Tetrahedron Letters 49 (2008) 6715–6719

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Friedel–Crafts acylation of aromatic compounds with carboxylic acids in the presence of P_2O_5/SiO_2 under heterogeneous conditions

Amin Zarei [a,*], Abdol R. Hajipour [b,c], Leila Khazdooz [c]

[a] Department of Science, Islamic Azad University, Fasa Branch, PO Box No. 364, Fasa, 7461713591 Fars, Iran
[b] Department of Pharmacology, University of Wisconsin, Medical School, 1300 University Avenue, Madison, 53706-1532 WI, USA
[c] Pharmaceutical Research Laboratory, College of Chemistry, Isfahan University of Technology, Isfahan 84156, Iran

ARTICLE INFO

Article history:
Received 29 June 2008
Revised 31 August 2008
Accepted 12 September 2008
Available online 17 September 2008

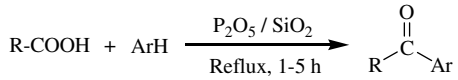
Keywords:
Friedel–Crafts acylation
Carboxylic acids
P_2O_5/SiO_2

ABSTRACT

A convenient and efficient procedure for the Friedel–Crafts acylation of aromatic compounds with carboxylic acids in the presence of P_2O_5/SiO_2 is described. Both aromatic and aliphatic carboxylic acids reacted easily to afford the corresponding aromatic ketones. The use of non-toxic and inexpensive materials, simple and clean work-up, short reaction times and good yields of the products are the advantages of this method.

Friedel–Crafts acylation is one of the most important methods to prepare aromatic ketones, which are used in manufacturing fine and speciality chemicals as well as pharmaceuticals.[1] Typical procedures include the use of acid chlorides or acid anhydrides as acylating agents and an excess amount of aluminium trichloride as a Lewis acid, which entails environmental pollution and a tedious work-up. In order to minimize these problems, several catalytic Friedel–Crafts acylations have been developed.[2] A literature survey indicates that the use of carboxylic acids as acylating agents is a superior method with respect to procedures utilizing acyl chlorides and anhydrides. Zeolites,[3] heteropolyacids and their salts,[4] clay,[5] alumina/TFAA,[6] $MeSO_3H$/graphite[7] and Lewis acids[8] are reported to catalyze Friedel–Crafts acylations using carboxylic acids as acylating agents. Recently, the use of catalysts and reagents on solid supports has been developed because such reagents not only simplify purification processes but also help to prevent release of reaction residues into the environment.[9]

Although there are many reports using phosphorus pentoxide as a reagent in organic reactions,[10] P_2O_5 is difficult to handle due to its moisture sensitivity at room temperature. P_2O_5 on silica gel (P_2O_5/SiO_2) is easy to prepare and to handle, and can be removed from the reaction mixture by simple filtration.[11] Herein, we report an efficient and convenient procedure for the conversion of carboxylic acids to the corresponding aryl ketones in the presence of P_2O_5/SiO_2. These reactions are easily carried out under heterogeneous and reflux conditions (Scheme 1).



R= Aryl, Alkyl, Alkenyl

Scheme 1.

The acylation reactions were carried out by heating a stirring mixture of the carboxylic acid, aromatic compound and P_2O_5/SiO_2 at reflux.[12,13] However, for reagents such as anisole, 1,3-dimethoxybenzene, 2-methoxynaphthalene, naphthalene, anthracene, 2-methylthiophene, thioanisole and biphenyl, the acylation reactions were carried out in 1,2-dichloroethane under reflux conditions.[14] The products were isolated by simple filtration of the reaction mixture and then by usual work-up. These reaction conditions were successfully applied for the preparation of different aryl ketones from electron-rich and electron-poor aromatic compounds. The results of this study are presented in Table 1. The reactions are remarkably clean, convenient and no chromatographic separation was necessary to obtain spectroscopically pure compounds, except in a few cases (Table 1, entries 26, 29 and 30). Using this reagent, acylation occurs at the *para* position with good selectivity. However, in cases where the *para* positions are blocked (Table 1, entries 2 and 16), the acyl group is introduced *ortho* to the substituent. This procedure also succeeds for the acylation of thiophene and 2-methylthiophene (Table 1, entries 8, 9 and 20), as well as polycyclic aromatic hydrocarbons (Table 1, entries 7, 11, 26 and 27), producing the corresponding acylated products in good yields. These reactions are rapid even with higher carboxylic acids.

