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High-yielding synthesis of 2-arylacrylamides via homogeneous catalytic aminocarbonylation of α-iodostyrene and α,α′-diiodo-1,4-divinylbenzene

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Abstract

Highly reactive iodoalkenes (α-iodostyrene and α,α′-diiodo-1,4-divinylbenzene) were prepared and used as substrates in palladium-catalysed aminocarbonylation reaction. Regardless of the type of amine nucleophile the corresponding *N*-substituted phenylacrylamides have been formed chemoselectively in nearly quantitative yields. High isolated yields (up to 83%) have been achieved both with unfunctionalised simple amines and amino acid methyl esters under mild reaction conditions.

Keywords: Aminocarbonylation; Carbon monoxide; Amino acid; Palladium; α-Iodostyrene

1. Introduction

Palladium-catalysed carbonylation reactions, carried out in the presence of various nucleophiles like amines and alcohols, belong to the most widely used homogeneous catalytic reactions in synthetic chemistry.[1] There are a number of applications concerning the synthesis of simple building blocks and the functionalisation of biologically important skeletons.[2] Aminocarbonylation plays a special role among these reactions, since those carboxamides which are difficult to prepare via the conventional carboxylic acid–carboxylic halide–carboxamide route (e.g., with bulky substituents at the amide nitrogen) can be synthesised from easily available starting materials.[3] In addition to the enol-triflates and aryl triflates the corresponding iodo analogues, iodoalkenes and iodoaromatics have been used for aminocarbonylation reaction. The homogeneous catalytic synthesis of unsaturated carboxamides or aryl carboxamides with various structures has been published also by our group.[4,5]

The application of styrene-derived iodoaromatics (2-iodo- and 4-iodostyrene) is well known in polymer chemistry [6–8] and in homogeneous cross-coupling (Stille-coupling).[9] Several applications are known for the application of iodostyrene possessing the iodo substituent in the unsaturated side chain. (*E*)-β-Iodostyrene as an iodoalkene coupling partner has been reacted in copper-mediated Stille cross-coupling with 1,3,5-tris[(*E*)-2-(tributylstannyl)vinyl]benzene.[10] α-Iodostyryl group can be introduced by the application of α-iodostyrene in Heck-[11] and Stille-coupling[12] reactions, in analogous reaction using 2-pyridylsilanes,[13] as well as its addition to aldehydes.[14,15]

The bromo analogue, (*E*)-β-bromostyrene, however, has been used more frequently in various transition metal-catalysed reactions. Its electrochemical carboxylation was carried out in the presence of nickel(II) catalysts.[16] It was also used as a substrate in palladium-catalysed asymmetric Kumada–Corriu coupling,[17] in multiple coupling reactions with norbornane and dicyclopentadiene,[18] in the reaction with chlorovinylsilanes resulting in β-substituted vinylsilanes[19] and in the functionalisation of cephem skeleton.[20]

The α-bromostyrene, the close analogue of our title substrates, has also been applied in several homogeneous catalytic reactions, such as in palladium-catalysed cross-coupling and consecutive [4+4] cycloaddition sequence,[21] in sequential amination/Heck cyclisation,[22] in direct amination with secondary and primary amines resulting in enamines and imines,

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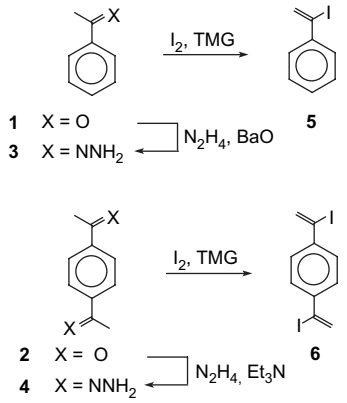
respectively.[23] The three-component coupling reaction involving allene brought about allylic silanes.[24] Several cyanoate complexes of iron, cobalt or nickel act as efficient catalyst in cross-coupling with organic halides.[25]

Encouraged by the increasing importance of the selective synthesis of unsaturated carboxamides, especially that of 2-arylacrylamides, as potential building blocks and their applicability as substrate in asymmetric synthesis, we decided to investigate the possibility of extending the scope of aminocarbonylation to α-iodostyrene derivatives expected to be highly reactive substrates. Accordingly, the clean and nearly quantitative aminocarbonylation of α-iodostyrene and α,α′-diiodo-1,4-divinylbenzene with simple primary and secondary amines, as well as with amino acid methyl esters is reported in the present paper.

2. Results and discussion

*2.1. Synthesis of α-iodostyrene (**5**) and α,α′-diiodo-1,4-divinylbenzene (**6**)*

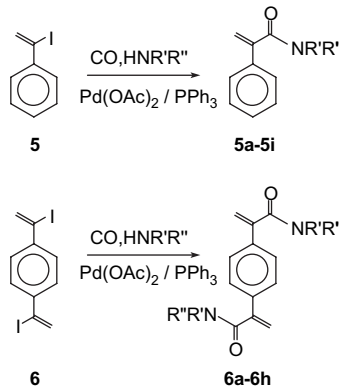
The above two iodoalkenes have been synthesised by the known methodology of Barton et al. [26] with some modifications (See Section 4). The conventional ketone–hydrazone–iodoalkene route has been used. Accordingly, acetophenone (**1**) and 1,4-diacetylbenzene (**2**) have been converted to the corresponding hydrazones (**3** and **4**) using barium oxide or triethylamine, respectively. Compounds **3** and **4** were reacted with iodine in the presence of a base (TMG=*N*,*N*,*N*′,*N*′-tetramethylguanidine) resulting in α-iodostyrene (**5**) and α,α′-diiodo-1,4-divinylbenzene (**6**), respectively (Scheme 1). The 'iodovinyl' product-forming step has been carried out under argon providing strictly moisture- and oxygen-free conditions.



