/C	Reflux/8	61
8	EtOH/water	K ₂ CO ₃	Pd/C	Reflux/2	Mixture
	,		$Pd(OAc)_2$	Reflux/2	Mixture
9	EtOH/water	K ₂ HPO ₄	Pd/C	Reflux/2	96
			$Pd(OAc)_2$	Reflux/2	95
10	EtOH/water	K ₃ PO ₄	Pd/C	Reflux/2	94
			$Pd(OAc)_2$	Reflux/2	90
11	Acetone/water	K2HPO4	Pd/C	Reflux/2	87
12	Acetone/water	$(NH_4)_2SO_4$	Pd/C	Reflux/2	
13	PEG2000/water	$(NH_4)_2SO_4$	Pd/C	Reflux/2	
14	PEG2000/water	K ₂ HPO ₄	Pd/C	Reflux/2	89

Table 1. Effect of different solvents on the Heck reaction of C_6H_5I with MA under reflux conditions^{*a*}

^{*a*}Reaction condition: 3 mmol PhI, 3.3 mmol methyl acrylate, 3 mol% Pd/C, 8 mmol base (or phase separation salts), and solvent (10 mL), reflux at 80 °C for corresponding time by GC or TLC.

^bIsolated yield.

^cAdded CTAB

PEG2000/(NH₄)₂SO₄ system (entries 12 and 13). We got similar results in the ATPS catalyzed by Pd(OAc)₂. From all those experimental data in Table 1, we consider that the ATPS is better than the pure water, ethanol, dimethylformamide (DMF), and other traditional solvents for the Heck reaction. The catalytic activity of Pd/C is similar to that of Pd(OAc)₂ and it can be reused, so we finally consider that EtOH/K₂HPO₄ ATPS as solvent catalyzed by Pd/C is the optimal condition for the Heck reaction.

Taking the reaction of C_6H_5I with methyl acrylate as a model in the ethanol/ water two-phase system, we also scanned the effects of other bases such as KOH, NaOH, Na₂CO₃, NaHCO₃, KH₂PO₄, and DBU (1,8-diazabicyclo[5.4.0]undec-7ene). All those bases could not separate the mixture into two phases, so the reaction conditions are like the traditional condition (Scheme 2). Among the bases, KOH, NaOH, and Na₂CO₃ made the most of methyl cinnamate to decompose into cinnamic acid (Table 2, entries 1–3). NaHCO₃, KH₂PO₄, and DBU gave moderate yields of 78–86% (Table 2, entries 4–6). It must be pointed that only K₂HPO₄,



Scheme 1.



 K_3PO_4 , and K_2CO_3 can make the ethanol aqueous separate into two phases, whereas KOH, NaOH, Na₂CO₃, DBU, NaHCO₃, and KH₂PO₄ do not have separation phenomena.

The typical experimental procedure for the Pd/C catalyzed Heck-type crosscoupling reactions is as follows: The reaction was carried out simply by treatment of a solution of aryl halides (3 mmol), olefin (3.3 mmol, 1.1 eq), and 3 mol% Pd/C in an ATPS (6 mL ethanol, 4 mL water, 8 mmol K₂HPO₄) reflux for an appropriate period of time until there was complete consumption of the starting material, as monitored by thin-layer chromatography (TLC). After the reaction, the mixture was filtered to recycle the catalyst, and the residue mixture fell into two phases automatically. The supernatant phase, which contains 96% of the product, was separated out and another 6 mL were added to extract the residue (about 4% of product in the water phase). It was dried over Na₂SO₄. The solvent was filtered and evaporated. The product was purified by chromatography on silica (eluent: EtOAc/petroleum ether = 1:15). The purity of the isolated product was determined by gas chromatographic (GC) analysis or ¹H NMR. The results are summarized in Table 3. In fact, iodobenzene reacted with various olefins and gave the corresponding products with 86–96% yields in a short time (Table 3, **3a–3f**). From the GC/MS spectra, we found the doubly substituted product of 1.4% exists when 2-BrC_6H_4 I reacts with excess olefin, but the C-I bond is the main reaction position (3d-3f). 2-Methylsulfanyl iodobenzene (**3r**) yielded 35%, probably because of the steric effect of the S-methyl group. Aryl bromides proceeded from moderate to satisfactory yields (3g-3l). The reactant, having an electron-withdrawing group (3j-3l), reacted better and gave greater yield than those having an electronic-donating group (3g-3i). Similar conditions brought