* Corresponding author. Tel.: +98 9171302528; fax: +98 7313333411.
E-mail address: aj_zarei@yahoo.com (A. Zarei).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.09.062

Table 1
Direct acylation of aromatic compounds with carboxylic acids in the presence of P_2O_5/SiO_2 under reflux conditions

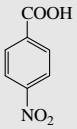
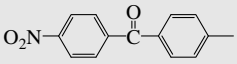
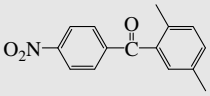
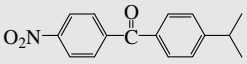
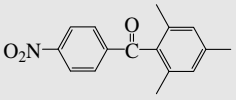
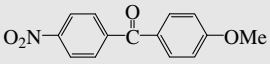
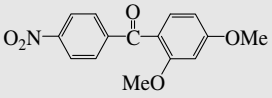
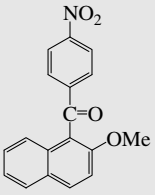
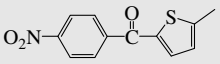
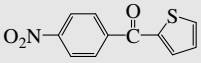
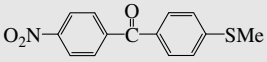
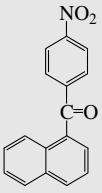
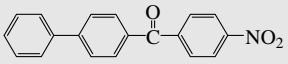
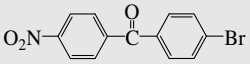
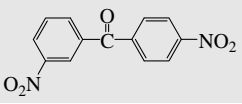
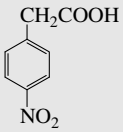
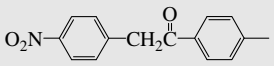
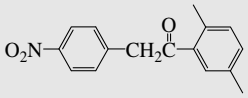
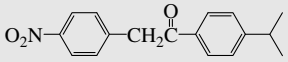
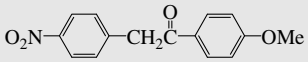
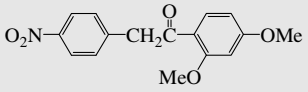
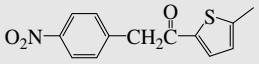
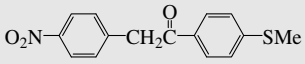
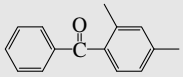
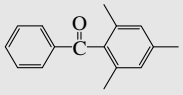
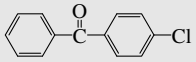
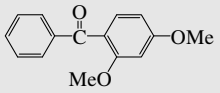
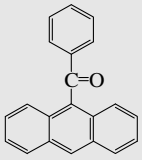
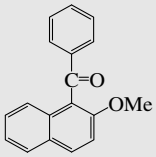
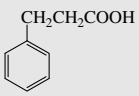
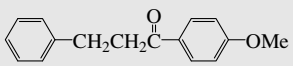
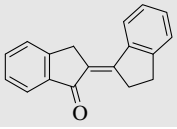
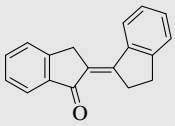
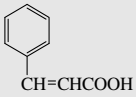
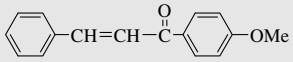
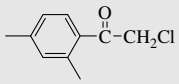
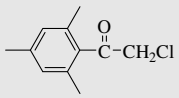
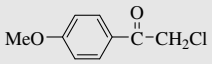
Entry	Carboxylic acid	Aromatic hydrocarbon	Product	Time (h)	Yield[a] (%)
1		Toluene		5	68
2		*p*-Xylene		3	70
3		Cumene		3	52
4		Mesitylene		2	66
5[be]		Anisole		5	67
6[c]		1,3-Dimethoxybenzene		3	78
7[d]		2-Methoxynaphthalene		2	86
8[b]		2-Methylthiophene		3	58
9		Thiophene		3	52
10[b]		Thioanisole		5	62
11[d,f]		Naphthalene		2	88
12[d]		Biphenyl		3	85
13		Bromobenzene		3	37
14		Nitrobenzene		3	0

Table 1 (*continued*)

Entry	Carboxylic acid	Aromatic hydrocarbon	Product	Time (h)	Yield[a] (%)
15		Toluene		3	80
16		*p*-Xylene		3	76
17		Cumene		3	45
18[b]		Anisole		5	88
19[c]		1,3-Dimethoxybenzene		3	90
20[b]		2-Methylthiophene		3	55
21[c]		Thioanisole		5	60
22		*m*-Xylene		3	82
23		Mesitylene		2	80
24		Chlorobenzene		5	28
25[c]		1,3-Dimethoxybenzene		3	84
26[d]		Anthracene		3	57
27[d]		2-Methoxynaphthalene		3	76
28[b]		Anisole		3	86
29		Toluene		3	16

