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SYNTHESIS OF ENOL ESTERS AND ENOL LACTONES VIA PALLADIUM-CATALYZED CARBONYLATION OF ARYL AND ALKENYL HALIDES

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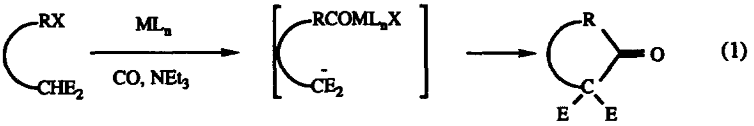
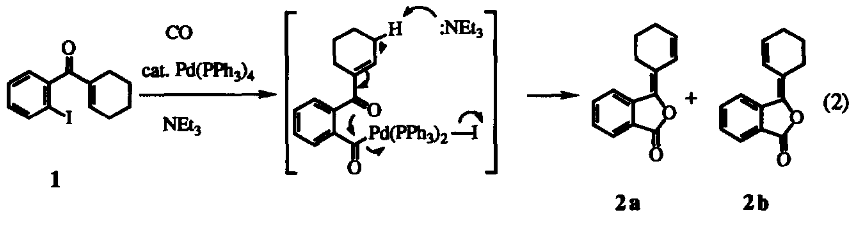
SUMMARY: Acylpalladium species derivable via oxidative addition of a Pd-phosphine complex with aryl and alkenyl iodides and CO insertion can react, either intramolecularly or intermolecularly, with enolates generated in situ to give the corresponding enol esters and enol lactones.

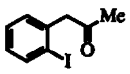
We have recently reported that acylpalladium derivatives generated in situ via oxidative addition-migratory insertion can be intramolecularly trapped by certain in-situ-generated enolates at the C terminus to give five- through seven-membered ketones[2] (eq. 1). In these cases the corresponding O-enolate trapping, i.e., trapping at the O terminus, would have produced seven- through nine-membered enol lactones whose formation is thought to be comparatively unfavorable. In fact, we earlier encountered one isolated example of trapping by O-enolate in an unwanted conversion of 1 into a 1:1 mixture of 2a and 2b, which was thought to proceed as shown in eq. 2.[3,4]



E= anion-stabilizing C and/or S groups



We now report that the Pd-catalyzed carbonylation of alkenyl and aryl halides in the presence of suitable enolate precursors may proceed via O-enolate trapping both intramolecularly and intermolecularly. Evaluation of the previous results summarized in eqs. 1 and 2 suggested to us that O-enolate trapping might favorably compete with C-enolate trapping in cases where formation of five- or six-membered enol lactones is feasible. To test the possibility we prepared 3-6.[5] Their carbonylation with CO (600 psi), NEt_3 (1.5-2 equiv), and 5 mol% of $Cl_2Pd(PPh_3)_2$ or $Pd(PPh_3)_4$ in THF-MeCN at 100°C overnight produced the corresponding enol lactones 7-10[6] in the yields indicated in parentheses.[7] Examination of the reaction mixtures failed to detect any of the possible C-enolate trapping products, such as 11 and 12 in the reaction of 3. The preferential formation of 10 rather than 13 from 6 indicates that, under comparable situations, O-enolate trapping must be favored over C-enolate trapping.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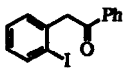
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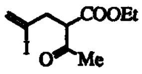
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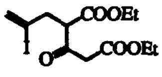
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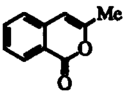
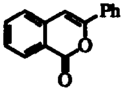
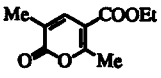
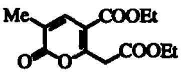
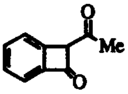

7 (84 % GLC, 77 % isol.)


8 (93 % NMR, 89 % isol.)


9 (76 % GLC, 56 % isol.)


