ELSEVIER

Heck reactions of 2-substituted enol ethers with aryl bromides catalysed by a tetraphosphine/palladium complex

Ahmed Battace,[a] Touriya Zair,[b] Henri Doucet[a],* and Maurice Santelli[a],*

[a]*Laboratoire de Synthèse Organique, UMR 6180 CNRS, Université d'Aix-Marseille III: Chirotechnologies: catalyse et biocatalyse, Faculté des Sciences de Saint Jérôme, Avenue Escadrille Normandie-Niemen, 13397 Marseille Cedex 20, France*
[b]*Laboratoire de Chimie Organique Appliquée, Faculté des Sciences, Université Moulay Ismail, BP 4010, Beni M'mhammed, 50000 Meknes, Morocco*

Abstract—*cis,cis,cis*-1,2,3,4-Tetrakis(diphenylphosphinomethyl)cyclopentane/[PdCl(C$_3$H$_5$)]$_2$ efficiently catalyses the Heck reaction of β-substituted enol ethers with aryl bromides. Employing β-methoxystyrene, 3-ethoxyacrylonitrile or methyl 3-methoxyacrylate, the regioselective α-arylation of these enol ethers was observed in all cases, and mixtures of *Z* and *E* isomers were generally obtained, which in many cases yielded a single ketone product after acid treatment. The stereoselectivity of this reaction depends on steric and electronic factors, and better stereoselectivities in favour of *Z* isomers were observed with electron-rich or sterically congested aryl bromides. Better yields were obtained for this reaction with electron-rich or sterically congested aryl bromides than with electron-poor aryl bromides. This observation suggests that with these β-substituted enol ethers the rate-limiting step of the catalytic cycle is not the oxidative addition of the aryl bromide to the palladium complex.
© 2005 Elsevier Ltd. All rights reserved.

The palladium-catalysed Heck vinylation reaction is one of the most powerful methods for the formation of C–C bonds.[1] The efficiency of several catalysts for the reaction of aryl halides with acrylates or styrene derivatives has been studied in detail. On the other hand, the reaction involving 1,2-disubstituted alkenes has attracted less attention. These alkenes are less reactive than terminal alkenes. Most of the results described with 1,2-disubstituted alkenes were obtained with cinnamates, crotonates or benzalacetone.[2,3] A few results have been described with 2-substituted enol ethers.[4–6] For example, the reaction of ethyl (*E*)-3-ethoxy acrylate and iodobenzene, 4-iodoanisole or 3-iodopyridine can be performed with Pd–C (5%) as catalyst.[4] The reaction involving 3,3,3-trifluoro-1-methoxypropene and iodobenzene, 4-iodonitrobenzene, 3-iodopyridine or iodo-4-bromobenzene with Pd(OAc)$_2$ (3%)/PPh$_3$ (6%) as catalyst and Ag$_2$CO$_3$ as base (1 equiv) also proceeds.[5] 1-Butoxy-prop-1-ene reacts with iodobenzene or 4-bromonitrobenzene employing Pd(PPh$_3$)$_4$ (1%), but mixtures of isomers and low yields were obtained.[6] To our knowl-

edge, the Heck reaction involving β-methoxystyrene[7] or 3-ethoxyacrylonitrile has not been described. Moreover, there still remains a need for a general protocol for Heck reactions in the presence of 2-substituted enol ethers especially with aryl bromides.

In order to obtain stable and efficient palladium catalysts, we have prepared the new tetraphosphine ligand, *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane or Tedicyp[8] (Fig. 1). We have already reported the results obtained in allylic substitution,[8] for Suzuki cross-coupling[9] and for Sonogashira alkynylation[10] using Tedicyp as the ligand. We have also reported several results for Heck vinylation.[11–13] We had observed that with our catalyst, good results could be obtained for the reaction of *n*-butylvinyl ether or ethyleneglycol vinyl ether with aryl bromides.[12] Satisfactory results in terms of substrate/catalyst ratio were also been obtained for the reaction with disubstituted alkenes
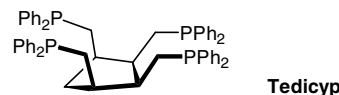
* Corresponding authors. Tel.: +33 4 91 28 84 16; fax: +33 4 91 98 38 65 (H.D.); tel.: +33 4 91 28 88 25 (M.S.); e-mail addresses: henri.doucet@univ.u-3mrs.fr; m.santelli@univ.u-3mrs.fr

Figure 1.

such as methyl crotonate, ethyl cinnamate or benz-alacetone.[13] In order to further establish the requirements for a successful Heck reaction with our catalytic system, we herein report on the reaction of a variety of aryl bromides with the 2-substituted enol ethers: β-methoxystyrene, 3-ethoxyacrylonitrile or methyl 3-methoxyacrylate.

