

mass) Calcd for  $C_{15}H_{24}O$ : 220.1827. Found: 220.1827.

**Preparation of the  $^{18}O$  Analogue of 4.** To a solution containing ketal-ketone D (884 mg) in 2 mL of dry THF was added 1  $\mu$ L of concentrated HCl and 67 mg of  $H_2^{18}O$  (99%, Stohler). The mixture was stirred for 4 h, quenched by adding 30 mL of  $CH_2Cl_2$ , washed with 10%  $NaHCO_3$  and brine, and dried over  $K_2CO_3$ . Mass spectral analysis showed only 12%  $^{18}O$  incorporation so the procedure was repeated and allowed to stir overnight. Removal of solvent after the same workup procedure gave 788 mg (89%) of the ketone. Mass spectral analysis showed 51%  $^{18}O$  incorporation.  $^{13}C$  NMR analysis of the carbonyl peak at 209.7 ppm showed two lines with the upfield resonance shifted by 0.052 ppm also showing 51% incorporation.

This ketone was then treated three times with  $(CH_3)_3S^+I^-$  in order to achieve an 89% yield of the diastereomeric mixture of epoxide E. Progress of this reaction was monitored by gas chromatography. High-resolution  $^{13}C$  NMR spectroscopy on the epoxide carbons of the major diastereomer of E revealed it to have  $^{13}C^{18}O$  satellites at 0.044 and 0.034 ppm upfield of the normal  $^{13}C$  resonances at 56.3 and 54.2 ppm, respectively. Integration of these resonances indicated 50% labeling of  $^{18}O$  still existed.

Epoxide E- $^{18}O$  was subsequently treated with 5 N HCl, as noted above for the unlabeled substrates, to yield 4- $^{18}O$  in 70%. Mass spectral analysis of the furan showed 50%  $^{18}O$  incorporation.  $^{13}C$  NMR analysis showed the peaks at 151.9 and 137.0 ppm to give two lines each. The isotope peak for the 151.9 ppm carbon was shifted 0.041 ppm upfield, while the isotope peak for the 137.0 ppm resonance was shifted 0.036 ppm.

**Oxidation of Furan 4.** To a stirred solution of furan 4 (100 mg) in 10 mL of  $CH_2Cl_2$  at 0  $^\circ C$  was added dropwise 2 equiv of mCPBA in 5 mL of  $CH_2Cl_2$ . After being stirred for 15 min, the reaction was washed with 5%  $Na_2S_2O_3$ , 10%  $NaHCO_3$ , and brine and dried over  $K_2CO_3$ . Removal of solvent gave the keto lactone 5 in 70% yield: IR (neat) 1760, 1666, 1652  $cm^{-1}$ ;  $^1H$  (NMR) 7.6 (1 H, s), 2.8 (2 H, m), 2.5 (2 H, m), 1.78 (3 H, s), 1.1-1.6 (16 H, m) ppm;  $^{13}C$  NMR 202.1 (s), 169.9 (s), 138.5 (d), 120.1 (s), 43.4 (t), 34.2 (t), 29.6 (t), 27.2 (t), 26.7 (t), 26.2 (t), 26.0 (t), 25.8 (t), 24.4 (t), 22.9 (t), 14.9 (q), ppm; mass spectrum,  $m/e$  (relative intensity) 252 ( $M^+$ ), 224, 73 (100). Anal. (accurate mass) Calcd for  $C_{15}H_{24}O_3$ : 252.1719. Found: 252.1749.

**Oxidation of  $^{18}O$  Analogue of 4.** In an analogous experiment, the  $^{18}O$ -labeled 4 was oxidized and separated from its reaction mixture as noted above for compound 4. Mass spectral analysis of the product showed 50%  $^{18}O$  incorporation. A  $^{13}C$  NMR spectrum of the product 5- $^{18}O$  showed two lines at 169.9 ppm with the upfield isotope resonance shifted by 0.043 ppm which corroborated the 50%  $^{18}O$  incorporation. Similar analysis of the vinyl carbon at 138.5 ppm failed to show an isotope resonance.

**Acknowledgment.** We wish to express their gratitude for financial support of this research by Montana State University and the National Science Foundation Grants CHE 7826160 and CHE 8115565.