(*continued on next page*)

Table 1 (*continued*)

Entry	Carboxylic acid	Aromatic hydrocarbon	Product	Time (h)	Yield[a] (%)
30		*m*-Xylene		3	23
31[b]		Anisole		3	88
32	Cl^-CH_2COOH	*m*-Xylene		2	72
33		Mesitylene		1	70
34[b,g]		Anisole		3	70

[a] The yield, based on the starting acid, refers to the isolated pure products which were characterized from their spectral data and were compared with authentic samples.[15,16]
[b] The molar ratio of aromatic compound/carboxylic acid is 5/1.5 and the reaction is carried out in 1,2-dichloroethane under reflux conditions.
[c] The molar ratio of aromatic compound/carboxylic acid is 3/1.5 and the reaction is carried out in 1,2-dichloroethane under reflux conditions.
[d] The molar ratio of aromatic compound/ carboxylic acid is 1/1.5 and the reaction is carried out in 1,2-dichloroethane under reflux conditions.
[e] 15% of the *ortho*-isomer was detected by ^1H NMR spectroscopy.
[f] 18% of the β-isomer was detected by ^1H NMR spectroscopy.
[g] 12% of the *ortho*-isomer was detected by ^1H NMR spectroscopy.

However, for deactivated aromatic rings such as bromobenzene and chlorobenzene (Table 1, entries 13 and 24), the corresponding 4-acylated products were obtained in low yields. With nitrobenzene, no product was obtained (Table 1, entry 14). The reaction between 3-phenylpropionic acid and anisole in the presence of P_2O_5/SiO_2 produced the corresponding 4-acylated product in high yield (Table 1, entry 28); however, the reaction between 3-phenylpropionic acid and toluene or *m*-xylene produced 2,3-dihydro-3′*H*-[1,2′]biindenyliden-1′-one as a major product of a subsequent aldol condensation (Table 1, entries 29 and 30).

According to our observations, the present method occurs by in situ generation of a carboxylic anhydride derived from a mixed carboxylic-phosphoric anhydride.[17,18]

To evaluate the role of the SiO_2, we studied the acylation of anisole with 4-nitrobenzoic acid, 4-nitrophenylacetic acid, 3-phenylpropionic, cinnamic acid and 2-chloroacetic acid in the absence of SiO_2. These reactions were carried out in refluxing 1,2-dichloroethane in the presence of P_2O_5 alone. We found that the yields using P_2O_5/SiO_2 were greater (average, 20%) than those with P_2O_5 alone under the same conditions. The effect of SiO_2 may be due to good dispersion of P_2O_5 on the surface of silica gel leading to significant improvements in its reactivity. SiO_2 as a support may also minimize cross contamination between the product and H_3PO_4 generated during the course of the reaction.[9,17]

In conclusion, P_2O_5/SiO_2 is an inexpensive, easily available, noncorrosive and environmentally benign compound. In this work, we have reported a convenient and efficient procedure for the preparation of aryl ketones in good yields and short reaction times. The notable advantages of this methodology are direct use of a wide variety of carboxylic acids, operational simplicity, generality, good regioselectivity, availability of reactants and easy work-up.

Acknowledgements

We gratefully acknowledge the funding support received for this project from the Islamic Azad University of Fasa and the Isfahan University of Technology (IUT).