Scheme 1. Synthesis of the iodoalkenes (**5** and **6**) from the corresponding ketones via their hydrazones.

*2.2. Aminocarbonylation of **5** and **6***

α-Iodostyrene (**5**) was reacted with *tert*-butylamine (**a**), aniline (**b**), piperidine (**c**), morpholine (**d**), methyl glycinate (**e**), methyl alaninate (**f**), methyl valinate (**g**), methyl prolinate (**h**) and benzyl prolinate (**i**) under atmospheric and high pressure (40 bar) carbon monoxide in the presence of in situ generated palladium(0)-triphenylphosphine catalysts (Scheme 2). Palladium(II) acetate was used as catalytic precursor and reduced to Pd(0) as described previously in detail.[27,28]



	R'	R"
a	H	*t*-Bu
b	H	Ph
c	-$(CH_2)_5$-	
d	-$(CH_2)_2O(CH_2)_2$-	
e	H	CH_2COOCH_3
f	H	$CH(CH_3)COOCH_3$
g	H	$CH(CH(CH_3)_2)COOCH_3$
h	-$CH(COOCH_3)(CH_2)_3$-	
i	-$CH(COOCH_2Ph)(CH_2)_3$-	

Scheme 2. Palladium-catalysed aminocarbonylation of **5** and **6**.

The reactivity of **5**, compared to several types of iodoalkenes, proved to be exceptionally high. All of the resulting *N*-substituted 2-phenylacrylamides (**5a–5i**) have been obtained with practically complete conversion and isolated in 63–83% yields after column chromatography (Section 4). Even those amines which have shown decreased reactivity in aminocarbonylation of various iodoalkenes, i.e., arylamine (**b**) and sterically hindered secondary amines (**h** and **i**), provided excellent isolated yields (Table 1).

By carrying out the aminocarbonylation of **5** under increased carbon monoxide pressure (40 bar), the expected carboxamides (**5a–5i**) have been obtained in yields similar to those obtained under normal carbon monoxide pressure (Table 1). It is worth noting that double carbonylation resulting in keto-carboxamides was not observed using GC–MS neither at atmospheric pressure nor at elevated carbon monoxide pressure, so the reaction is said to be completely chemoselective.

The 'bis-iodovinyl' type substrate **6** has been reacted with the same amines of various structures **a–h** as in case of **5** (Scheme 2). The bis-carboxamides (**6a–6h**) have been obtained in excellent yields except for **6b**. (The lower reactivity of the aniline nucleophile resulted in complex mixtures including some carboxylic acids formed from hydroxycarbonylation of **6** in the presence of traces of water. The isolation of the expected amide **6b** failed.) Due to the excellent reactivity of the 'iodovinyl' functionality, substrate **6** was practically completely converted almost in all cases even under atmospheric carbon monoxide pressure (Table 2).

Table 1
Palladium-catalysed aminocarbonylation of **5**[a]

Amine	Reaction time [h]	p(CO) [bar]	Isolated yield[b] (amide) [%]
t-BuNH$_2$ (**a**)	22	1	83 (**5a**)
t-BuNH$_2$ (**a**)	22	40	82 (**5a**)
Aniline (**b**)	22	1	70 (**5b**)
Aniline (**b**)	22	40	68 (**5b**)
Piperidine (**c**)	22	1	79 (**5c**)
Piperidine (**c**)	22	40	77 (**5c**)
Morpholine (**d**)	22	1	74 (**5d**)
Morpholine (**d**)	22	40	73 (**5d**)
GlyOMe (**e**)	22	1	76 (**5e**)
GlyOMe (**e**)	22	40	73 (**5e**)
AlaOMe (**f**)	22	1	72 (**5f**)
AlaOMe (**f**)	22	40	71 (**5f**)
ValOMe (**g**)	22	1	69 (**5g**)
ValOMe (**g**)	22	40	67 (**5g**)
ProOMe (**h**)	66	1	67 (**5h**)
ProOMe (**h**)	66	40	65 (**5h**)
ProOBz (**i**)	66	40	63 (**5i**)

[a] Reaction conditions: 0.025 mmol Pd(OAc)$_2$; 0.05 mmol PPh$_3$, 1 mmol α-iodostyrene (**5**); 3 mmol nonfunctionalised amine (or 1.1 mmol amino acid methyl ester hydrochloride); 10 mL DMF.
[b] Practically complete conversion (>98%) has been obtained in all cases.

Table 2
Palladium-catalysed aminocarbonylation of **6**[a]

Amine	Isolated yield[b] (amide) [%]
t-BuNH$_2$ (**a**)[c]	80 (**6a**)
Piperidine (**c**)	75 (**6c**)
Morpholine (**d**)	73 (**6d**)
GlyOMe (**e**)	70 (**6e**)
AlaOMe (**f**)	70 (**6f**)
ValOMe (**g**)	66 (**6g**)
ProOMe (**h**)	62 (**6h**)

[a] Reaction conditions (unless otherwise stated): 0.025 mmol Pd(OAc)$_2$; 0.05 mmol PPh$_3$, 1 mmol α,α′-diiodo-1,4-divinylbenzene (**6**); 3 mmol nonfunctionalised amine (or 1.1 mmol amino acid methyl ester); p(CO)=1 bar; 10 mL DMF, 22 h.
[b] Practically complete conversion (>98%) has been obtained in all cases.
[c] p(CO)=40 bar.