**Registry No.** 4, 66090-18-4; 4- $^{18}O$ , 93943-14-7; 5, 93943-11-4; 5- $^{18}O$ , 93943-15-8; A, 4017-60-1; B, 93943-07-8; C, 93943-08-9; D, 93943-09-0; D- $^{18}O$ , 93943-12-5; E, 93943-10-3; E- $^{18}O$ , 93943-13-6; MCPBA, 937-14-4;  $(EtO)_2CO$ , 105-58-8;  $H_2^{18}O$ , 14314-42-2; MeLi, 917-54-4;  $Me_3S^+I^-$ , 2181-42-2; cyclododecanone, 830-13-7.

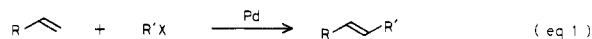
### Facile Synthesis of $\beta$ -Aryl- or $\beta$ -Alkenyl- $\beta$ -methyl- $\alpha,\beta$ -unsaturated Carbonyl Compounds by Palladium-Catalyzed Reaction of 1,2-Dien-4-ols with Aryl or Alkenyl Halides

Isao Shimizu, Teruo Sugiura, and Jiro Tsuji\*

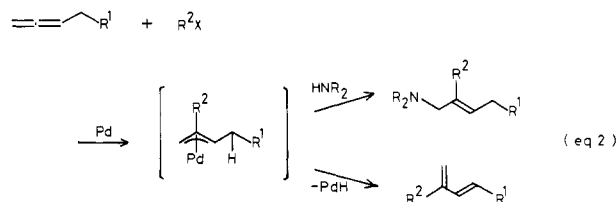
Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

Received July 10, 1984

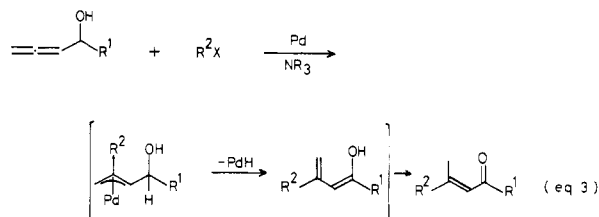
Catalytic arylation or alkenylation of olefins by way of olefin insertion to aryl- or alkenylpalladium known as the Heck reaction is a useful carbon-carbon bond forming reaction (eq 1).<sup>1</sup> We have found that phenyl- or alke-



nylpalladium complexes, formed in situ from phenyl or alkenyl halides and a Pd(0) complex, reacts with 1,2-dienes regioselectively to form (2-phenyl- or (2-alkenyl- $\pi$ -allyl)-palladium intermediates which undergo amination to give 2-phenyl or 2-alkenyl allylic amines (eq 2).<sup>2</sup> In the reaction



of halides with 1,2-dienes in the absence of nucleophiles, 1,3-dienes are formed by  $\beta$ -elimination of PdH from ( $\pi$ -allyl)palladium complexes. In this paper, we report the facile synthesis of  $\beta$ -methyl- $\alpha,\beta$ -unsaturated ketones or aldehydes by palladium-catalyzed reaction of 1,2-dien-4-ols with aryl or alkenyl halides in the presence of tertiary amines (eq 3).<sup>3</sup>



Reaction of 2,3-butadien-1-ol (**1a**) with iodobenzene was carried out under various conditions in the presence of *N*-methylpyrrolidine or triethylamine. As shown in Table I, 3-methylcinnamaldehydes were obtained as *E/Z* mixtures in good yields by using 1,2-bis(diphenylphosphino)ethane (dppe) as a ligand of palladium in  $Me_2SO$  or  $CH_3CN$ . Dioxane and toluene are not good solvents for this reaction. 4-Phenyl- and 4-isobutyl-1,2-butadien-4-ol (**1b** or **1c**) also reacted with aryl halides at 110  $^\circ C$  to give the corresponding unsaturated ketones respectively.