10 (40 % GLC)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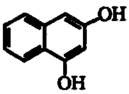
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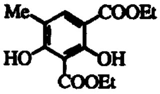
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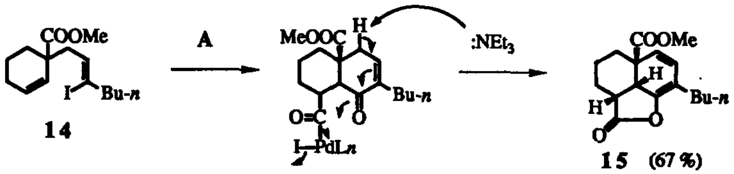
The results presented above provide a ready explanation for the initially puzzling but highly efficient cyclization of 14 to give 15 vis-a-vis the previously reported corresponding reaction of 16 to give 17.[8] It is noteworthy that three carbon-carbon and two carbon-oxygen bonds are formed in this reaction, which most probably proceeds as shown in eq. 3. The spectral properties of 15 are as follows, and its stereochemistry has been established by ^{1}H 2D NOESY NMR spectroscopy: IR(neat) 1815 (s), 1760 (sh, m), 1735 (s), 1710 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, *J* = 7 Hz, 3H), 1.1-1.5 (m, 6H), 1.6-1.75 (m, 2H), 2.0-2.3 (m, 4H), 2.95 (dt, *J* = 12 and 7 Hz, 1H), 3.64 (br d, *J* = 8 Hz, 1H), 3.79 (s, 3H), 5.69 (br d, *J* = 10 Hz, 1H), 5.86 (d, *J* = 10 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.90, 20.56, 22.26, 26.22, 27.21, 30.34, 31.39, 37.92, 38.29, 47.35, 52.80, 109.63, 124,82, 126.82, 145.72, 175.42, 176.86; High resolution MS calcd, 290.1518; found, 290.1518.



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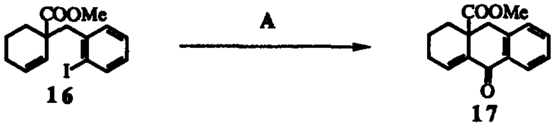
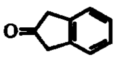


(4)

A = CO (600 psi), 3-5 % $Pd(PPh_3)_4$, NEt_3 (1.5-2 equiv.), THF-MeCN, 100 °C, overnight.

The favorable results presented above prompted us to investigate the feasibility of intermolecular O-enolate trapping. To this end, 18-20 were chosen as enolate sources. Their reaction with PhI under the standard carbonylation conditions as in the previous cases indeed produced 21-23[9] in the yields indicated in parentheses. On the other hand, the corresponding reactions of cyclohexanone, acetophenone, and 2-phenylacetophenone failed to yield the desired O-enolate trapping products under comparable conditions.[10] The reaction of 19 with (E)-β-iodostyrene and (E)-1-iodo-1-hexene in the presence of CO (600 psi), NEt_3 (1.5 equiv), and 5 mol% of $Cl_2Pd(PPh_3)_2$ at 100°C produced 24[11] and 25[12] in 56 and 76% isolated yields, respectively. In the case of 24 the intermediary formation of 26 was observed. Since the reaction of 19 with cinnamoyl chloride in the absence of a palladium catalyst does produce 26 which is gradually converted to 24,[13] the cyclization step is not likely to be catalyzed by a Pd complex even in its presence.



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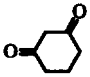

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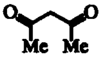

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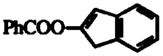
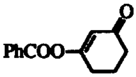
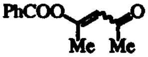


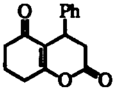
21 (53 % GLC)



22 (63 % GLC 56 % isol.)



23 (25 % isol E/Z = 1)



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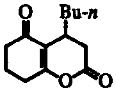

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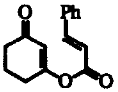

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REFERENCES AND NOTES

(1) On leave from NKK Corporation, Japan.

(2) Negishi, E.; Zhang, Y.; Shimoyama, I.; Wu, G. J. Am. Chem. Soc. 1989, 111, 8018.

(3) Negishi, E.; Tour, J. M. Tetrahedron Lett. 1986, 27, 4869.

(4) For a related O-enolate trapping, see Roberto, D.; Catellani, M.; Chiusoli, G. P. Tetrahedron Lett. 1988, 29, 2115.

(5) o-Iodobenzyl bromide was converted to 3 and 4 via its reaction with the ethoxyethyl-protected cyanohydrin derivatives of acetaldehyde and benzaldehyde, respectively, under the influence of LDA or NaH. Treatment of propargyl alcohol with Me_3SiI followed by bromination with NBS-Me_2S provided 2-iodo-3-bromopropene. Its reaction with ethyl acetoacetate and diethyl acetonedicarboxylate under the influence of NaH gave 5 and 6, respectively.