Entry	Base	Yield (%) ^b	
1	КОН	Mix	
2	NaOH	Mix	
3	Na ₂ CO ₃	Mix	
4	NaHCO ₃	81	
5	KH ₂ PO ₄	86	
6	DBU	78	

Table 2. Effect of different bases on the Heck reaction in $ethanol/water^{a}$

^{*a*}Reaction condition: 3 mmol PhI, 3.3 mmol methyl acrylate, 8 mmol base, 3 mol% Pd/C, ethanol 6 ml, and water 4 ml, reflux at 80 °C for corresponding time by GC.

^bIsolated yield.

Compound	ArX	$Olefin^b$	Time (h)	Yield ^c (%)
3a	C ₆ H ₅ I	MA	1.5	96
3b	C ₆ H ₅ I	BA	1.5	93
3c	C ₆ H ₅ I	PTEA	2.0	86
3d	$2-BrC_6H_4I$	MA	1.5	92^d
3e	2-Br C_6H_4I	BA	1.5	94^d
3f	2-Br C_6H_4I	PTEA	2.0	87^d
3g	$4-CH_3C_6H_4Br$	MA	4.0	90
3h	$4-CH_3C_6H_4Br$	BA	4.0	85
3i	$4-CH_3C_6H_4Br$	PTEA	8.0	82
3i	$3-NO_2C_6H_4Br$	MA	2.0	94
3k	$3-NO_2C_6H_4Br$	BA	2.0	93
31	$3-NO_2C_6H_4Br$	PTEA	2.0	89
3m	2-Bromothiophene	MA	4.0	89
3n	2-Bromothiophene	BA	4.0	85
30	2-Bromothiophene	PTEA	6.0	80
3q	$4-NO_2C_6H_4Cl$	MA	8.0	87
3p	$4-NO_2C_6H_4Cl$	BA	8.0	88
3r	2-CH ₃ SC ₆ H ₄ I	MA	6.0	35
3a	C ₆ H ₅ Cl	MA	24	Trace

Table 3. Heck reaction of aryl or heteraryl halides with olefins^a

^{*a*}Reaction condition: 3 mmol ArX, 3.3 mmol olefin, 8 mmol K₂HPO₄, and 3 mol % Pd/C, aqueous two-phase system (10 mL) reflux at 80 °C for corresponding time by GC or TLC.

^bMA: $CH_2 = CHCO_2CH_3$, BA: $CH_2 = CHCO_2(Bu-n)$, PTEA: $CH_2 = CHCO_2CH_2CH_2SPh$.

^cIsolated yield.

^dExit about 1.4–2.0% double-substituted product from the GC/MS.

about the coupling of heteroaryl substrates such as 2-bromothiophene, which also gave a moderate yield of 80-89%. Unfortunately, aryl chloride did not react well, even when prolonging the reaction time at high temperature, except 1-chloro-4-nitrobenzene (**3p**, **3q**). All of the reactions were clean, and (*E*)-cinnamates were the only products.

Pd/C remained completely in the ATPS after the reaction, so it could be reused. Iodobenzene and methyl acrylate were chosen as reactants. After the Pd/C was filtered out of the first reaction, the catalyst was irradiated by ultrasound for 0.5 h at room temperature in pure water. Then another portion of iodobenzene and methyl acrylate was added. The procedure was repeated four times, and the catalyst system proceeded well with a little loss of activity (Table 4, entry 1, runs 1–5). When we decreased the amount of Pd/C to 1.5 mol%, the reaction still

		Isolated yield (%)				
Entry	Run 1	Run 2	Run 3	Run 4	Run 5	
1	94	90	82	74	78	
2 ^{<i>a</i>}	84	76	70	62	60	

Table 4. Recycling of the catalyst system

^aIn entry 2, 1.5 mol% Pd/C was used.

proceeded well, and good yields were obtained in the following four runs (Table 4, entry 2, runs 1–5).