3. Conclusions

Palladium-catalysed aminocarbonylation proved to be an efficient method for the functionalisation of α-iodovinyl substituted aromatics, α-iodostyrene and α,α′-diiodo-1,4-divinylbenzene using the great variety of amine nucleophiles. It could be stated that the exceptional reactivity of the iodostyrene substrates compared to cyclic and open-chain iodoalkenes, the clean and nearly quantitative aminocarbonylation enabled the facile synthesis of 2-arylacrylamide type synthetic building blocks. These could also serve as intermediates of chiral building blocks, which are available via asymmetric hydrogenation.

Furthermore, the easy work-up of the reaction mixtures obtained with these substrates makes these reactions of synthetic importance. The use of iodoalkenes as synthetic substitutes for the corresponding enol-triflates is supported not only by green chemistry principles but also by their advantageous synthetic properties as substrates in homogeneous catalytic reactions. The advantage of this methodology has been illustrated by several types of skeletons of biological importance, like tropane-alkaloids[29] and steroids.[30]

4. Experimental

4.1. General procedures

^{1}H and ^{13}C NMR spectra were recorded in CDCl$_3$ on a Varian Inova 400 spectrometer at 400.13 MHz and 100.62 MHz, respectively. Chemical shifts δ are reported in ppm relative to residual CHCl$_3$ (7.26 ppm and 77.00 ppm for ^{1}H and ^{13}C, respectively). Elemental analyses were measured on a 1108 Carlo Erba apparatus. Samples of the catalytic reactions were analysed with a Hewlett Packard 5830A gas chromatograph fitted with a capillary column coated with OV-1.

4.2. Synthesis of α-iodostyrene (5)

Acetophenone (**1**) (40 g, 0.33 mol), freshly distilled hydrazine hydrate (98%, 18.36 g, 0.36 mol) and barium oxide (12.60 g) in absolute ethanol (50 mL) were heated for 5 h at 90 °C. After completion of the reaction, ether (100 mL) was added and filtered and the mixture was dried over sodium hydroxide for a day. At last it was evaporated to give the hydrazone (**3**) derivative. The product was used in the next step without further purification.

To a stirred solution of iodine (58.73 g, 0.231 mol) in dichloromethane (150 mL) the mixture of 1,1,3,3-tetramethylguanidine (TMG, 115.88 g, 1.006 mol) and acetophenone hydrazone (**3**) (15 g, 0.112 mol) in dichloromethane (30 mL) was added dropwise at room temperature. After the addition was complete, the mixture was stirred for half an hour. Then the solvent was evaporated and the residue was heated at 90 °C under argon atmosphere for 2 h. The mixture was poured into water (400 mL) and extracted with ether (three times 100 mL). The combined organic layer was washed with 1 N aqueous HCl (three times 50 mL), water (50 mL), 5% aqueous NaHCO$_3$ (twice 50 mL), water (50 mL), saturated aqueous Na$_2$S$_2$O$_3$ (10 mL) and water (twice 50 mL) again, dried over sodium sulfate and evaporated. Purification by column chromatography (silicagel, petroleum ether) gave pure **5** as a yellow viscous material. Yield: 8.51 g; 33%.

α-Iodostyrene[31–33] *(**5**)*: δ_H (400 MHz, CDCl$_3$) 7.52 (d, 7.2 Hz, 2H, Ph); 7.30–7.41 (m, 3H, Ph); 6.48 (br s, 1H, =CH); 6.07 (br s, 1H, =CH). δ_C (100.6 MHz, CDCl$_3$) 141.7; 133.7; 128.8; 128.4; 127.3; 107.5. MS *m/z* (rel int. %): 230 (21), 103 (100), 77 (42). Analysis calculated for C$_8$H$_7$I (230.05): C, 41.77; H, 3.07; found: C, 41.51; H, 3.16. The spectral data above are in accordance with the literature data.

4.3. Synthesis of α,α′-diiodo-1,4-divinylbenzene (6)

1,4-Diacetylbenzene (**2**) (10 g, 0.062 mol), triethylamine (31.19 g, 0.308 mol) and freshly distilled hydrazine hydrate (98%, 7.41 g, 0.148 mmol) in absolute ethanol (30 mL) were heated for 5 h at 90 °C. After completion of the reaction the

mixture was evaporated, dichloromethane was added and the solution dried over sodium sulfate for a day. The organic phase was then evaporated to give the hydrazone (**4**) derivative. The product was used in the next step without further purification.

To a stirred solution of iodine (75.12 g, 0.296 mol) in dichloromethane (150 mL), 1,1,3,3-tetramethylguanidine (TMG, 71.02 g, 0.617 mmol) and 1,4-diacetylbenzene dihydrazone (**4**) (11.73 g, 0.062 mol) in dichloromethane (50 mL) were added dropwise at room temperature. After the addition was completed, the mixture was stirred for half an hour. Then the solvent was evaporated and the residue was heated at 90 °C under argon atmosphere for 2 h. The mixture was poured into water (450 mL) and extracted with ether (three times 150 mL). The combined organic layer was washed with 1 N aqueous HCl (three times 50 mL), water (50 mL), 5% aqueous $NaHCO_3$ (twice 50 mL), water (50 mL), saturated aqueous $Na_2S_2O_3$ (10 mL) and water (twice 50 mL) again, dried over sodium sulfate and evaporated. Purification by column chromatography (silicagel, petroleum ether) gave pure **6** as a yellow solid material. Yield: 5.06 g; 22%.

