Facile β-Alkoxycarbonylation and β-Acylation of α,β-Unsaturated Lactones and Esters *via* the Phosphoniosilylation Process†

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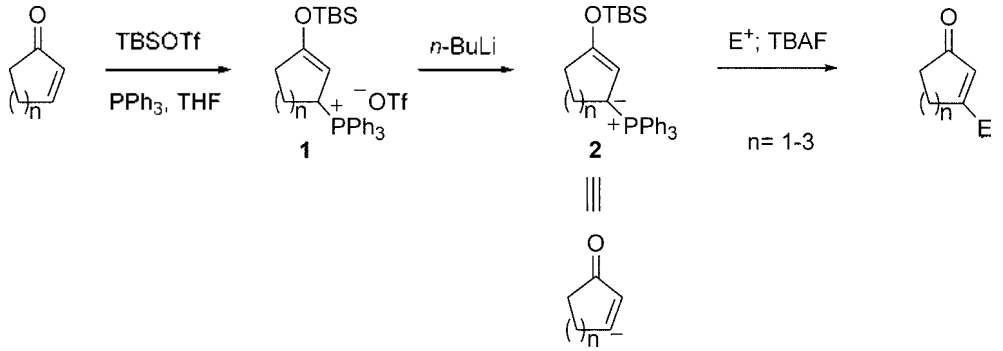
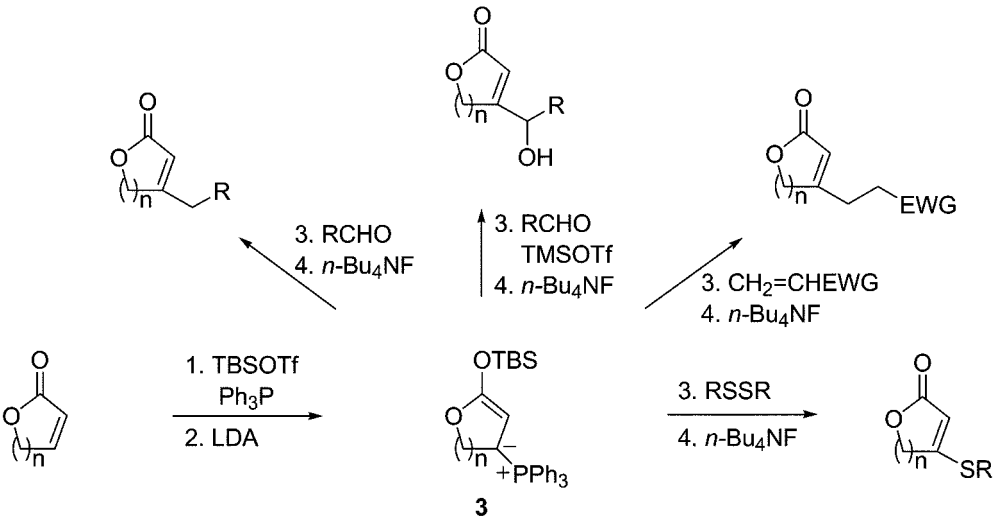
β-Functionalization of α,β-unsaturated carbonyl compounds can be effected by a variety of methods, which generally involve either by the organometallic conjugate addition procedures followed by enolate trapping and subsequent oxidation[1] or by the dipole reversal process involving the conversion of α,β-unsaturated carbonyl compounds into β-acylvinyl anion equivalents. However, the former procedures are sometimes inadequate and the requisite organocuprates are difficult to obtain.[2] In the case of enones, very efficient and practical β-functionalization methods utilizing the phosphoniosilylation process, one of the latter processes, have been previously developed by Kozikowski, Kim and Lee (Scheme 1).[3-5] Recently, we have reported that such procedure can also be employed to α,β-unsaturated lactones and esters by effecting β-alkylation, β-hydroxyalkylation, β-conjugate addition of them, and β-sulfenylation (Scheme 2).[6] The feasible formation of ylides **3** from phosphoniosilylation products of α,β-unsaturated lactones and esters by using lithium diisopropylamide (LDA) as a base was the key to the success in these β-functionalizations. Encouraged by



Scheme 1



Scheme 2

†Dedicated to Professor Yong Hae Kim for his distinguished achievements in organic chemistry.