CONCLUSIONS

In summary, an efficient ATPS for the Heck-type cross-coupling reaction has been developed. In the presence of Pd/C, coupling of various aryl halides with olefins were carried out efficiently to afford the desired products in moderate to excellent yields. The procedure is operationally simple and comparable. The use of an ATPS reaction medium and traditional Pd catalysts promise further opportunities in batch processing and catalyst recycling.

EXPERIMENTAL

All reagents were used as received. ¹H NMR and ¹³C NMR were recorded at 300 MHz and 75 MHz with a Bruker Avance 300 spectrometer. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as an internal standard. Infrared (IR) spectra were obtained using a Bruker Equinox 55 Fourier transform (FT)–IR spectrophotometer in KBr pellets. Melting points were obtained with a XT4A melting-point apparatus and were uncorrected. GC analyses were conducted using a Trace GC/Thermo Finnigan equipped with an SE-54 capillary column (25 m) and an FID detector. Melting points were determined by using a Büchi B-540 melting-point apparatus and are uncorrected.

Aryl or heteroaryl halide (3 mmol), MA (3.3 mmol, BA or PTEA) (see Note *b* in Table 3 for MA, BA, and PTEA definitions), 6 mL ethanol, 4 mL water, 1.4 g K₂HPO₄, and 5% Pd/C (0.09 mmol) were placed in a 25-ml, two-necked flask. The mixture was heated and refluxed to about 80 °C in an air atmosphere for the required time with magnetic stirring. After cooling to room temperature, the mixture was filtered to recycle the catalyst, and the residue mixture fell into two phases automatically. The supernatant phase, which contains 96% of the product was separated out, and then another 6 mL were added to extract the residue (about 4% of product in the water phase), which was dried over Na₂SO₄. The solvent was filtered and evaporated. The product was purified by chromatography on silica (eluent: EtOAc/ petroleum ether = 1:15). The purity of the isolated product was determined by GC analysis or ¹H NMR.

(E)-Methyl Cinnamate (3a)

White solid, mp 35–36 °C (lit.^[17] 34–35 °C); ¹H NMR (CDC1₃, 300 MHz) δ : 7.70 (d, J = 15.9 Hz, 1H), 7.50–7.53 (m, 2H), 7.37–7.42 (m, 3H), 6.45 (d, J = 15.9 Hz, Hz, 1H), 3.80 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 167.4, 144.8, 134.4, 130.3, 128.9, 128.1, 117.8, 51.6; IR (KBr) ν : 2365, 1708, 1632, 1152, 856 cm⁻¹.

(E)-n-Butyl Cinnamate (3b)

Oil;^[18,19] ¹H NMR (CDCl₃, 300 MHz) δ : 7.79 (d, J = 16.0 Hz, 1H), 7.61–7.63 (m, 2H), 7.46–7.49 (m, 3H), 6.55 (d, J = 16.0 Hz, 1H), 4.33 (t, J = 6.6 Hz, 2H),

1.80–1.85 (m, 2H), 1.48–1.61 (m, 2H), 1.07 (t, J = 7.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 167.0, 144.5, 134.5, 130.2, 128.8, 128.0, 118.3, 64.4, 30.8, 19.2, 13.7; IR (film) ν : 3068, 2959, 1712, 1638, 1467, 1327, 767, 684 cm⁻¹.

(E)-2-(Phenylsulfanyl)ethyl Cinnamate (3c)

Oil; ¹H NMR (CDC1₃, 300 MHz) δ : 7.68 (d, J = 16.1 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.23–7.53 (m, 10H), 6.42 (d, J = 16.1 Hz, 1H), 4.40 (t, J = 6.6 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ : 166.7, 145.3, 135.2, 134.3, 130.3, 129.2, 129.0, 128.8, 128.2, 126.6, 117.7, 63.1, 32.5; IR (film) ν : 3038, 2825, 1716, 1618, 1469, 1121, 749, 594 cm⁻¹. Anal. calcd. for C₁₇H₁₆O₂S: C, 71.80; H, 5.67. Found: C, 71.83; H, 5.68.