This reaction is useful for the preparation of conjugated enones having other carbonyl groups in the same molecules, which are difficult to prepare by the well-known directed aldol condensation method.<sup>4</sup> The keto aldehyde **2f** was readily obtained in 61% yield by the reaction of *p*-bromobenzaldehyde with **1c** by using palladium-dppe catalyst. The aldehyde group was unaffected in this reaction. Reaction of alkenyl halide with **1** afforded conjugated dienyl carbonyl compounds in good yields. Thus, this method offers an efficient synthetic method for polyconjugated carbonyl compounds.<sup>5</sup>

### Experimental Section

**General Methods.** Dioxane and toluene were distilled from benzophenone ketyl.  $Me_2SO$  was distilled from  $CaH_2$  under reduced pressure.  $CH_3CN$  was distilled from  $P_2O_5$ .  $^1H$  NMR spectra were taken with a Hitachi R-24A (60 MHz) or a JEOL FX-90Q (90 MHz) spectrometer.  $^{13}C$  NMR spectra were recorded

(1) Heck, R. F. *Acc. Chem. Res.* 1979, 12, 146-151, *Org. React.* (N.Y.) 1982, 27, 345-390.

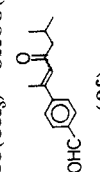
(2) Shimizu, I.; Tsuji, J. *Chem. Lett.* 1984, 233-236.

(3) For ketone synthesis by palladium-catalyzed reaction of allylic alcohols, see: (a) Chalk, A. J.; Magennis, S. A. *J. Org. Chem.* 1976, 41, 273-278. (b) Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* 1976, 41, 265-272. (c) Patel, B. A.; Heck, R. F. *J. Org. Chem.* 1978, 43, 3898-3903. (d) Kao, L.-C.; Stakem, F. G.; Patel, B. A.; Heck, R. F. *J. Org. Chem.* 1982, 47, 1267-1277.

(4) See: Mukaiyama, T. *Org. React.* (N.Y.) 1982, 28, 203-331.

(5) Stork, G.; Kraus, G. A. *J. Am. Chem. Soc.* 1976, 98, 2351-2352.

Table I. Palladium-Catalyzed Reactions of 1,2-Dien-4-ols and Organic Halides

| run | 1,2-dien-4-ol   | halide                               | ligand                     | amine                 | solvent                | temp, °C | time, h | product  | yield, %<br>(E/Z)     |
|-----|---|--------------------------------------|----------------------------|-----------------------|------------------------|----------|---------|--|-----------------------|
| 1   | $\text{CH}_2=\text{C}=\text{CHCH}_2\text{OH}$ (1a)              | PhI                                  | dppe                       | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 0.8     | $\text{PhC}(\text{CH}_3)=\text{CHCHO}$ (2a)  | 88 (7/3) <sup>b</sup> |
| 2   | 1a  | PhI                                  | dppe                       | NMP                   | $\text{Me}_2\text{SO}$ | 80       | 0.8     | 2a   | 76 (5/2) <sup>b</sup> |
| 3   | 1a  | PhI                                  | dppe                       | NMP                   | $\text{CH}_3\text{CN}$ | 81       | 5       | 2a   | 67 (5/3) <sup>b</sup> |
| 4   | 1a  | PhI                                  | dppe                       | NMP                   | dioxane                | 80       | 22      | 2a   | 33 (2/1) <sup>b</sup> |
| 5   | 1a  | PhI                                  | dppe                       | NMP                   | toluene                | 80       | 22      | 2a   | 17 (2/1) <sup>b</sup> |
| 6   | 1a  | PhI                                  | dppe                       | $\text{Et}_3\text{N}$ | $\text{CH}_3\text{CN}$ | 81       | 24      | 2a   | 69 (3/2) <sup>b</sup> |
| 7   | 1a  | PhI                                  | dppe                       | $\text{Et}_3\text{N}$ | $\text{Me}_2\text{SO}$ | 80       | 1       | 2a   | 57 (7/3) <sup>b</sup> |
| 8   | 1a  | PhI                                  | none                       | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 1.5     | 2a   | 54                    |
| 9   | 1a  | PhI                                  | $\text{PPPh}_3$            | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 0.2     | 2a   | 84 (5/3) <sup>b</sup> |
| 10  | 1a  | PhI                                  | $\text{P}(\text{o-tol})_3$ | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 0.2     | 2a   | 59 (5/3) <sup>b</sup> |
| 11  | 1a  | PhI                                  | $\text{P}(\text{OEt})_3$   | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 2       | 2a   | 40 (7/3) <sup>b</sup> |
| 12  | 1a  | PhI                                  | $\text{P}(\text{OPh})_3$   | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 1.5     | 2a   | 55 (8/3) <sup>b</sup> |
| 13  | 1a  | $\text{PhCH}=\text{CHBr}$            | dppe                       | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 4       | $\text{PhCH}=\text{CHC}(\text{CH}_3)=\text{CHCHO}$ (2b)                                | 69                    |
| 14  | $\text{CH}_2=\text{C}=\text{CHCH}(\text{OH})\text{Ph}$ (1b)     | PhI                                  | dppe                       | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 1.5     | (E)- $\text{PhC}(\text{CH}_3)=\text{CHCOPh}$ (2c)                                      | 65                    |
| 15  | 1b  | $\text{PhCH}=\text{CHBr}$            | dppe                       | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 1.5     | (E,E)- $\text{PhCH}=\text{CHC}(\text{CH}_3)=\text{CHCOPh}$ (2d)                        | 94 (2/1) <sup>c</sup> |
| 16  | $\text{CH}_2=\text{C}=\text{CHCH}(\text{OH})(i\text{-Bu})$ (1c) | $\text{PhCH}=\text{CHBr}$            | dppe                       | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 4       | $\text{PhCH}=\text{CHC}(\text{CH}_3)=\text{CHCO}(i\text{-Bu})$ (2e)                    | 77 (2/1) <sup>c</sup> |
| 17  | 1c  | $p\text{-BrC}_6\text{H}_4\text{CHO}$ | dppe                       | NMP                   | $\text{Me}_2\text{SO}$ | 110      | 3       |  (2f) | 61 (8/1) <sup>c</sup> |