*α,α′-Diiodo-1,4-divinylbenzene (**6**)*: δ_H (400 MHz, $CDCl_3$) 7.45 (s, 4H, C_6H_4); 6.50 (br s, 1H, =CH); 6.09 (br s, 1H, =CH). δ_C (100.6 MHz, $CDCl_3$) 142.0; 127.9; 127.8; 106.0. MS *m/z* (rel int. %): 382 (11), 255 (100), 128 (62), 102 (9), 76 (5). Analysis calculated for $C_{10}H_8I_2$ (381.98): C, 31.44; H, 2.11; found: C, 31.29, H, 2.31. Mp 65 °C.

4.4. Aminocarbonylation experiments at normal pressure

In a typical experiment a solution of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PPh_3 (13.1 mg, 0.05 mmol), 0.5 mmol iodo substrate (**5**), 1.5 mmol nonfunctionalised amine (**a**–**d**) (or 0.55 mmol amino acid methyl ester (**e**–**h**) hydrochloride) were dissolved in 10 mL of DMF under argon. Triethylamine (0.5 mL) was added to the homogeneous yellow solution and the atmosphere was changed to carbon monoxide. The colour changed to dark red. The reaction was conducted for 22 h at 50 °C. Some metallic palladium was formed at the end of the reaction which was filtered off. (A sample of this solution was immediately analysed by GC–MS.) The mixture was then concentrated and evaporated to dryness. The residue was dissolved in chloroform (20 mL) and washed with water (20 mL). The organic phase was thoroughly washed twice with 5% HCl (20 mL), saturated $NaHCO_3$ (20 mL), brine (20 mL), dried over Na_2SO_4 and concentrated to a yellow waxy material or a thick oil. Chromatography (silica, chloroform, then chloroform/ethanol=4/1) yielded the desired compounds as yellow solids.

By carrying out the reaction with **6**, a solution of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PPh_3 (13.1 mg, 0.05 mmol), 0.5 mmol iodo substrate (**6**), 3.0 mmol nonfunctionalised amine (**a**–**d**) (or 1.1 mmol amino acid methyl ester (**e**–**h**) hydrochloride) were dissolved in 10 mL of DMF under argon. Triethylamine (1.0 mL) was added to the homogeneous yellow solution and further steps were carried out as above.

4.5. Aminocarbonylation experiments at high pressure

The DMF solution of the catalyst precursor and reactants (amounts given in Section 4.4) was transferred under argon into a 100 mL stainless steel autoclave. The reaction vessel was pressurised up to 40 bar total pressure with carbon monoxide and the magnetically stirred mixture was heated in an oil bath at 50 °C for 22 h. The work-up procedure is identical with that given above.

4.6. Characterisation of the products

*N-tert-Butyl-2-phenylacrylamide (**5a**)*: δ_H (400 MHz, $CDCl_3$) 7.30–7.42 (m, 5H, Ph); 6.00 (br s, 1H, =CH); 5.54 (br s, 1H, NH); 5.52 (br s, 1H, =CH). δ_C (100.6 MHz, $CDCl_3$) 166.8; 146.0; 137.3; 128.5; 128.3; 127.9; 120.7; 51.5; 28.6. IR (KBr (cm^{-1})): 3259 (NH); 1646 (CON). MS *m/z* (rel int. %): 203 (38), 188 (32), 146 (24), 131 (45), 103 (100), 77 (23). Analysis calculated for $C_{13}H_{17}NO$ (203.28): C, 76.81; H, 8.43; N, 6.89; found: C, 76.65; H, 8.52; N, 6.60; R_f (10% EtOAc/$CHCl_3$) 0.76; R_f (5% EtOAc/$CHCl_3$) 0.69; yellow solid, mp 70–72 °C.

*N-Phenyl-2-phenylacrylamide (**5b**)*:[34–37] δ_H (400 MHz, $CDCl_3$) 7.58 (br s, 1H, NH); 7.10–7.55 (m, 10H, 2×Ph); 6.22 (br s, 1H, =CH); 5.70 (br s, 1H, =CH). δ_C (100.6 MHz, $CDCl_3$) 165.5; 145.2; 137.7; 136.6; 128.9; 128.6; 128.4; 128.1; 124.6; 122.7; 120.0. IR (KBr (cm^{-1})): 3230 (NH); 1651 (CON). MS *m/z* (rel int. %): 223 (46), 146 (3), 103 (100), 77 (30). Analysis calculated for $C_{15}H_{13}NO$ (223.27): C, 80.69; H, 5.87; N, 6.27; found: C, 80.49; H, 5.96; N, 6.02; R_f (10% EtOAc/$CHCl_3$) 0.82; yellow solid, mp 138–140 °C. The spectral data were in accordance with the literature data.

*2-Phenyl-1-piperidin-1-yl-propenone (**5c**)*:[38] δ_H (400 MHz, $CDCl_3$) 7.20–7.42 (m, 5H, Ph); 5.65 (br s, 1H, =CH); 5.29 (br s, 1H, =CH); 3.60–3.70 (m, 2H, NCH_2); 3.25–3.31 (m, 2H, NCH_2); 1.60 (br s, 4H, $(CH_2)_2$); 1.32 (br s, 2H, CH_2). δ_C (100.6 MHz, $CDCl_3$) 169.1; 145.2; 135.7; 129.8; 128.5; 125.6; 113.2; 47.9; 42.3; 26.2; 25.3; 24.4. IR (KBr (cm^{-1})): 1634 (CON). MS *m/z* (rel int. %): 215 (100), 214 (80), 103 (90), 77 (33). Analysis calculated for $C_{14}H_{17}NO$ (215.30): C, 78.10; H, 7.96; N, 6.51; found: C, 77.89; H, 8.11; N, 6.40; R_f (10% EtOAc/$CHCl_3$) 0.55; yellow solid, mp 170–173 °C. The spectral data were in accordance with the literature data.