(E)-Methyl 2-Bromocinnamate (3d)

Oil;^[20] ¹H NMR (CDC1₃, 300 MHz) δ : 8.06 (d, J = 15.9 Hz, 1H), 7.60–7.64 (m, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.21–7.25 (m, 1H), 6.40 (d, J = 15.9 Hz, 1H), 3.83 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 166.8, 143.2, 134.5, 133.4, 131.2, 127.7, 127.1, 125.3, 120.7, 51.9; IR (KBr) ν : 2365, 1708, 1632, 1152, 856 cm⁻¹. Anal. calcd. for C₁₀H_{9Br}O₂: C, 49.82; H, 3.76. Found: C, 49.83; H, 3.73.

(E)-n-Butyl 2-Bromocinnamate (3e)

Oil;^[21] ¹H NMR (CDC1₃, 300 MHz) & 8.04 (d, J = 15.9 Hz, 1H), 7.61 (d, J = 8.5 Hz, 2H), 7.32 (t, J = 7.4 Hz, 1H), 7.19–7.25 (m, 1H), 6.39 (d, J = 15.9 Hz, 1H), 4.23 (t, J = 6.6 Hz, 2H), 1.62–1.75 (m, 2H), 1.39–1.50 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) & 166.5, 143.1, 134.8, 133.5, 131.1, 128.0, 127.3, 126.5, 121.1, 64.2, 31.1, 19.1,13.4; IR (KBr) ν : 2808, 2306, 1695, 1605, 1158, 852, 714 cm⁻¹. Anal. calcd. for C₁₃H₁₅BrO₂: C, 55.14; H, 5.34. Found: C, 55.12; H, 5.38.

(E)-2-(Phenylsulfanyl)ethyl 2-Bromocinnamate (3f)

Oil; ¹H NMR (CDC1₃, 300 MHz) δ : 8.08 (d, J = 16.1 Hz, 1H), 7.58–7.64 (m, 2H), 7.44 (d, J = 7.5 Hz, 2H), 7.19–7.36 (m, 5H), 6.38 (d, J = 16.1 Hz, 1H), 4.40 (t, J = 6.6 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ : 166.1, 143.6, 135.0, 134.4, 133.5, 131.3, 129.9, 129.1, 127.8, 127.7, 126.6, 125.4, 120.4, 63.1, 32.4; IR (KBr) ν : 2816, 2351, 1702, 1612, 1155, 974, 856, 658 cm⁻¹. Anal. calcd. for C₁₇H₁₅BrO₂S: C, 56.21; H, 4.16. Found: C, 56.23; H, 4.18.

(E)-Methyl 3-p-Tolyl Acrylate (3g)

White solid;^[17,18] mp 56.5–57.4 °C (lit.^[21] 60–62 °C); ¹H NMR (CDCl₃, 300 MHz) δ : 7.63 (d, J = 16 Hz, 1H), 7.44 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 6.46 (d, J = 16 Hz, 1H), 3.82 (s, 3H), 2.3 (s, 3H); ¹³C NMR (CDCl₃) δ : 167.5, 144.8, 140.6, 131.6, 129.5, 128.0, 116.6, 51.6, 21.4; IR (KBr) 2922, 1709, 1631, 1168 cm⁻¹.

(E)-n-Butyl 3-p-Tolyl Acrylate (3h)

Oil;^[18] ¹H NMR (CDCl₃, 300 MHz) δ : 7.75 (d, J = 16.0 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 6.50 (d, J = 16.0 Hz, 1H), 4.20 (t, J = 6.7 Hz, 2H), 2.48 (s, 3H), 1.75–1.85 (m, 2H), 1.51–1.61 (m, 2H), 1.08 (t, J = 7.4 Hz, 3H);¹³C NMR (75 MHz, CDCl₃) δ : 13.8, 19.3, 21.5, 30.8, 64.4, 117.3, 128.1, 129.7, 131.9, 140.7, 144.6, 167.3; IR (film) ν : 3015, 2959, 1712, 1608, 1514, 983, 813 cm⁻¹.