The regioselectivity of the insertion of Heck reaction is controlled both by the electronic properties of the alkenes and by steric factors. Electron-poor alk-1-enes such as acrylates, acrylonitrile or styrene generally lead very selectively to the β-arylated alkenes. On the other hand, electron-rich alk-1-enes such as n-butylvinyl ether often gave mixtures of α- and β-arylated alkenes.[1] Electronic effects do indeed play a major role in arylations of enol ethers. With our Tedicyp/palladium catalyst, we had observed with n-butylvinyl ether that, in all cases, mixtures of linear and branched products were obtained.[12a] For these reasons, the regioselectivity of reaction with the unsymmetrical disubstituted alkenes: β-methoxystyrene, 3-ethoxyacrylonitrile or methyl 3-methoxyacrylate can be predicted and should lead to regioselective insertions to give the isomers **a** and **b** of Scheme 1.

For this study, based on previous results,[12,13] DMF was chosen as the solvent. The reactions were performed under argon employing a 1:2 ratio of [Pd(C₃H₅)Cl]₂/Tedicyp as catalyst. We first studied the reactivity of β-methoxystyrene with 4-t-butylbromobenzene using a few bases at 100–150 °C. Low conversions were observed in the presence of 1 mol % catalyst with K₂CO₃, Na₂CO₃ or NaOAc as bases or at 100–130 °C. The best yield was obtained with NaHCO₃ at 150 °C. Next, we examined the reaction of β-methoxystyrene with several aryl bromides employing 1% catalyst (Scheme 1, Table 1, entries 1–14). As expected, with this alkene, we observed a regioselective addition of the aryl bromides to give the corresponding β-aryl-β-methoxystyrene derivatives. The Tedicyp–Pd catalyst system is tolerant of a variety of aryl bromides for the reaction with β-methoxystyrene. Electron-poor aryl bromides such as 4-bromoacetophenone or 4-bromobenzaldehyde led to the coupling adducts in lower conversions and yields than the reactions performed with electron-rich 4-t-

butylbromobenzene, 4-bromotoluene or 4-bromoanisole (Table 1, entries 1–7). This observation indicates that the rate-limiting step of the reaction with this enol ether is not the oxidative addition of the aryl bromide to the palladium complex, but probably the insertion of the enol ether in the Ar–Pd bond. We also studied the influence of *ortho*-substituents on the aryl bromide for this reaction and we observed that 1-bromonaphthalene, 2-methylbromobenzene or 2,4,6-trimethylbromobenzene gave similar yields than 4-methylbromobenzene (Table 1, entries 11–13). However, for steric reasons, with 2,4,6-trimethylbromobenzene the Z isomer was selectively obtained. The heteroaromatic substrates 3-bromoquinoline and β-methoxystyrene also led to the expected adduct in good yield (Table 1, entry 14). The mixtures of stereoisomers obtained with β-methoxystyrene were hydrolysed into the corresponding ketones using a mixture of THF/H₂O/HCl (or H₂SO₄). The stereoselectivity of this reaction is irrelevant as the outcome of these reaction is the ketone product.

Next, we studied the reactivity of 3-ethoxyacrylonitrile (Table 1, entries 15–26). With this enol ether, very low conversions were obtained with 4-bromoacetophenone or 4-trifluoromethylbromobenzene. On the other hand, with 4-fluorobromobenzene, 4-bromotoluene, 4-t-butylbromobenzene or 6-methoxy-2-bromonaphthalene complete conversions and good yields of arylated ethoxyacrylonitrile were obtained (Table 1, entries 15–18). These *para*-substituted aryl bromides gave regioselectively 3-aryl-3-ethoxyacrylonitrile derivatives but mixtures of Z (12–35%) and E (88–65%) isomers were obtained.