*1-Morpholin-4-yl-2-phenyl-propenone (**5d**)*: δ_H (400 MHz, $CDCl_3$) 7.24–7.42 (m, 5H, Ph); 5.70 (br s, 1H, =CH); 5.33 (br s, 1H, =CH); 3.55–3.80 (m, 4H, 2×OCH_2); 3.42 (br s, 2H, CH_2); 3.32 (br s, 2H, CH_2). δ_C (100.6 MHz, $CDCl_3$) 169.3; 144.4; 135.3; 128.8; 128.5; 125.6; 114.4; 66.7 (double intensity); 47.3; 41.9. IR (KBr (cm^{-1})): 1639 (CON). MS *m/z* (rel int. %): 217 (52), 132 (22), 103 (100), 77 (36). Analysis calculated for $C_{13}H_{15}NO_2$ (217.27): C, 71.87; H, 6.96; N, 6.45; found: C, 71.73; H, 7.08; N, 6.38; R_f (10% EtOAc/$CHCl_3$) 0.40; R_f (50% EtOAc/$CHCl_3$) 0.61; golden highly viscous material.

*(2-Phenyl-acryloylamino)-acetic acid methyl ester (**5e**)*: δ_H (400 MHz, $CDCl_3$) 7.3–7.45 (m, 5H, Ph); 6.34 (br s, 1H, NH); 6.12 (br s, 1H, =CH); 5.63 (br s, 1H, =CH); 4.08 (d, 9 Hz, 2H, CH_2); 3.70 (s, 3H, OCH_3). δ_C (100.6 MHz,

$CDCl_3$) 170.1; 167.5; 144.2; 136.6; 128.6; 128.5; 128.0; 122.4; 52.2; 41.4. IR (KBr (cm^{-1})): 3332 (NH); 1752 (COO); 1665 (CON). MS *m/z* (rel int. %): 219 (22), 160 (12), 146 (18), 131 (35), 103 (100), 77 (29). Analysis calculated for $C_{12}H_{13}NO_3$ (219.24): C, 65.74; H, 5.98; N, 6.39; found: C, 65.64; H, 5.81; N, 6.23; R_f (10% EtOAc/$CHCl_3$) 0.46; R_f (20% EtOAc/$CHCl_3$) 0.60; yellow solid, mp 68–70 °C.

*2-(2-Phenyl-acryloylamino)-propionic acid methyl ester (**5f**)*: δ_H (400 MHz, $CDCl_3$) 7.30–7.50 (m, 5H, Ph); 6.38 (br s, 1H, NH); 6.07 (br s, 1H, =CH); 5.60 (br s, 1H, =CH); 4.64 (quintet, 7.2 Hz, 1H, C*H*CH_3); 3.70 (s, 3H, OCH_3); 1.4 (d, 7.2 Hz, 3H, CHC*H*$_3$). δ_C (100.6 MHz, $CDCl_3$) 173.2; 166.9; 144.4; 136.6; 128.6; 128.5; 128.0; 122.1; 52.4; 48.3; 18.1. IR (KBr (cm^{-1})): 3327 (NH); 1744 (COO); 1662 (CON). MS *m/z* (rel int. %): 233 (4), 174 (56), 131 (42), 103 (100), 77 (24). Analysis calculated for $C_{13}H_{15}NO_3$ (233.27): C, 66.94; H, 6.48; N, 6.00; found: C, 66.78; H, 6.62; N, 5.76; R_f (10% EtOAc/$CHCl_3$) 0.60; R_f (20% EtOAc/$CHCl_3$) 0.75; golden highly viscous material.

*3-Methyl-2-(2-phenyl-acryloylamino)-butyric acid methyl ester (**5g**)*: δ_H (400 MHz, $CDCl_3$) 7.30–7.50 (m, 5H, Ph); 6.20 (br s, 1H, NH); 6.09 (s, 1H, =CH); 5.62 (br s, 1H, =CH); 4.60 (m, 1H, C*H*NH); 2.15 (m, 1H, C*H*$(CH_3)_2$; 0.91 (d, 7.2 Hz, 3H, CHC*H*$_3$); 0.8 (d, 7.2 Hz, 3H, CHC*H*$_3$). δ_C (100.6 MHz, $CDCl_3$) 173.8; 167.2; 144.5; 136.6; 132.4; 128.6; 128.0; 122.1; 57.4; 52.1; 31.1; 18.9; 17.7. IR (KBr (cm^{-1})): 3352 (NH); 1743 (COO); 1666 (CON). MS *m/z* (rel int. %): 261 (6), 202 (43), 131 (29), 103 (100), 77 (20). Analysis calculated for $C_{15}H_{19}NO_3$ (261.32): C, 68.94; H, 7.33; N, 5.36; found: C, 68.70; H, 7.12; N, 5.06; R_f (10% EtOAc/$CHCl_3$) 0.64; dark yellow bright highly viscous material.