References and notes

1. Heaney, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 2, p 733.
2. (a) Kawada, A.; Mitamura, S.; Kobayashi, S. *Synlett* **1994**, 545; (b) Matsuo, J.; Odashima, K.; Kobayashi, S. *Synlett* **2000**, 403; (c) Effenberger, F.; Buckel, F.; Maier, A. H.; Schmider, J. *Synthesis* **2000**, 1427; (d) Bartoli, G.; Bosco, M.; Marcantoni, E.; Massaccesi, M.; Rinaldi, S.; Sambri, L. *Tetrahedron Lett.* **2002**, *43*, 6331; (e) Repichet, S.; Roux, C. L.; Roques, N.; Dubac, J. *Tetrahedron Lett.* **2003**, *44*, 2037; (f) Firouzabadi, H.; Iranpoor, N.; Nowrouzi, F. *Tetrahedron* **2004**, *60*, 10843; (g) Sartori, G.; Maggi, R. *Chem. Rev.* **2006**, *106*, 1077.
3. (a) Wang, Q. L.; Ma, Y.; Ji, X.; Yan, H.; Qiu, Q. *Chem. Commun.* **1995**, 2307; (b) Singh, A. P.; Pandey, A. K. *J. Mol. Catal. A* **1997**, *123*, 141; (c) Pandey, A. K.; Singh, A. P. *Catal. Lett.* **1997**, *44*, 129; (d) De Castro, C.; Primo, J.; Corma, A. *J. Mol. Catal. A* **1998**, *134*, 215.
4. (a) Izumi, Y.; Ogawa, M.; Nohara, W.; Urabe, K. *Chem. Lett.* **1992**, 1987; (b) Kaur, J.; Kozhevnikov, I. V. *Chem. Commun.* **2002**, 2508; (c) Firouzabadi, H.; Iranpoor, N.; Nowrouzi, F. *Tetrahedron Lett.* **2003**, *44*, 5343.
5. Chiche, B.; Finiels, A.; Gautheir, C.; Geneste, P. *J. Mol. Catal.* **1987**, *42*, 229.
6. Ranu, B. C.; Ghosh, K.; Jana, U. *J. Org. Chem.* **1996**, *61*, 9546.
7. Sarvari, M. H.; Sharghi, H. *Synthesis* **2004**, 2165.
8. (a) Suzuki, K.; Kitagawa, H.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3729; (b) Kobayashi, S.; Moriwaki, M.; Hachiya, I. *Tetrahedron Lett.* **1996**, *37*, 4183; (c) Kawamura, M.; Cui, D. M.; Hayashi, T.; Shimada, S. *Tetrahedron Lett.* **2003**, *44*, 7715.
9. Clark, J. H. In *Catalysis of Organic Supported Inorganic Reagents*; VCH: New York, 1994; p 2.
10. (a) Eaton, C. L. *J. Org. Chem.* **1973**, *38*, 4071; (b) Basavaiah, D.; Bakthadoss, M.; Reddy, G. J. *Synthesis* **2001**, 919; (c) Kato, Y.; Okada, S.; Tomimoto, K.; Mase, T. *Tetrahedron Lett.* **2001**, *42*, 4849.
11. (a) Hajipour, A. R.; Zarei, A.; Khazdooz, L.; Zahmatkesh, S.; Ruoho, A. E. *Phosphorus, Sulfur, Silicon* **2006**, *181*, 387; (b) Mirjalilli, F.; Zolfigol, M. A.;

Bamoniri, A. H.; Khazdooz, L. *Bull. Korean Chem. Soc.* **2003**, *24*, 1009; (c) Hajipour, A. R.; Koshki, B.; Ruoho, A. E. *Tetrahedron Lett.* **2005**, *46*, 5503; (d) Eshghi, H.; Hassankhani, A. *Synth. Commun.* **2006**, *36*, 2211; (e) Tamaddon, F.; Khoobi, M.; Keshavarz, E. *Tetrahedron Lett.* **2007**, *48*, 3643.