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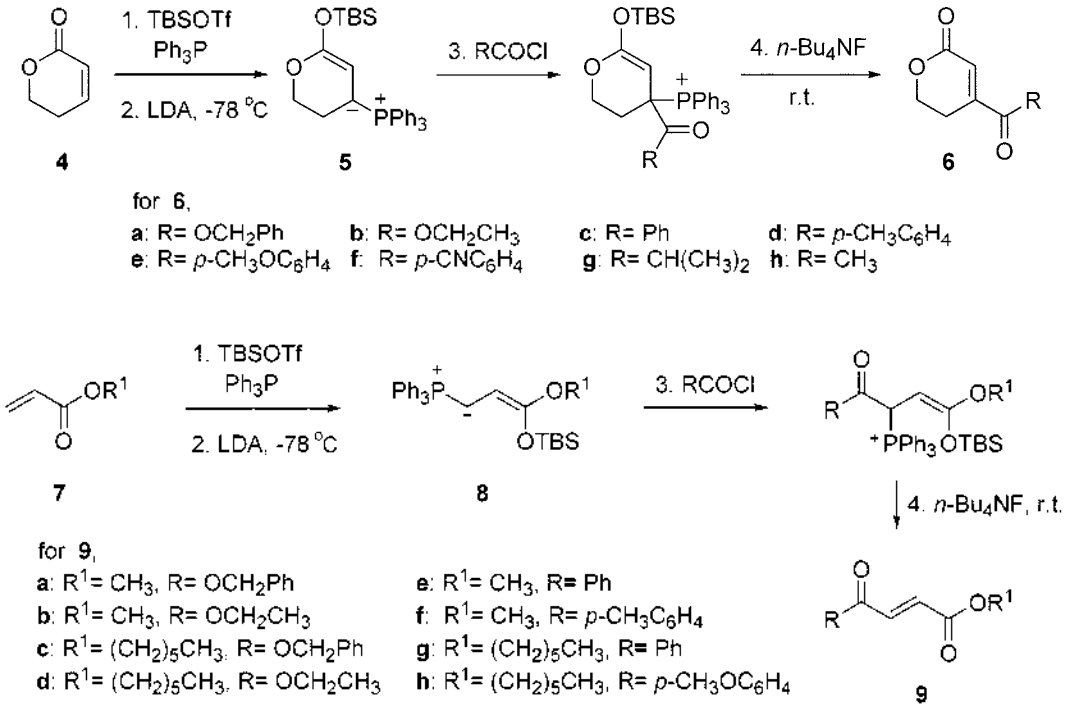


Scheme 3

these results, we have investigated the possibility of β-alkoxycarbonylation and β-acylation of α,β-unsaturated lactones and esters. Herein, we now wish to report efficient β-alkoxycarbonylation and β-acylation of α,β-unsaturated lactones and esters.

Kim has demonstrated that alkoxycarbonylation and acylation of enones at the β-position can be achieved by the reaction of ylides **2**, derived from the phosphoniosilylation products **1** of enones, with alkyl chloroformates and acid halides in good yields.[4b] Since various β-functionalization, namely, β-alkylation, β-hydroxyalkylation, β-conjugate addition and β-sulfenylation of α,β-unsaturated lactones and esters could be executed by the phosphoniosilylation process,[6] we envisaged that β-alkoxycarbonylation and β-acylation of ylides **5** and **8** can also be achieved. Thus, we have examined the reaction of ylides **5** and **8**, derived from phosphoniosilylation products of lactone **4** and ester **7**, with alkyl chloroformates and acid halides, as shown in Scheme 3.