Employing the sterically congested aryl bromides: 2-bromotoluene, 1-bromonaphthalene, 2,4,6-trimethyl-bromobenzene or 2,4,6-triisopropylbromobenzene larger amounts of Z isomers were formed (66–93%) (Table 1, entries 21–24). On the other hand, with the π-electron deficient heteroaromatic substrates, 3-bromo-pyridine or 3-bromoquinoline, the E isomers were obtained in 91% and 90% selectivities, respectively (Table 1, entries 25 and 26). The separation of Z and E 3-aryl-3-ethoxyacrylonitrile isomers was possible by chromatography on silica gel.

R^1 = H, Me, *i*Pr, *t*Bu, OMe, F, CF₃, MeCO, CHO
R^2 = Me and R^3 = CO₂Me
R^2 = Et and R^3 = CN
R^2 = Me and R^3 = Ph
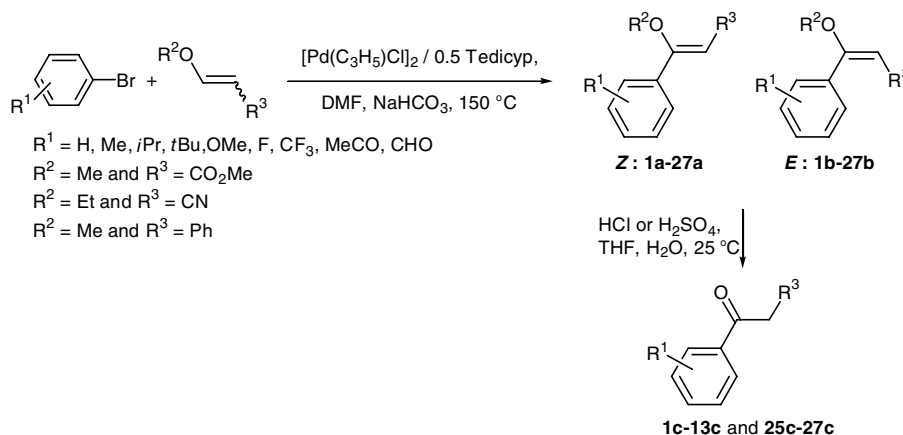
Scheme 1.

Table 1. Heck reactions with 2-substituted enol ethers catalysed by the Tedicyp–palladium complex (Scheme 1)[14,15]

Entry	Aryl halide	Alkene	Ratio Z (**a**)/E(**b**)	Isolated product	Yield[c] (%)
1	4-Bromoacetophenone	β-Methoxystyrene[a]	65/35	**1c**	58
2	4-Bromobenzaldehyde	β-Methoxystyrene[a]	69/31	**2c**	60
3	4-Trifluoromethylbromobenzene	β-Methoxystyrene[a]	72/28	**3c**	62
4	4-Fluorobromobenzene	β-Methoxystyrene[a]	67/33	**4c**	78
5	4-Bromotoluene	β-Methoxystyrene[a]	62/38	**5c**	80
6	4-*t*-Butylbromobenzene	β-Methoxystyrene[a]	63/37	**6c**	79
7	4-Bromoanisole	β-Methoxystyrene[a]	54/46	**7c**	77[d]
8	6-Methoxy-2-bromonaphthalene	β-Methoxystyrene[a]	51/49	**8c**	82
9	Iodobenzene	β-Methoxystyrene[a]	33/67	**9c**	79
10	Bromobenzene	β-Methoxystyrene[a]	66/34	**9c**	74
11	1-Bromonaphthalene	β-Methoxystyrene[a]	57/43	**10c**	84
12	2-Methylbromobenzene	β-Methoxystyrene[a]	62/32	**11c**	79
13	2,4,6-Trimethylbromobenzene	β-Methoxystyrene[a]	100/0	**12c**	74[d]
14	3-Bromoquinoline	β-Methoxystyrene[a]	71/29	**13c**	73
15	4-Fluorobromobenzene	3-Ethoxyacrylonitrile[b]	12/88	**14a,b**	79
16	4-Bromotoluene	3-Ethoxyacrylonitrile[b]	35/65	**15a,b**	76
17	4-*t*-Butylbromobenzene	3-Ethoxyacrylonitrile[b]	30/70	**16a,b**	82
18	6-Methoxy-2-bromonaphthalene	3-Ethoxyacrylonitrile[b]	27/73	**17a,b**	84
19	Iodobenzene	3-Ethoxyacrylonitrile[b]	40/60	**18a,b**	80
20	Bromobenzene	3-Ethoxyacrylonitrile[b]	23/77	**18a,b**	88
21	1-Bromonaphthalene	3-Ethoxyacrylonitrile[b]	75/25	**19a,b**	81
22	2-Bromotoluene	3-Ethoxyacrylonitrile[b]	77/23	**20a,b**	77
23	2,4,6-Trimethylbromobenzene	3-Ethoxyacrylonitrile[b]	66/34	**21a,b**	73[d]
24	2,4,6-Triisopropylbromobenzene	3-Ethoxyacrylonitrile[b]	93/7	**22a,b**	76
25	3-Bromopyridine	3-Ethoxyacrylonitrile[b]	9/91	**23a,b**	78
26	3-Bromoquinoline	3-Ethoxyacrylonitrile[b]	10/90	**24a,b**	80
27	4-*t*-Butylbromobenzene	Methyl (*E*)-3-methoxyacrylate	49/51[e]	**25c**	62
28	4-Bromoanisole	Methyl (*E*)-3-methoxyacrylate	ND[e,f]	**26c**	60[d]
29	2-Bromotoluene	Methyl (*E*)-3-methoxyacrylate	ND[e,f]	**27c**	56