<sup>a</sup> Isolated yield. <sup>b</sup> GLC analysis. <sup>c</sup> NMR analysis.

on a JEOL FX-90Q (22.5 MHz) instrument. Chemical shifts are given in  $\delta$  units relative to tetramethylsilane as an internal standard. Splitting patterns are designated with s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Infrared spectra were recorded on a JASCO IRA-2 spectrophotometer. 2,3-Butadien-1-ol (1a) and 1-phenyl-2,3-butadien-1-ol (1b) were prepared according to the literature.<sup>6</sup>

**6-Methyl-1,2-heptadien-4-ol (1c).** A solution of *n*-BuLi (1.6 M hexane solution, 44 mL, 70 mmol) was added to a solution of propargyl chloride (7.5 g, 0.1 mol) in dry ether at  $-78^\circ\text{C}$  for 20 min. Isovaleraldehyde (9.5 g, 0.11 mol) was added to the reaction mixture at  $-78^\circ\text{C}$ , and the resulting mixture was stirred at  $-40^\circ\text{C}$  for 2.5 h and then at room temperature for 3 h. A 3 N HCl solution was added to the mixture, and the mixture was extracted with ether. The extract was washed with saturated  $\text{NaHCO}_3$  solution and brine and dried over  $\text{MgSO}_4$ . Evaporation of the solvent under reduced pressure gave 1-chloro-6-methyl-2-heptyn-4-ol (15.1 g), which was used without further purification:  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  0.92 (d,  $J = 6$  Hz, 6 H,  $\text{CH}_3$ ), 1.05–2.30 (m, 3 H,  $-\text{CH}_2-$ ,  $\text{CH}(\text{Me})_2$ ), 4.11 (d,  $J = 2$  Hz, 2 H,  $\text{ClCH}_2$ ), 4.35 (m, 1 H,  $-\text{CH}(\text{OH})-$ ).