Upon examining various reaction conditions with 5,6-dihydro-2*H*-pyran-2-one **4** and benzyl chloroformate as model unsaturated lactone and alkoxycarbonyl chloride, respectively, it was found that efficient β-alkoxycarbonylation of **4** could be accomplished by the reaction of ylide **5** with benzyl chloroformate at −78 °C and subsequent treatment with tetra-*n*-butylammonium fluoride (TBAF) at −78 °C to rt in the same pot. The results of β-alkoxycarbonylation of α,β-unsaturated lactones and esters, employing these reaction conditions, are shown in Table 1. This process works well with alkyl chloroformates in six-membered lactone **4** series (entries 1 and 2), and α,β-unsaturated esters **7** series (entries 3-6) in which products were obtained in moderate to good yields (57-65%). The success in β-alkoxycarbonylation of α,β-unsaturated lactones and esters prompted us to investigate the possibility of β-acylation of α,β-unsaturated lactones and esters. By reacting ylides **5** and **8** with acid chlorides instead of alkyl chloroformates in the same process, the acylation could also be achieved. The results are given in Table 2. With aromatic acid chlorides (entries 1-4, 7-10), the yields attending this procedure were much better than those reported in enone series,[4b] although relatively low in some cases (entries 4, 7, and 9). With aliphatic acid chlorides (entries 5 and 6), the yields were generally poor as indicated in the reaction with isobutyric chloride (30%, entry 5), although better than those reported in enone series.[4b] With acetyl chloride, no significant amounts of desired product were obtained. The poor yields in these cases were assumed to be due in part to competitive acylation by diisopropylamine produced during ylide generation by LDA. If the use of amide bases is avoided, such competitive acylation would not be a problem. However, at the present time, the use of amide base was inescapable, since other bases such as alkyllithiums and metal hydrides are not suitable for the generation of ylides **5** and **8**. Therefore, attempts to improve the yields were made, mainly based on the use of other acylating agents such as acetyl bromide, acetyl imidazole and isobutyryl imidazole, acetyl cyanide, and 2,4-dinitrophenyl acetate (and isobutyrate). However, these attempts were not fruitful. No significant amounts of desired products were obtained with these acylating agents except for acetyl cyanide (entry 6).

The results illustrate the efficiency, applicability and limitation of the present method. Especially, it is noteworthy that these overall conversions can be accomplished by four-

Table 1. β-Alkoxycarbonylation of α,β-Unsaturated Lactones (Esters)

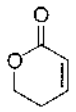
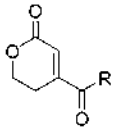
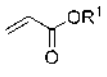
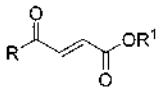
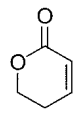
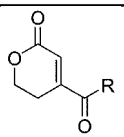
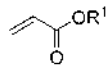
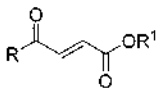
Entry	Unsaturated lactone (ester)	RCOCl	Product	Yield (%)
				
1	〃	R = OCH_2Ph	**6a**	58
2	〃	R = OCH_2CH_3	**6b**	65
				
3	R' = CH_3	R = OCH_2Ph	**9a**	59
4	〃	R = OCH_2CH_3	**9b**	63
5	R' = $(CH_2)_5CH_3$	R = OCH_2Ph	**9c**	61
6	〃	R = OCH_2CH_3	**9d**	57

Table 2. β-Acylation of α,β-Unsaturated Lactones (Esters)

Entry	Unsaturated lactone (ester)	RCOCl	Product	Yield (%)
				
1	〃	R = Ph	**6c**	73
2	〃	R = *p*-$CH_3C_6H_4$	**6d**	67
3	〃	R = *p*-$CH_3OC_6H_4$	**6e**	78
4	〃	R = *p*-CNC_6H_4	**6f**	28
5	〃	R = $CH(CH_3)_2$	**6g**	30
6	〃	R = CH_3	**6h**	22[a]
				
7	R = CH_3	R = Ph	**9e**	39
8	〃	R = *p*-$CH_3C_6H_4$	**9f**	61
9	R = $(CH_2)_5CH_3$	R = Ph	**9g**	39
10	〃	R = *p*-$CH_3OC_6H_4$	**9h**	56

[a]Cyano group was used as a leaving group instead of chloride group.

step one pot procedure from α,β-unsaturated lactones and esters without any isolation of the intermediates.

In summary, we have shown that the phosphoniosilylation of α,β-unsaturated latctones and esters, in combination with alkoxycarbonylation and acylation reaction, provides a convinient tool for β-alkoxycarbonylation and β-acylation of α,β-unsaturated lactones and esters.