Conditions: catalyst [Pd(C$_3$H$_5$)Cl]$_2$/Tedicyp 1:2, see Ref. 7 (0.01 equiv), ArX (1 equiv), enol ether (2 equiv), NaHCO$_3$ (2 equiv), DMF, 20 h, 150 °C, under argon, isolated yields, ratio Z/E calculated with ^{1}H NMR of the crude mixtures.

[a] Ratio Z/E: 2/98.
[b] Ratio Z/E: 35/65.
[c] Isolated yields of the mixture of Z (**a**)+E (**b**) isomers (entries 15–26) or hydrolysed products **c** (entries 1–14 and 27–29).
[d] The reaction performed under similar conditions with [Pd(C$_3$H$_5$)Cl]$_2$/PPh$_3$ 1:4 as catalyst gave **7c**, **12c** or **26c** in 16–25% yields and **21a,b** in 38% yield.
[e] Partial deprotection into the corresponding ketones **c** was observed before treatment with HCl or H$_2$SO$_4$.
[f] Not determined.

Finally, we performed a few reactions with methyl (*E*)-3-methoxyacrylate (Table 1, entries 27–29). The formation of mixtures of Z and E 3-aryl-3-methoxyacrylates was observed, and, with this alkene a partial hydrolysis of the arylated enol ethers occurs during the Pd-catalysed reactions to give directly the 3-aryl-3-oxopropionic acid methyl esters. The formation of side-products was also observed with this alkene. Hydrolysis of these mixtures gave the 3-aryl-3-oxopropionic acid methyl esters in moderate yields.

A few reactions were also performed with these 2-substituted enol ethers using PPh$_3$ as ligand, but low yields of adducts were obtained and side products were formed with this catalytic system.

In summary, with the Tedicyp/palladium complex, the Heck vinylation of several aryl bromides with 2-substituted enol ethers can be performed in high regioselectivities and good yields. The reactivity of three 2-substituted enol ethers has been studied: β-methoxystyrene, 3-ethoxyacrylonitrile and methyl (*E*)-3-methoxyacrylate. In all cases, regioselective α-arylations of these enol ether have been observed. The stereoselectivity of the reactions strongly depends on the electron properties and the steric hindrance of the aryl bromides. As expected, larger amounts of Z isomers were obtained with sterically congested aryl bromides. Higher reactions rates were observed with the electron-rich than with electron-deficient aryl bromides. This observation indicates that the rate-limiting step of this reaction is not the oxidative addition of the aryl bromide to the palladium complex, but more likely the insertion of the enol ether in the Ar–Pd bond of the intermediate: Ar(X)Pd(RCH=CHOR′) to give Ar(R)CH–CH(PdX)(OR′). Steric factors may also be important for the reductive elimination step with our bulky tetraphosphine ligand. Steric strain is a driving force in many Pd catalysed reactions. With our systems a catalytic intermediate might be a P$_2$PdArX(alkene) penta-coordinate complex type with two arms of the ligand detached. Apart from achieving excellent regiocontrol, another advantage is that β-methoxystyrene, 3-ethoxyacrylonitrile and methyl (*E*)-3-methoxyacrylate are commercially available. The hydrolysis of these arylated enolesters gives a very simple access to a wide variety of acetophenone derivatives.