To a solution of crude 1-chloro-6-methyl-2-heptyn-4-ol (15.1 g) in dry ether (80 mL) was added a solution of  $\text{LiAlH}_4$  (3.8 g, 0.1 mol) in dry ether (80 mL) at such a rate as to keep gentle reflux of ether. The mixture was warmed for an additional 30 min under reflux and then cooled to  $0^\circ\text{C}$ . A 3 N HCl solution was added dropwise with vigorous stirring until refluxing of the ether had ceased. The ethereal layer was decanted and the white slurry was extracted with ether. The combined ethereal solution was washed with saturated  $\text{NaHCO}_3$  and brine and dried over  $\text{MgSO}_4$ . After evaporation of the solvent, the residue was distilled to give 6-methyl-1,2-heptadien-4-ol (1c) (7.3 g, 82.7% based on BuLi): bp  $68^\circ\text{C}$  (10 torr);  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  0.88 (d,  $J = 6$  Hz, 6 H,  $\text{CH}_3$ ), 1.32 (dd,  $J = 8, 6$  Hz, 1 H,  $-\text{CHH}-$ ), 1.39 (dd,  $J = 8, 6$  Hz, 1 H,  $-\text{CHH}-$ ), 1.52–2.05 (m, 1 H,  $\text{CH}(\text{Me})_2$ ), 3.80–4.35 (m, 1 H,  $-\text{CH}(\text{OH})-$ ), 4.60–4.85 (m, 2 H,  $\text{CH}_2=\text{C}=\text{C}=\text{C}$ ), 5.11 (dt,  $J = 5$  Hz, 7 Hz, 1 H,  $=\text{C}=\text{CH}-$ ); IR (neat) 3300, 1960, 845  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_8\text{H}_{14}\text{O}$ : C, 76.14; H, 11.18. Found: C, 76.02; H, 11.09.

**General Procedure for the Preparation of  $\beta$ -Methyl- $\alpha,\beta$ -unsaturated Carbonyl Compounds 2 by the Palladium-Catalyzed Reaction of Organic Halides with 1,2-Dien-4-ols.** Organic halides (1 mmol), 1,2-dien-4-ols 1 (1 mmol), and amine (1 mL) were added to a solution of  $\text{Pd}(\text{OAc})_2$  (11.2 mg, 0.05 mmol) and phosphine or phosphite [0.2 mmol except dppe (0.1 mmol)] in dry solvent (3 mL). The mixture was stirred at  $80$ – $110^\circ\text{C}$ , and the reaction was monitored by TLC. After the reaction was complete, the mixture was passed through a Florisil column. Purification by column chromatography on  $\text{SiO}_2$  with hexane-ether (5:1) gave enal or enone 2.

**3-Phenyl-2-butenal (2a):** IR (neat) 1660, 1480, 1450, 1390, 1150, 760, 690  $\text{cm}^{-1}$ . (E)-2a:  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  2.50 (s, 3 H,  $\text{CH}_3$ ), 6.20 (d,  $J = 7$  Hz, 1 H,  $=\text{CH}-$ ), 7.15–7.60 (m, 5 H, Ph), 10.08 (d,  $J = 7$  Hz, 1 H, CHO). (Z)-2a:  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  2.25 (s, 3 H,  $\text{CH}_3$ ), 5.89 (d,  $J = 8$  Hz, 1 H,  $=\text{CH}-$ ), 7.10–7.20 (m, 5 H, Ph), 9.20 (d,  $J = 8$  Hz, 1 H, CHO).

**3-Methyl-5-phenyl-2,4-pentadienal (2b):** IR (neat) 1660, 1500, 1450, 1390, 960, 750, 690  $\text{cm}^{-1}$ . (E,E)-2b:  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  2.25 (s, 3 H,  $\text{CH}_3$ ), 5.90 (d,  $J = 8$  Hz, 1 H,  $=\text{CHCHO}$ ), 6.65 (d,  $J = 18$  Hz, 1 H,  $=\text{CH}-$ ), 7.00 (d,  $J = 18$  Hz, 1 H,  $\text{PhCH}=\text{C}$ ), 7.00–7.65 (m, 5 H, Ph), 10.10 (d,  $J = 8$  Hz, 1 H, CHO). (Z,E)-2b:  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  2.05 (s, 3 H,  $\text{CH}_3$ ), 5.80 (d,  $J = 8$  Hz, 1 H,  $=\text{CHCHO}$ ), 6.79 (d,  $J = 17$  Hz, 1 H,  $=\text{CH}-$ ), 7.00–7.55 (m, 5 H, Ph), 7.77 (d,  $J = 17$  Hz, 1 H,  $\text{PhCH}=\text{C}$ ), 10.24 (d,  $J = 8$  Hz, 1 H, CHO).

**(E)-1,3-Diphenyl-2-buten-1-one (2c):** IR (neat) 1680, 1600, 1500, 1450, 760, 690  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  2.55 (s, 3 H,  $\text{CH}_3$ ), 7.05 (s, 1 H,  $=\text{CH}-$ ), 7.15–7.80 (m, 8 H, Ph, meta and para position H of benzoyl), 7.80–8.00 (m, 2 H, ortho position H of benzoyl).