Experimental Section

The general procedure for β-alkoxycarbonylation and β-acylation of α,β-unsaturated lactones (esters). To a solution of triphenylphosphine (292 mg, 1.10 mmol) in tetrahydrofuran (3.0 mL) was added TBSOTf (263 μL, 1.10 mmol) and 5,6-dihydro-2*H*-pyran-2-one (86.1 μL, 1.00 mmol). After being stirred at room temperature for 1.5 h, the reaction mixture was cooled to −78 °C and LDA, prepared from diisopropylamine (252 μL, 1.80 mmol) and *n*-butyllithium (1.06 mL of 1.41 *M* solution in hexanes, 1.50 mmol) in THF, was added dropwise to give a dark brown-colored solution. The mixture was stirred at −78 °C for 1 h and benzoyl chloride (174 μL, 1.50 mmol) was added to the ylide solution. After the reaction mixture was stirred for 1 h, TBAF (2.0 mL of 1 *M* solution in THF, 2.0 mmol) was added. After being warmed to room temperature, the reaction mixture was stirred for 1 h. The extractive work-up and flash column chromatography gave 4-benzoyl-5,6-dihydro-pyran-2-one (**6c**) (147 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 6.84 Hz, 2H), 7.65 (t, J = 7.32 Hz, 1H), 7.52 (t, J = 7.81 Hz, 2H), 6.36 (s, 1H), 4.56 (t, J = 6.35 Hz, 2H), 2.85 (t, J = 6.35 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.3, 163.7, 151.3, 135.1, 133.8, 129.5, 128.8, 125.7, 66.8, 24.0. IR (neat) 3063, 2976, 2884, 1726, 1711, 1655, 1593, 1471, 1081 cm^{-1}.

6-Oxo-3,6-dihydro-2*H*-pyran-4-carboxylic acid phenyl ester (6a). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.34 (m, 5H), 6.79 (s, 1H), 5.28 (s, 2H), 4.44 (t, J = 5.86 Hz, 2H), 2.71 (t, J = 5.86 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 163.3, 145.2, 134.8, 128.7, 128.7, 128.4, 126.1, 67.7, 66.5, 23.5. IR (neat) 3042, 2971, 2904, 1726, 1706, 1660, 1639, 1480, 1096 cm^{-1}.

6-Oxo-3,6-dihydro-2*H*-pyran-4-carboxylic acid ethyl ester (6b). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (s, 1H), 4.45 (t, J = 6.10 Hz, 2H), 4.31 (q, J = 7.32 Hz, 2H), 2.71 (s, J = 6.10 Hz, 2H), 1.35 (t, J = 7.32 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 163.5, 145.5, 125.7, 66.5, 62.1, 23.5, 14.0. IR (neat) 3094, 2996, 2914, 1721, 1703, 1655, 1096 cm^{-1}.

But-2-enedioic acid benzyl ester methyl ester (9a). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.34 (m, 5H), 6.91 (s, 2H), 5.25 (s, 2H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 166.0, 136.6, 136.6, 133.9, 132.1, 128.9, 128.8, 52.3, IR (neat) 3047, 2966, 2940, 2889, 2863, 1731, 1701, 1647, 1445, 1163, 989 cm^{-1}.

But-2-enedioic acid ethyl ester methyl ester (9b). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (s, 2H), 4.27 (q, J = 7.32 Hz, 2H), 3.82 (s, 3H), 1.33 (t, J = 7.32 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 164.9, 133.9, 133.1, 61.3, 52.3, 14.1. IR (neat) 2986, 2940, 2858, 1731, 1690, 1655, 1163, 989 cm^{-1}.

But-2-enedioic acid benzyl ester hexyl ester (9c). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.35 (m, 5H), 6.90 (s, 2H), 5.25 (s, 2H), 4.20 (t, J = 6.84 Hz, 2H), 1.71-1.65 (m, 2H), 1.40-1.35 (m, 2H), 1.34-1.29(m, 4H), 0.90 (t, J = 6.84 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 164.8, 135.2, 134.1, 133.2, 128.6, 128.5, 128.3, 67.1, 65.5, 31.4, 28.4, 25.5, 22.5, 14.0. IR (neat) 3037, 2966, 2935, 2868, 1726, 1696, 1655, 1460, 1158, 989 cm^{-1}.