References and notes

1. For reviews on the palladium-catalysed Heck reaction see: (a) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2; (b) Beletskaya, I.; Cheprakov, A. *Chem. Rev.* **2000**, *100*, 3009; (c) Withcombe, N.; Hii (Mimi), K. K.; Gibson, S. *Tetrahedron* **2001**, *57*, 7449; (d) Littke, A.; Fu, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176; (e) Farina, V. *Adv. Synth. Catal.* **2004**, *346*, 1553; (f) Bedford, R. B.; Cazin, C. S. J.; Holder, D. *Coord. Chem. Rev.* **2004**, *248*, 2283; (g) Dupont, J.; Consorti, C. S.; Spencer, J. *Chem. Rev.* **2005**, *105*, 2527.

2. For selected examples of Heck reactions with cinnamates or crotonates: (a) Melpolder, J.; Heck, R. *J. Org. Chem.* **1976**, *41*, 265; (b) Cortese, N.; Ziegler, C.; Hrnjez, B.; Heck, R. *J. Org. Chem.* **1978**, *43*, 2952; (c) Moreno-Mañas, M.; Pérez, M.; Roser, P. *Tetrahedron Lett.* **1996**, *37*, 7449; (d) Gürtler, C.; Buchwald, S. *Chem. Eur. J.* **1999**, *5*, 3107; (e) Littke, A.; Fu, G. *J. Am. Chem. Soc.* **2001**, *123*, 6989; (f) Calo, V.; Nacci, A.; Monopoli, A.; Lopez, L.; di Cosmo, A. *Tetrahedron* **2001**, *57*, 6071.

3. For examples of Heck reactions with (*E*)-benzalacetone or (*E*)-benzalacetophenone: (a) Cacchi, S.; Arcadi, A. *J. Org. Chem.* **1983**, *48*, 4236; (b) Amorese, A.; Arcadi, A.; Bernocchi, E.; Cacchi, S.; Cerrini, S.; Fereli, W.; Ortar, G. *Tetrahedron* **1989**, *45*, 813.

4. For examples of Heck reactions with ethyl (*E*)-3-ethoxy acrylate: Sakamoto, T.; Kondo, Y.; Kashiwagi, Y.; Yamanaka, H. *Heterocycles* **1988**, *27*, 257.

5. For examples of Heck reactions with 3,3,3-trifluoro-1-methoxypropene: Shi, G.-Q.; Huang, X.-H.; Hong, F. *J. Chem. Soc., Perkin Trans. 1* **1996**, 763.

6. For examples of Heck reactions with 1-butoxyprop-1-ene: Andersson, C. M.; Hallberg, A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3529.

7. For reactions with related substrates, see: (a) Nilsson, P.; Larhed, M.; Hallberg, A. *J. Am. Chem. Soc.* **2001**, *123*, 8217; (b) Nilsson, P.; Larhed, M.; Hallberg, A. *J. Am. Chem. Soc.* **2003**, *125*, 3430.

8. Laurenti, D.; Feuerstein, M.; Pèpe, G.; Doucet, H.; Santelli, M. *J. Org. Chem.* **2001**, *66*, 1633.

9. Feuerstein, M.; Laurenti, D.; Bougeant, C.; Doucet, H.; Santelli, M. *Chem. Commun.* **2001**, 325.

10. Feuerstein, M.; Berthiol, F.; Doucet, H.; Santelli, M. *Org. Biomol. Chem.* **2003**, 2235.

11. (a) Feuerstein, M.; Doucet, H.; Santelli, M. *J. Org. Chem.* **2001**, *66*, 5923; (b) Feuerstein, M.; Doucet, H.; Santelli, M. *Synlett* **2001**, 1980; (c) Berthiol, F.; Feuerstein, M.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2002**, *43*, 5625; (d) Berthiol, F.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2003**, *44*, 1221; (e) Berthiol, F.; Doucet, H.; Santelli, M. *Synlett* **2003**, 841; (f) Lemhadri, M.; Doucet, H.; Santelli, M. *Tetrahedron* **2004**, *60*, 11533; (g) Berthiol, F.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2004**, *45*, 5633; (h) Berthiol, F.; Doucet, H.; Santelli, M. *Eur. J. Org. Chem.* **2005**, 1367; (i) Battace, A.; Zair, T.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2005**, *690*, 3790.