(6) 7 and 8 [Hauser, F. M.; Baghdanov, V. M. *J. Org. Chem.* 1988, *53*, 4676]. 9: IR (neat) 1738 (s), 1709 (s), 1632 (s), 1378 (s), 1261 (s), 1161 (s), 1083 (s), 1025 (s), 778 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.37 (s, *J* = 7 Hz, 3H), 2.11 (s, 3H), 2.63 (s, 3H), 4.33 (q, *J* = 7 Hz, 2H), 7.63 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.32, 16.29, 20.05, 61.50, 109.54, 122.12, 140.09, 162.77, 164.74, 168.43; High resolution MS calcd for $C_{10}H_{12}O_4$ 196.0736; found 196.0736. 10: IR (neat) 1745 (s), 1718 (s), 1084 (s), 1029 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.27 (t, *J* = 7 Hz, 3H), 1.35 (t, *J* = 7 Hz, 3H), 2.14 (d, *J* = 1.3 Hz, 3H), 4.03 (s, 2H), 4.20 (q, *J* = 7 Hz, 2H), 4.31 (q, *J* = 7 Hz, 2H), 7.66 (d, *J* = 1.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.19, 16.49, 39.47, 61.83, 111.11, 123.91, 139.53, 162.21, 163.03, 164.16, 168.11; High resolution MS calcd for $C_{13}H_{16}O_6$ 268.0947; found 268.0945.

(7) Typically, 4 (0.32 g, 1 mmol), NEt_3 (0.15 g, 1.5 mmol), MeCN (2 mL), THF (0.5 mL) and $Cl_2Pd(PPh_3)_2$ (0.035 g, 0.05 mmol) were placed in an autoclave, and CO (600 psi) was introduced. After 18 h at 100°C, the mixture was worked up with ether and aqueous $NaHCO_3$, washed with brine and dried over $MgSO_4$. Column chromatography (ether/hexane = 1/2) provided 0.20 g (89%, 93% by NMR) of 8.

(8) Zhang, Y.; O'Connor, B.; Negishi, E. *J. Org. Chem.* 1988, *53*, 5588.

(9) 21: IR (Nujol) 1739 (s), 1450 (s), 1281 (m), 1060 (m), 850 (s), 749 (s), 712 (s), 700 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.70 (s, 2H), 6.77 (s, 1H), 7.1-8.2 (m, 9H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 38.04, 115.51, 121.40, 123.79, 124.78, 127.07, 128.96, 129.71, 130.43, 134.00, 137.71, 143.30, 156.33, 164.35; High resolution MS calcd for $C_{16}H_{12}O_2$ 236.0837; found 236.0836. 22 [Goldblum, A.; Mechoulam, R. *J. Chem. Soc. Perkin Trans. I* 1977, 1889]. 23 [Larkin, J.; Murray, M. G.; Nonhebel, D. C.; Mitchell, A. D. *J. Chem. Soc. Perkin Trans. I* 1976, 380].

(10) See, however, Drent, E. *Eur. Pat. Appl. EP* 218282 and 218283 (*Chem. Abstr.* 1987, *107*, 154886h and 154887j).

(11) Margaretha, P. *Tetrahedron Lett.* 1970, 1449.

(12) 25: IR (neat) 1790 (s), 1653 (s), 1381 (s), 1185 (s), 1120 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.87 (t, *J* = 7 Hz, 3H), 1.1-1.5 (m, 6H), 2.0-2.2 (m, 2H), 2.4-2.8 (m, 6H), 2.9-3.1 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.92, 20.75, 22.62, 27.31, 28.20, 28.59, 33.32, 33.63, 36.85, 119.14, 167.25, 167.34, 197.40; High resolution MS calcd for $C_{13}H_{18}O_3$ 222.1256; found 222.1259.

(13) For a report of a similar cyclization reaction which curiously describes an unsuccessful attempt to cyclize a similar cinnamoyl derivative, see Monroe, B. M. *J. Heterocyclic Chem.* 1969, *6*, 917.

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