12. P_2O_5/SiO_2 was prepared by mixing phosphorus pentoxide (3 g) and 3 g of dried Silica Gel 60 (0.063–0.200 mm, previously heated at 120 °C for 24 h) in a round bottomed flask with a glass spatula. After 10 min, a fine and homogenous powder was obtained. This reagent was heated in an oven at 120 °C for 1 h and then stored in a sealed flask for later use. *General procedure for the acylation of aromatic compounds using carboxylic acids and P_2O_5/SiO_2*: To a mixture of a carboxylic acid (1.5 mmol) and an aromatic compound (5 mL), P_2O_5/SiO_2 (0.6 g) was added and the reaction mixture was stirred under reflux conditions for the appropriate reaction times (Table 1). After completion of the reaction (monitored by TLC), the mixture was diluted with EtOAc and filtered. The organic layer was washed with 10% $NaHCO_3$ solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to give the corresponding pure aryl ketone.
13. *Typical procedure for the acylation of toluene using 4-nitrophenylacetic acid and P_2O_5/SiO_2*: To a mixture of 4-nitrophenylacetic acid (1.5 mmol, 0.27 g) and toluene (5 mL), P_2O_5/SiO_2 (0.6 g) was added and the reaction mixture was stirred under reflux conditions for 3 h. After cooling, the mixture was diluted with EtOAc (15 mL) and after vigorous stirring was filtered. The residue was extracted with EtOAc (2×10 mL) and the collected organic layer was washed with 10% $NaHCO_3$ solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to give 1-(*p*-tolyl)-2-(4-nitrophenyl)ethanone in 80% yield (0.15 g, Table 1, entry 15).
14. *Typical procedure for the acylation of 1,3-dimethoxybenzene using 4-nitrobenzoic acid and P_2O_5/SiO_2 in 1,2-dichloroethane under reflux conditions*: To a mixture of 4-nitrobenzoic acid (1.5 mmol, 0.25 g), 1,3-dimethoxybenzene (3 mmol, 0.4 mL) and 1,2-dichloroethane (5 mL), P_2O_5/SiO_2 (0.6 g) was added and the reaction mixture was stirred under reflux conditions for 3 h. After cooling, the mixture was diluted with CH_2Cl_2 (15 mL) and after vigorous stirring was filtered. The residue was extracted with CH_2Cl_2 (2×10 mL) and the collected organic layer was washed with 10% $NaHCO_3$ solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude product was washed with cold *n*-hexane to give (2,4-dimethoxyphenyl)(4-nitrophenyl)methanone in 78% yield (0.165 g, Table 1, entry 6).
15. (a) Yamashita, M. *Bull. Chem. Soc. Jpn.* **1928**, *3*, 180; (b) Ray, F. E.; Moomaw, W. A. *J. Am. Chem. Soc.* **1933**, *55*, 3833; (c) Hey, D. H.; Jackson, E. R. B. *J. Chem. Soc.* **1936**, 802; (d) Adams, R.; Theobald, C. W. *J. Am. Chem. Soc.* **1943**, *65*, 2208; (e) Goncalves, R.; Kegelman, M. R.; Brown, E. V. *J. Org. Chem.* **1952**, *17*, 705; (f) Fuson, R. C.; Emmons, W. D.; Smith, S. G. *J. Am. Chem. Soc.* **1955**, *77*, 2503; (g) Metz, G. *Synthesis* **1972**, 614; (h) Goeckner, N. A.; Snyder, H. R. *J. Org. Chem.* **1973**, *38*, 481; (i) Sawada, S.; Miyasaka, T.; Arakawa, K. *Chem. Pharm. Bull.* **1977**, *25*, 3370; (j) Krespan, C. G. *J. Org. Chem.* **1979**, *44*, 4924; (k) Rappoport, Z.; Pross, N. *J. Org. Chem.* **1980**, *45*, 4309; (l) *Dictionary of Organic Compounds*, 5th ed., Chapman and Hall, 1982; (m) Santo, R. D.; Costi, R.; Artico, M.; Massa, S.; Musiu, C.; Scintu, F.; Putzolu, M.; Colla, P. L. *Eur. J. Med. Chem.* **1997**, *32*, 143; (n) Shirude, S. T.; Patel, P.; Giridhar, R.; Yadav, M. R. *Indian J. Chem.* **2006**, *45B*, 1080.