(E)-2-(Phenylthio)ethyl 3-p-Tolyl Acrylate (3i)

Oil; ¹H NMR (CDC1₃, 300 MHz) δ : 7.63 (d, J = 16.1 Hz, 1H), 7.50 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.23–7.53 (m, 5H), 6.46 (d, J = 16.1 Hz, 1H), 4.40 (t, J = 6.6 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ : 166.5, 145.5, 135.2, 134.9, 130.5, 130.2, 129.0, 128.8, 128.1, 126.2, 114.1, 63.1, 32.5, 18.5; IR (KBr) ν : 3035, 2908, 2865, 1609, 1445, 965, 819, 756, 693 cm⁻¹. Anal. calcd. for C₁₈H₁₈O₂S: C, 72.45; H, 6.08. Found: C, 72.46; H, 6.03.

(E)-Methyl 3-(3-Nitrophenyl)acrylate (3j)

White solid;^[21] mp 115–116 °C (lit.^[22] 113–114 °C); ¹H NMR (CDC1₃, 300 MHz) δ : 8.36 (s, 1H), 8.22 (d, J=8.0 Hz, 1H), 7.82 (d, J=7.6 Hz, 1H), 7.70 (d, J=16.0 Hz, 1H), 7.58 (t, J=8.5 Hz, 1H), 6.57 (d, J=16.0 Hz, 1H), 3.83 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 166.6, 148.7, 141.9, 136.1, 133.6, 129.9, 124.5, 122.4, 120.9, 52.0; IR (KBr) ν : 2819, 2512, 1705, 1595, 1515, 1343, 1155, 858 cm⁻¹.

(E)-n-Butyl 3-(3-Nitrophenyl)acrylate (3k)

White solid, mp 48–49 °C (lit.^[22,23] 47–48 °C); ¹H NMR (CDC1₃, 300 MHz) δ : 8.38 (s, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.71 (d, J = 16.0 Hz, 1H), 7.59 (t, J = 8.5 Hz, 1H), 6.57 (d, J = 16.0 Hz, 1H), 4.24 (t, J = 6.6 Hz, 2H), 1.66–1.75 (m, 2H), 1.38–1.51 (m, 2H), 0.97 (t, J = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 166.2, 148.7, 141.6, 136.3, 133.6, 129.0, 124.4, 122.4, 121.6, 64.8, 30.7, 19.1, 13.7; IR (KBr) ν : 2851, 2516, 2313, 1709, 1645, 1550, 1321, 958 cm⁻¹.

(E)-2-(Phenylthio)ethyl 3-(3-Nitrophenyl)acrylate (31)

White solid, mp 65–66 °C; ¹H NMR (CDC1₃, 300 MHz) δ : 8.36 (s,1H), 8.25 (d, J = 8.1 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 16.3 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.45 (d, J = 8.5 Hz, 2H), 7.21–7.39 (m, 3H), 6.50 (d, J = 16.3 Hz, 1H), 4.42 (t, J = 6.6 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ : 165.8, 148.7, 142.2, 136.1, 135.1, 133.6, 130.1, 129.9, 129.1, 126.7, 124.6, 122.5,120.8, 63.6, 32.6; IR (KBr) ν : 3025, 1709, 1602, 1508, 1339, 958, 850, 755 cm⁻¹. Anal. calcd. for C₁₇H₁₅NO₄S: C, 61.99; H, 4.59. Found: C, 61.95; H, 4.62.

(E)-Methyl 3-(Thiophen-2-yl)acrylate (3m)

Oil;^[23,24] ¹H NMR (300 MHz, CDCl₃) δ : 7.68 (d, J = 16.1 Hz, 1H), 7.32 (d, J = 5.2 Hz, 1H), 7.23 (d, J = 5.6 Hz, 1H), 7.04 (dd, J = 5.2 Hz; J = 5.6 Hz, 1H), 6.23 (d, J = 16.1 Hz, 1H), 3.85 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 165.5, 141.3, 139.8, 130.2, 128.8, 128.2, 116.3, 52.6; IR (film) ν : 2952, 1701, 1624, 1306 cm⁻¹.