But-2-enedioic acid ethyl ester hexyl ester (9d). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (s, 2H), 4.27 (q, J = 6.84

Hz, 2H), 4.20 (t, J = 6.84 Hz, 2H), 1.71-1.66 (m, 2H), 1.41-1.35 (m, 2H), 1.35-1.28 (m, 7H), 0.91 (t, J = 6.84 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 165.0, 133.7, 133.6, 65.5, 61.3, 31.4, 28.5, 25.5, 22.5, 14.1, 14.0. IR (neat) 3069, 2976, 2940, 2863, 1731, 1696, 1657, 1163, 989 cm^{-1}.

4-(4-Methylbenzoyl)-5,6-dihydropyran-2-one (6d). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 6.35 Hz, 2H), 7.32 (d, J = 7.81 Hz, 2H), 6.34 (s, 1H), 4.56 (t, J = 6.11 Hz, 2H), 2.84 (t, J = 6.11 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.9, 163.8, 151.7, 145.0, 132.5, 129.8, 129.5, 125.0, 66.8, 24.2, 21.7. IR (neat) 3063, 2955, 2863, 1711, 1696, 1650, 1563, 1450, 1173, 823 cm^{-1}.

4-(4-Methoxybenzoyl)-5,6-dihydropyran-2-one (6e). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 8.79 Hz, 2H), 6.99 (d, J = 9.28 Hz, 2H), 6.30 (s, 1H), 4.56 (t, J = 6.35 Hz, 2H), 3.91 (s, 3H), 2.83 (t, J = 6.35 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6, 164.4, 163.8, 152.1, 132.1, 127.7, 124.1, 114.2, 66.8, 55.6, 24.4. IR (neat) 3073, 2955, 2832, 1726, 1710, 1650, 1562, 1465, 1264, 1034, 1173, 843 cm^{-1}.

4-(6-Oxo-3,6-dihydro-2*H*-pyran-4-carbonyl)benzonitrile (6f). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.30 Hz, 2H), 7.83 (d, J = 8.30 Hz, 2H), 6.36 (s, 1H), 4.58 (t, J = 6.10 Hz, 2H), 2.86 (t, J = 6.10 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.0, 163.1, 150.1, 138.6, 132.6, 129.8, 127.1, 117.5, 117.0, 66.7, 23.6. IR (thin film) 3067, 2950, 2904, 2244, 1726, 1675, 1650, 1603, 1462, 1081, 866 cm^{-1}.

4-Isobutyryl-5,6-dihydropyran-2-one (6g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.62 (s, 1H), 4.46 (t, J = 6.35 Hz, 2H), 3.29-3.22 (m, 1H), 2.66 (t, J = 6.35 Hz, 2H), 1.17 (d, J = 6.84 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7, 164.3, 150.1, 124.1, 66.8, 35.3, 22.6, 18.8, 18.7. IR (neat) 3083, 2986, 2945, 2884, 1731, 1690, 1629, 1199 cm^{-1}.

4-Acetyl-5,6-dihydropyran-2-one (6h). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64 (s, 1H), 4.46 (t, J = 6.10 Hz, 2H), 2.66 (t, J = 6.10 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 164.2, 150.9, 125.3, 66.8, 25.7, 22.1. IR (neat) 3080 (C=C-H), 2976, 2935, 2879, 1711, 1690, 1663, 1096 cm^{-1}.

4-Oxo-4-phenylbut-2-enoic acid methyl ester (9e). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 7.32 Hz, 2H), 7.94 (d, J = 15.6 Hz, 1H), 7.64 (t, J = 7.32 Hz, 1H), 7.53 (t, J = 7.32 Hz, 2H), 6.91 (d, J = 15.6 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 164.7, 135.2, 133.6, 133.5, 128.6, 128.5, 128.3, 67.1, 52.3. IR (neat) 3078, 2960, 2935, 2858, 1726, 1680, 1660, 1608, 1450, 1178, 988 cm^{-1}.