*1-(2-Phenyl-acryloyl)-pyrrolidine-2-carboxylic acid methyl ester (**5h**)*: δ_H (400 MHz, $CDCl_3$) 7.25–7.50 (m, 5H, Ph); 5.71 (br s, 1H, =CH); 5.41 (br s, 1H, =CH); 4.58 (m, 1H, NCH); 3.72 (s, 3H, OCH_3); 3.30 (t, 7.4 Hz, 2H, NCH_2); 1.7–2.22 (m, 4H, $(CH_2)_2$). δ_C (100.6 MHz, $CDCl_3$) 172.5; 169.2; 145.4; 135.3; 128.7; 128.4; 126.0; 115.0; 58.4; 52.1; 48.5; 29.3; 24.8. IR (KBr (cm^{-1})): 1744 (COO); 1639 (CON). MS *m/z* (rel int. %): 259 (14), 200 (67), 131 (40), 103 (100), 77 (22). Analysis calculated for $C_{15}H_{17}NO_3$ (259.30): C, 69.48; H, 6.61; N, 5.40; found: C, 69.30; H, 6.52; N, 5.26; R_f (10% EtOAc/$CHCl_3$) 0.31; R_f (20% EtOAc/$CHCl_3$) 0.53; dark yellow bright highly viscous material.

*1-(2-Phenyl-acryloyl)-pyrrolidine-2-carboxylic acid benzyl ester (**5i**)*: δ_H (400 MHz, $CDCl_3$) 7.25–7.50 (m, 5H, Ph); 5.74 (br s, 1H, =CH); 5.43 (br s, 1H, =CH); 5.20 (AB-dd, 2H, CH_2Ph); 4.65 (m, 1H, NCH); 3.30 (t, 7.4 Hz, 2H, NCH_2); 1.7–2.25 (m, 4H, $(CH_2)_2$). δ_C (100.6 MHz, $CDCl_3$) 171.9; 169.3; 145.5; 135.7; 135.3; 128.7; 128.6; 128.5; 128.3; 128.1; 126.0; 115.2; 66.9; 58.6; 48.5; 29.4; 24.8. IR (KBr (cm^{-1})): 1743 (COO); 1640 (CON). MS *m/z* (rel int. %): 335 (6), 200 (87), 131 (44), 103 (100), 77 (22). Analysis calculated for $C_{21}H_{21}NO_3$ (335.40): C, 75.20; H, 6.31; N, 4.18; found: C, 75.02; H, 6.42; N, 4.01; R_f (10% EtOAc/$CHCl_3$) 0.50; R_f (20% EtOAc/$CHCl_3$) 0.65; dark yellow bright highly viscous material.

*N-tert-Butyl-2-[4-(1-tert-butylcarbamoyl-vinyl)-phenyl]acryl amide (**6a**)*: δ_H (400 MHz, $CDCl_3$) 7.38 (s, 4H, C_6H_4); 5.91 (br s, 2H, =CH); 5.60 (br s, 2H, NH); 5.57 (br s, 2H, =CH); 1.36 (s, 18H, 2×$C(CH_3)_3$). δ_C (100.6 MHz, $CDCl_3$) 166.9; 145.6; 137.1; 127.9; 120.1; 51.6; 28.6. IR (KBr (cm^{-1})): 3328 (NH); 1644 (CON). MS *m/z* (rel int. %): 328 (70), 313 (30), 272 (21), 228 (100), 172 (47), 128 (45), 57 (43). Analysis calculated for $C_{20}H_{28}N_2O_2$ (328.45): C, 73.14; H, 8.59; N, 8.53; found: C, 73.01, H, 8.73; N, 8.29; R_f (4% EtOH/$CHCl_3$) 0.79; R_f (50% EtOAc/$CHCl_3$) 0.70; off-white solid, mp 180–183 °C.

*2-{4-[1-(Piperidine-carbonyl)-vinyl]-phenyl}-1-piperidin-1-yl-propenone (**6c**)*: δ_H (400 MHz, $CDCl_3$) 7.38 (s, 4H, C_6H_4); 5.67 (br s, 2H, =CH); 5.28 (br s, 2H, =CH); 3.60 (br s, 4H, NCH_2); 3.23 (br s, 4H, NCH_2); 1.55 (br s, 8H, 4×CH_2); 1.30 (br s, 4H, 2×CH_2). δ_C (100.6 MHz, $CDCl_3$) 168.8; 144.6; 135.7; 126.0; 113.5; 47.9; 42.3; 26.2; 25.5; 24.4. IR (KBr (cm^{-1})): 1628 (CON). MS *m/z* (rel int. %): 352 (100), 323 (4), 269 (26), 241 (34), 207 (10), 186 (17), 128 (37), 98 (77). Analysis calculated for $C_{22}H_{28}N_2O_2$ (352.48): C, 74.97; H, 8.01; N, 7.95; found: C, 74.85, H, 8.11; N, 7.76; R_f (4% EtOH/$CHCl_3$) 0.53; R_f (50% EtOAc/$CHCl_3$) 0.43; off-white solid, mp 171–172 °C.

*2-{4-[1-(Morpholin-4-yl-carbonyl)-vinyl]-phenyl}-1-morpholin-4-yl-propenone (**6d**)*: δ_H (400 MHz, $CDCl_3$) 7.42 (s, 4H, C_6H_4); 5.78 (br s, 2H, =CH); 5.37 (br s, 2H, =CH); 3.60–3.80 (m, 8H, 4×CH_2); 3.30–3.50 (m, 8H, 4×CH_2). δ_C (100.6 MHz, $CDCl_3$) 169.0; 143.6; 135.6; 126.1; 114.9; 66.7; 47.3; 41.9. IR (KBr (cm^{-1})): 1632 (CON). MS *m/z* (rel int. %): 356 (83), 328 (10), 271 (26), 207 (43), 128 (40), 100 (100). Analysis calculated for $C_{20}H_{24}N_2O_4$ (356.42): C, 67.40; H, 6.79; N, 7.86; found: C, 67.57, H, 6.92; N, 7.58; R_f (4% EtOH/$CHCl_3$) 0.50; R_f (50% EtOAc/$CHCl_3$) 0.61; pale brown solid, mp 185–190 °C.