(E)-n-Butyl 3-(Thiophen-2-yl)acrylate (3n)

Oil;^[23,25] ¹H NMR (300 MHz, CDCl₃) δ : 7.76 (d, J = 15.7 Hz, 1H), 7.35 (d, J = 4.9 Hz, 1H), 7.23 (d, J = 3.4 Hz, 1H), 7.04 (dd, J = 3.7 Hz; J = 6.7 Hz, 1H), 6.23 (d, J = 15.7 Hz, 1H), 4.18 (t, J = 6.6 Hz, 2H), 1.72–1.62 (m, 2H), 1.48–1.36 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H);¹³C NMR (75 MHz, CDCl₃) δ : 167.3, 140.0, 137.3, 131.3, 128.7, 128.5, 117.5, 64.8, 31.2, 19.6, 14.1; IR (film) ν : 2959, 1708, 1628, 1316 cm⁻¹.

(E)-2-(Phenylthio)ethyl 3-(Thiophen-2-yl)acrylate (30)

Oil; ¹H NMR (300 MHz, CDCl₃) δ : 7.61 (d, J = 15.9 Hz, 1H), 7.52–7.45 (m, 2H), 7.36 (q, J = 3.4 Hz, J = 6.8 Hz, 1H), 7.04 (d, J = 8.2 Hz, 2H), 6.42 (d, J = 15.9 Hz, 1H), 6.28–6.21 (m, 3H), 4.25 (t, J = 6.6 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ : 166.8, 141.2, 139.9, 133.2, 130.5, 129.9, 129.2, 128.8, 128.0, 124.6, 116.3, 64.8, 31.2; IR (film) ν : 2925, 1716, 1626, 1306, 983 cm⁻¹. Anal. calcd. for C₁₅H₁₄O₂S₂: C, 62.04; H, 4.86. Found: C, 62.02; H, 4.88.

(E)-Methyl 3-(4-Nitrophenyl)acrylate (3p)

Light yellow solid, mp 132.3–133.5 °C (lit.^[24,26] 133–135 °C); ¹H NMR (CDCl₃, 300 MHz) δ : 8.25 (d, J = 8.8 Hz, 2H), 7.73 (d, J = 16.3 Hz, 1H), 7.69–7.66 (m, 2H), 6.65 (d, J = 16.2 Hz, 1H), 3.83 (s, 3H); ¹³C NMR (CDCl₃) δ : 166.4, 148.5, 141.9, 140.5, 128.6, 124.2, 122.1, 52.1; IR (KBr) IR: 2959, 1709, 1641, 1599, 1518, 1343 cm⁻¹.

(E)-n-Butyl 3-(4-Nitrophenyl)acrylate (3q)

Light yellow solid, mp 62.8–65.3 °C (lit.^[24,27] 64–65 °C); ¹H NMR (CDCl₃, 300 MHz) δ : 8.25 (d, J = 8.8 Hz, 2H), 8.05 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 16.1 Hz, 1H), 6.86 (d, J = 16.1 Hz, 1H), 4.14 (t, J = 6.8 Hz, 2H), 1.65–1.70 (q, J = 6.8 Hz, 2H), 1.40–1.51 (m, 2H), 1.07 (t, J = 7.2 Hz, 3H); IR (KBr) ν : 3058, 2958, 1709, 1601, 1493, 1308, 982, 759 cm⁻¹.

(E)-Methyl 3-(2-(Methylthio)phenyl)acrylate (3r)

Oil; ¹H NMR (CDC1₃, 300 MHz) δ : 8.21 (d, J = 15.8 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.27–7.35 (m, 2H), 7.22 (t, J = 8.5 Hz, 1H), 6.40 (d, J = 15.8 Hz, 1H), 3.83 (s, 3H), 2.49 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 167.2, 141.8, 139.4, 134.8, 130.3, 127.5, 127.1, 125.7, 119.7, 51.7, 16.7; IR (KBr) ν : 2812, 2356, 1692, 1602, 1156, 858, 765 cm⁻¹. Anal. calcd. for C₁₁H₁₂O₂S: C, 63.43; H, 5.81. Found: C, 63.47; H, 5.86.

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