16. *Spectral data of new compounds*: *Table 1, entry 7*: Yellow solid; mp 172–174 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.25 (2H, d, J = 8.82 Hz), 7.98 (3H, m), 7.74 (1H, d, J = 7.35Hz), 7.52 (1H, d, J = 9.1 Hz), 7.4 (2H, m), 7.32 (1H, d, J = 9.1 Hz), 3.8 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.6, 155.5, 151.2, 143.3, 133.2, 132.3, 131, 129.6, 129.2, 128.7, 125.2, 124.6, 124.2, 122, 113.5, 57.2. EIMS *m/z* (%): 307 (M^+, 56), 290 (16), 276 (13), 260 (12), 185 (100), 142 (25), 127 (21), 120 (27), 114 (26), 106 (15), 92 (14), 76 (14), 43 (34). IR (KBr) cm^{-1}: 3040, 2920 1675, 1600, 1530, 1340, 1235, 1080, 890, 840, 800. Anal. Calcd for $C_{18}H_{13}NO_4$: C, 70.03; H, 4.23; N, 4.56. Found: C, 70.16; H, 4.21; N, 4.51. *Table 1, entry 8*: Yellow solid; mp 124–126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.16 (2H, d, J = 9.2 Hz), 7.97 (2H, d, J = 9.2 Hz), 7.44 (1H, d, J = 4.1 Hz), 6.87 (1H, d, J = 4.1 Hz), 2.6 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189, 149.1, 147, 143.2, 142.5, 136.5, 130, 127.2, 123.9, 16.3. EIMS *m/z* (%): 247 (M^+, 2), 246 (3), 232 (2), 125 (100), 106 (5), 97 (6), 78 (2), 53 (15), 45 (4). IR (KBr) cm^{-1}: 3060, 2875, 1630, 1590, 1520, 1450, 1350, 1300, 1050, 870, 840, 700. Anal. Calcd for $C_{12}H_9NSO_3$: C, 58.3; H, 3.64; N, 5.66; S, 12.95. Found: C, 58.22; H, 3.55; N, 5.76; S, 12.86. *Table 1, entry 10*: Bright yellow solid; mp 140–142 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.36 (2H, d, J = 9 Hz), 7.92 (2H, d, J = 9 Hz), 7.75 (2H, d, J = 8.4 Hz), 7.34(2H, d, J = 8.4 Hz), 2.6 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 196, 147.1, 143.8, 140.5, 135, 130.8, 130.7, 125.1, 123.7, 18.5. EIMS *m/z* (%): 273 (M^+, 47), 243 (24), 196 (10), 151 (100), 123 (13), 120 (45), 108 (18), 76 (16), 45 (20). IR (KBr) cm^{-1}: 3065, 2885, 1640, 1585, 1515, 1360, 1290, 1090, 935, 850. Anal. Calcd for $C_{14}H_{11}NSO_3$: C, 61.53; H, 4.03; N, 5.13; S, 11.71. Found: C, 61.62; H, 4.13; N, 5.04; S, 11.81. *Table 1, entry 16*: Yellow solid; mp 86–88 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.2 (2H, d, J = 8.5 Hz), 7.55 (1H, s), 7.4 (2H, d, J = 8.5Hz), 7.22 (1H, d, J = 8.05 Hz), 7.15 (1H, d, J = 8.05 Hz), 4.37 (2H, s), 2.42 (3H, s), 2.39 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 195.1, 145.3, 137, 134.5, 134, 133.2, 132.7, 131.1, 129.7, 128.4, 124.2, 48.1, 24.9, 21.6. IR (KBr) cm^{-1}: 3065, 2890, 1680, 1600, 1510, 1340, 1170, 985, 960, 820, 720. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.37; H, 5.57; N, 5.20. Found: C, 71.30; H, 5.50; N, 5.28. *Table 1, entry 17*: Yellow solid; mp 122–124 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.2 (2H, d, J = 8.3 Hz), 8 (2H, d, J = 7.96 Hz), 7.55 (2H, d, J = 8.28 Hz), 7.44 (2H, d, J = 7.93 Hz), 4.6 (2H, s), 2.99 (1H, septet, J = 6.8 Hz), 1.24 (6H, d, J = 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 195.8, 145.2, 143.1, 134.3, 131.3, 130.7, 130.6, 127, 123.6, 45.8, 34.5, 24.1. EIMS *m/z* (%): 283 (M^+, 2), 147 (100), 119 (9), 104 (8), 91 (15), 77 (7), 41 (5). IR (KBr) cm^{-1}: 3060, 2925, 1670, 1600, 1520, 1350, 1230, 990, 840, 725. Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.08; H, 6.05; N, 4.94%. Found: C, 72.15; H, 6.11; N, 5.01. *Table 1, entry 19*: Yellow solid; mp 119–121 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.18 (2H, d, J = 8.7 Hz), 7.85 (1H, d, J = 8.65 Hz), 7.38 (2H, d, J = 8.7 Hz), 6.55 (1H, dd, J_1 = 8.65 Hz, J_2 = 2.48 Hz), 6.48 (1H, d, J = 2.48 Hz), 4.4 (2H, s), 3.92 (3H, s), 3.88 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 194.5, 163, 160.1, 146.2, 142.3, 134.1, 131.4, 124.2, 117.5, 106.1, 98.7, 56.3, 56.1, 49.4. IR (KBr) cm^{-1}: 3045, 2920, 1660, 1600, 1515, 1355, 1310, 1270, 1140, 990, 830, 735. Anal. Calcd for $C_{16}H_{15}NO_5$: C, 63.78; H, 4.98; N, 4.65. Found: C, 63.71; H, 5.08; N, 4.72.
17. So, Y. H.; Heeschen, J. P. *J. Org. Chem.* **1997**, *62*, 3552.
18. Field, L. *J. Am. Chem. Soc.* **1952**, *74*, 394.