4-Oxo-4-*p*-tolylbut-2-enoic acid methyl ester (9f). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 15.6 Hz, 1H), 7.92 (d, J = 8.30 Hz, 2H), 7.32 (d, J = 8.30 Hz, 2H), 6.89 (d, J = 15.6 Hz, 1H), 3.86 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 166.1, 145.0, 136.8, 134.1, 131.7, 129.6, 129.0, 52.3, 21.8. IR (neat) 3041, 2960, 2935, 2863, 1731, 1675, 1660, 1608, 1450, 1173, 984, 846 cm^{-1}.

4-Oxo-4-phenylbut-2-enoic acid hexyl ester (9g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 7.33 Hz, 2H), 7.91 (d, J = 15.6 Hz, 1H), 7.64 (t, J = 7.33 Hz, 1H), 7.53 (t, J = 7.81 Hz, 2H), 6.90 (d, J = 15.6 Hz, 1H), 4.25 (t, J = 6.84 Hz, 2H), 1.75-1.67 (m, 2H), 1.44-1.38 (m, 2H), 1.37-1.30 (m, 4H), 0.91 (t, J = 6.84 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.6, 165.7, 136.6, 136.4, 133.8, 132.6, 128.9, 128.8, 65.6, 31.4, 28.5, 25.5, 22.5, 14.0. IR (neat) 3068, 2966, 2935, 2863, 1726, 1680, 1655, 1603, 1455, 1184, 989 cm^{-1}.

4-(4-Methoxyphenyl)-4-oxobut-2-enoic acid hexyl ester (9h). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 9.03 Hz, 2H), 7.92 (d, J = 15.6 Hz, 1H), 6.99 (t, J = 9.03 Hz, 2H), 6.88 (d, J = 15.6 Hz, 1H), 4.24 (t, J = 6.84 Hz, 2H), 3.90 (s, 3H), 1.74-1.69 (m, 2H), 1.44-1.39 (m, 2H), 1.38-1.31 (m, 4H), 0.91 (t, J = 7.08 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.7, 165.8, 164.2, 136.5, 131.9, 131.3, 129.7, 114.1, 65.5, 55.6, 31.4, 28.5, 25.6, 22.5, 14.0. IR (neat) 3073, 2971, 2940, 2863, 1731, 1675, 1657, 1603, 1470, 1265, 1173, 1040, 989, 845 cm^{-1}.

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References

1. (a) Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley-Interscience: New York, 1980. (b) Taylor, R. J. K. *Organocopper Reagents*; Oxford University Press: Oxford, 1994.
2. (a) Taylor, R. J. K. *Synthesis* **1985**, 364. (b) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1992. (c) Hulce, M. *Org. React.* **1990**, *38*, 225. (d) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.
3. (a) Kozikowski, A. P.; Jung, S. H. *J. Org. Chem.* **1986**, *51*, 3400. (b) Kozikowski, A. P.; Jung, S. H. *Tetrahedron Lett.* **1986**, *27*, 3227.
4. (a) Kim, S.; Lee, P. H. *Tetrahedron Lett.* **1988**, *29*, 5413. (b) Kim, S.; Lee, P. H.; Kim, S. S.; *Bull. Korean Chem. Soc.* **1989**, *10*, 218. (c) Kim, S.; Kim, Y. G.; Park, J. H. *Tetrahedron Lett.* **1991**, *32*, 2043. (d) Kim, S.; Park, J. H.; Kim, Y. G.; Lee, J. M. *J. Chem. Soc., Chem. Commun.* **1993**, 1188. (e) Kim, S.; Lee, B. S.; Park, J. H. *Bull. Korean Chem. Soc.* **1993**, *14*, 654.
5. (a) Lee, P. H.; Kim, S. *Bull. Korean Chem. Soc.* **1992**, *13*, 580. (b) Lee, P. H.; Cho, M.; Han, I.-S.; Kim, S. *Tetrahedron Lett.* **1999**, *40*, 6975.
6. (a) Jung, S. H.; Kim, J. H. *Bull. Korean Chem. Soc.* **2002**, *23*, 365. (b) Jung, S. H.; Kim, J. H. *Bull. Korean Chem. Soc.* **2002**, *23*, 1375. (c) Jung, S. H.; Kim, J. H.; Kim, H. J. *Bull. Korean Chem. Soc.* **2004**, *25*, 136.