12. (a) Feuerstein, M.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2002**, *43*, 2191; (b) Kondolff, I.; Doucet, H.; Santelli, M. *Synlett* **2004**, 1561.

13. Kondolff, I.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2003**, *44*, 8487.

14. As a typical experiment for reactions with β-methoxystyrene or methyl (*E*)-3-methoxyacrylate: (Table 1, entry 4) The reaction of 4-fluorobromobenzene (0.175 g, 1 mmol), β-methoxystyrene (0.268 g, 2 mmol) and NaHCO$_3$ (0.168 g, 2 mmol) at 150 °C over 20 h in dry DMF (5 mL) with *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphino-methyl)cyclopentane/[PdCl(C$_3$H$_5$)]$_2$ complex (0.01 mmol) under argon affords the corresponding products (*Z*)-1-methoxy-2-phenyl-1-(4-fluorophenyl)ethene (**4a**) and (*E*)-1-methoxy-2-phenyl-1-(4-fluorophenyl)ethene (**4b**) as a mixture of isomers. Ratio **4a** (*Z*)/**4b** (*E*) determined by ^{1}H NMR on the crude mixture: 67/33. Characteristic band of the mixture of isomers: ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 6.04$ (s, 1H, C*H*=C (*Z*)), 5.82 (s, 1H, C*H*=C (*E*)). This unseparable mixture of isomers was hydrolysed into the corresponding ketone using a mixture THF/H$_2$O/HCl to give 1-(4-fluorophenyl)-2-phenylethanone **4c** in 78% (0.167 g) isolated yield. ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 8.02$ (dd, *J* = 7.4 and 5.5 Hz, 2H), 7.35–7.20 (m, 5H), 7.11 (t, *J* = 7.4 Hz, 2H), 4.25 (s, 2H).

15. As a typical experiment for reactions with 3-ethoxyacrylonitrile: (Table 1, entry 21) The reaction of 1-bromonaphthalene (0.207 g, 1 mmol), 3-ethoxyacrylonitrile (0.194 g, 2 mmol) and NaHCO$_3$ (0.168 g, 2 mmol) at 150 °C over 20 h in dry DMF (5 mL) with *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane/[PdCl(C$_3$H$_5$)]$_2$ complex (0.01 mmol) under argon affords the corresponding products (*Z*)-3-ethoxy-3-naphthalen-1-ylacrylonitrile (**19a**) and (*E*)-3-ethoxy-3-naphthalen-1-ylacrylonitrile (**19b**) after evaporation and filtration on silica gel as a mixture of isomers in 81% (0.181 g) isolated yield. Ratio **19a** (*Z*)/**19b** (*E*) determined by ^{1}H NMR on the crude mixture: 75/25. These isomers were separated by chromatography on silica gel. Isomer *Z* **19a**: ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.92 (d, 1H, *J* = 8.3 Hz), 7.85 (m, 2H), 7.64 (d, 1H, *J* = 7.0 Hz), 7.60–7.47 (m, 3H), 4.90 (s, 1H), 4.07 (q, 2H, *J* = 7.0 Hz), 1.43 (t, 3H, *J* = 7.0 Hz). ^{13}C NMR (75 MHz, CDCl$_3$): δ 174.0, 133.6, 130.9, 130.4, 128.5, 127.7, 126.9, 126.3, 124.9, 124.6, 117.8, 74.2, 65.8, 14.1. Anal. Calcd for C$_{15}$H$_{13}$NO: C, 80.69; H, 5.87. Found: C, 80.48; H, 5.97. Isomer *E* **19b**: ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.00–7.85 (m, 3H), 7.62–7.45 (m, 4H), 4.71 (s, 1H), 3.93 (q, 2H, *J* = 7.0 Hz), 1.25 (t, 3H, *J* = 7.0 Hz). ^{13}C NMR (75 MHz, CDCl$_3$): δ 172.7, 133.2, 131.0, 130.8, 130.4, 128.5, 127.6, 127.5, 126.7, 125.0, 124.6, 116.6, 77.7, 66.9, 15.2. Anal. Calcd for C$_{15}$H$_{13}$NO: C, 80.69; H, 5.87. Found: C, 80.80; H, 5.78.