*(2-{4-[1-(Methoxycarbonylmethyl-carbamoyl)-vinyl]-phenyl}-acryloylamino)-acetic acid methyl ester (**6e**)*: δ_H (400 MHz, $CDCl_3$) 7.45 (s, 4H, C_6H_4); 6.25 (br s, 2H, NH); 6.14 (br s, 2H, =CH); 5.70 (br s, 2H, =CH); 4.14 (d, 7.5 Hz, 2H, NHC*H*$_2$); 3.75 (s, 3H, OCH_3). δ_C (100.6 MHz, $CDCl_3$) 163.9; 161.2; 137.5; 130.6; 122.0; 116.1; 46.1 35.2. IR (KBr (cm^{-1})): 3310 (NH); 1748 (COO); 1652 (CON). Analysis calculated for $C_{18}H_{20}N_2O_6$ (360.37): C, 59.99; H, 5.59; N, 7.77; found: C, 60.11, H, 5.75; N, 7.53; R_f (4% EtOH/$CHCl_3$) 0.42; R_f (50% EtOAc/$CHCl_3$) 0.15; white solid, mp 130–133 °C.

*(2-{4-[1-(1-Methoxycarbonyl-ethyl-carbamoyl)-vinyl]-phenyl}-acryloylamino)-propionic acid methyl ester (**6f**)*: δ_H (400 MHz, $CDCl_3$) 7.45 (s, 4H, C_6H_4); 6.28 (br s, 2H, NH); 6.10 (br s, 2H, =CH); 5.72 (br s, 2H, =CH); 4.70 (quintet, 7.1 Hz, 2H, NHC*H*); 3.75 (s, 6H, OCH_3); 1.42 (d, 7.1 Hz, 6H, CHC*H*$_3$). δ_C (100.6 MHz, $CDCl_3$) 167.0; 160.6; 137.6; 130.5; 122.0; 115.9; 46.2; 42.1; 11.9. IR (KBr (cm^{-1})): 3284 (NH); 1747 (COO); 1647 (CON). MS *m/z* (rel int. %): 388 (10), 329 (52), 258 (100), 198 (18), 128 (30). Analysis calculated for $C_{20}H_{24}N_2O_6$ (388.42): C, 61.85; H, 6.23; N, 7.21; found: C, 61.75, H, 6.43; N, 7.07; R_f (4% EtOH/$CHCl_3$) 0.56; R_f (50% EtOAc/$CHCl_3$) 0.44; white solid, mp 111 °C.

(2-{4-[1-(1-Methoxycarbonyl-2-methyl-propyl-carbamoyl)-vinyl]-phenyl}-acryloylamino)-3-methyl-butyric acid methyl

*ester (**6g**)*: δ_H (400 MHz, $CDCl_3$) 7.43 (s, 4H, C_6H_4); 6.21 (br s, 2H, NH); 6.10 (br s, 2H, =CH); 5.72 (br s, 2H, =CH); 4.65 (m, 2H, NHC*H*); 3.72 (s, 6H, OCH_3); 2.20 (m, 2H, C*H*$(CH_3)_2$); 1.90 (d, 7.0 Hz, 3H, $CH(CH_3)$); 1.95 (d, 7.0 Hz, 3H, C*H*(CH_3). δ_C (100.6 MHz, $CDCl_3$) 166.0; 161.0; 137.8; 125.8; 122.0; 115.9; 51.2; 45.9; 24.9; 12.8; 11.6. IR (KBr (cm^{-1})): 3376 (NH); 1742 (COO); 1655 (CON). MS *m/z* (rel int. %): 444 (58), 385 (67), 286 (100), 128 (65). Analysis calculated for $C_{24}H_{32}N_2O_6$ (444.53): C, 64.85; H, 7.26; N, 6.30; found: C, 64.97, H, 7.41; N, 6.08; R_f (4% EtOH/$CHCl_3$) 0.58; R_f (50% EtOAc/$CHCl_3$) 0.69; pale yellow solid, mp 100–102 °C.

*1-(2-{4-[1-(2-Methoxycarbonyl-pyrrolidine-1-carbonyl)-vinyl]-phenyl}-acryloyl)-pyrrolidine-2-carboxylic acid methyl ester (**6h**)*: δ_H (400 MHz, $CDCl_3$) 7.50 (s, 4H, C_6H_4); 5.79 (br s, 2H, =CH); 5.46 (br s, 2H, =CH); 4.60 (m, 2H, NCH); 3.78 (s, 6H, OCH_3); 3.30–3.40 (m, 4H, CH_2); 1.80–2.30 (m, 8H, CH_2). δ_C (100.6 MHz, $CDCl_3$) 166.3; 162.8; 138.6; 129.1; 120.2; 109.0; 52.2; 46.0; 42.3; 23.1; 18.5. IR (KBr (cm^{-1})): 1744 (COO); 1638 (CON). MS *m/z* (rel int. %): 440 (1), 253 (17), 128 (100). Analysis calculated for $C_{24}H_{28}N_2O_6$ (440.50): C, 65.44; H, 6.41; N, 6.36; found: C, 65.35, H, 6.62; N, 6.16; R_f (4% EtOH/$CHCl_3$) 0.44; yellow solid, mp 147–150 °C.

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References and notes

1. Skoda-Földes, R.; Kollár, L. *Curr. Org. Chem.* **2002**, *6*, 1097–1119.
2. *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Eds.; Wiley-VCH: Weinheim, 1996; *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vols. I–II.
3. Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation. Direct Synthesis of Carbonyl Compounds*; Plenum: New York, NY and London, 1991.
4. Ács, P.; Müller, E.; Rangits, G.; Lóránd, T.; Kollár, L. *Tetrahedron* **2006**, *62*, 12051–12056.
5. Müller, E.; Péczely, G.; Skoda-Földes, R.; Takács, E.; Kokotos, G.; Bellis, E.; Kollár, L. *Tetrahedron* **2005**, *61*, 797–802.
6. Huang, X.; Zhou, Q. *Tetrahedron Lett.* **2001**, *42*, 6373–6375.
7. Camps, M.; Jebri, A. *Eur. Polym. J.* **1994**, *30*, 1029–1035.
8. Hossain, M. D.; Kitamura, T. *Synthesis* **2006**, 1253–1256.
9. Khartulyari, A. S.; Kapur, M.; Maier, M. E. *Org. Lett.* **2006**, *8*, 5833–5836.
10. Jung, I.; Lee, T. W.; Kang, S. O.; Ko, J. J. *Synthesis* **2005**, 986–992.
11. Larock, R. C.; Yang, H. *Synlett* **1994**, 748–750.
12. Koo, B.; McDonald, F. E. *Org. Lett.* **2005**, *7*, 3621–3624.
13. Kamei, T.; Fujita, K.; Itami, K.; Yoshida, J. *Org. Lett.* **2005**, *7*, 4725–4728.
14. Takai, K.; Kimura, K.; Kuroda, T.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1983**, *24*, 5281–5284.
15. Chan, P. W. H.; Kamijo, S.; Yamamoto, Y. *Synlett* **2001**, 910–913.
16. Kuang, C. X.; Yang, Q.; Senboku, H.; Tokuda, M. *Chem. Lett.* **2005**, *34*, 528–529.
17. Hideo, H.; Fukuda, Y.; Kondo, K.; Okuno, H.; Murakami, Y.; Aoyama, T. *Tetrahedron* **2004**, *60*, 10701–10709.
18. Albrecht, K.; Demeijere, A. *Chem. Ber.* **1994**, *127*, 2539–2541.
19. Yamashita, H.; Roan, B. L.; Tanaka, M. *Chem. Lett.* **1990**, 2175–2176.
20. Tanaka, H.; Zhao, J. F.; Kumase, H. *J. Org. Chem.* **2001**, *66*, 570–577.
21. Lee, P. H.; Lee, K.; Kang, Y. J. *J. Am. Chem. Soc.* **2006**, *128*, 1139–1146.
22. Barluenga, J.; Fernadez, M. A.; Aznar, F.; Valdes, C. *Chem.—Eur. J.* **2005**, *11*, 2276–2283.
23. Barluenga, J.; Fernadez, M. A.; Aznar, F.; Valdes, C. *Chem.—Eur. J.* **2004**, *10*, 494–507.
24. Wu, M. Y.; Yang, F. Y.; Cheng, C. H. *J. Org. Chem.* **1999**, *64*, 2471–2474.
25. Kauffmann, T.; Nienaber, H. *Synthesis* **1995**, 207–211.
26. Barton, D. H. R.; Bashiardes, B.; Fourrey, J. L. *Tetrahedron Lett.* **1983**, *24*, 1605–1608.
27. Amatore, C.; Carre, E.; Jutand, A.; M'Barki, M. A.; Meyer, G. *Organometallics* **1995**, *14*, 5605–5614 and references cited therein.
28. Csákai, Z.; Skoda-Földes, R.; Kollár, L. *Inorg. Chim. Acta* **1999**, *286*, 93–97.
29. Horváth, L.; Berente, Z.; Kollár, L. *Lett. Org. Chem.* **2005**, *2*, 124–127.
30. Skoda-Földes, R.; Kollár, L. *Chem. Rev.* **2003**, *103*, 4095–4129.
31. Campos, P. J.; García, B.; Rodríguez, M. A. *Tetrahedron Lett.* **2002**, *43*, 6111–6112.
32. Lee, K.; Wiemer, D. F. *Tetrahedron Lett.* **1993**, *34*, 2433–2436.
33. Brown, H. C.; Somayaji, V.; Narasimhan, S. *J. Org. Chem.* **1984**, *49*, 4822–4827.
34. Li, Y.; Alper, H.; Yu, Z. *Org. Lett.* **2006**, *8*, 5199–5201.
35. Matteoli, U.; Scrivanti, A.; Beghetto, V. *J. Mol. Catal., A: Chem.* **2004**, *213*, 183–186.
36. El Ali, B.; El-Ghanam, A.; Fettouli, M.; Tijani, J. *Tetrahedron Lett.* **2000**, *41*, 5761–5764.
37. Koike, T.; Takahashi, M.; Arai, N.; Mori, A. *Chem. Lett.* **2004**, *33*, 1364–1365.
38. Turbanti, L.; Cerbai, G.; Bramanti, G.; Bianchini, P.; Tellini, N. *Chim. Ther.* **1967**, *2*, 354–365.