**(E,E)-3-Methyl-1,5-diphenyl-2,4-pentadien-1-one (2d):** mp  $138.0$ – $138.5^\circ\text{C}$  (MeOH) (lit.<sup>7</sup> mp  $138$ – $139^\circ\text{C}$ ); IR (neat) 1640,

(6) Brandsma, L.; Verkrujssse, H. D. "Synthesis of Acetylenes, Allenes and Cumulenes"; Elsevier: Amsterdam, 1981.

(7) Huang, Y.; Shen, Y.; Xin, Y.; Ma, J. *Sci. Sin. (Engl. Ed.)* 1980, 23, 1396–1404.

1570, 970, 760, 700  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 60 MHz)  $\delta$  2.36 (s, 3 H,  $\text{CH}_3$ ), 6.80-7.60 (m, 11 H), 7.75-8.00 (m, 2 H).

**2,6-Dimethyl-8-phenyl-5,7-octadien-4-one (2e) (E,Z mixture):** IR (neat) 1680, 1580, 1500, 960, 750, 690  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  0.92 (d,  $J = 6$  Hz, 6 H,  $\text{CH}_3$ ), 1.87-2.50 (m, 6 H,  $=\text{C}(\text{CH}_3)-$ ,  $-\text{CH}(\text{Me})_2$ ,  $-\text{CH}_2-$ ), 5.90, 6.08 (s, 1 H,  $=\text{CH}-$  ( $Z$  and  $E$ )), 6.40-8.50 (m, 7 H, Ph,  $-\text{CH}=\text{CH}-$ ). Anal. Calcd for  $\text{C}_{18}\text{H}_{20}\text{O}$ : C, 84.16; H, 8.82. Found: C, 84.03; H, 8.84.

**6-Methyl-2-(4-formylphenyl)-2-hepten-4-one (2f) (E,Z mixture):** IR (neat) 1700, 1600, 1250, 1170, 700  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CCl}_4$ , 60 MHz)  $\delta$  0.86 (d,  $J = 6$  Hz, 6 H,  $\text{CH}_3$ ), 1.70-2.50 (m, 3 H,  $-\text{CH}(\text{Me})_2$ ,  $-\text{CH}_2-$ ), 2.38 (s, 3 H,  $=\text{C}(\text{CH}_3)-$ ), 6.10 (s, 1 H,  $=\text{CH}-$ ), 7.05-7.55 (m, 4 H, Ph), 9.45 (s, 1 H, CHO);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 22.5 MHz) 18.20, 22.65, 25.19, 53.91, 126.35, 127.11, 129.60, 129.82, 136.43, 151.49, 191.37, 201.01. Anal. Calcd for  $\text{C}_{15}\text{H}_{18}\text{O}_2$ : C, 78.23; H, 7.88. Found: C, 78.25; H, 8.02.

**Acknowledgment.** This research was financially supported by the Grant-in-Aids for Scientific Research, A, No. 57430030, and Encouragement of Young Scientist, No. 58750681, from the Ministry of Education.

### Electroorganic Synthesis. 4. Facile Synthesis of Aromatic Aldehydes by Direct Anodic Oxidation of Para-Substituted Toluenes<sup>1</sup>

Ikuzo Nishiguchi\* and Tsuneaki Hirashima

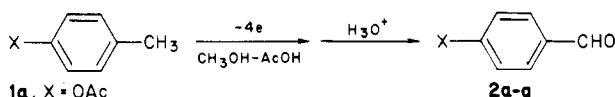
Osaka Municipal Technical Research Institute, 6-50,  
1-Chome, Morinomiya, Jyoto-ku, Osaka 536, Japan

Received August 21, 1984

Highly selective oxidation of ring-substituted toluenes to aromatic aldehydes may be one of the most important reactions in organic synthesis and industrial chemistry because of much usefulness of the latter compounds as key intermediates for production of a variety of fine or speciality chemicals such as pharmaceutical drugs, dyestuffs, pesticides, and perfume compositions.

Although numerous methods using a variety of oxidizing agents such as chromyl chloride,<sup>2</sup> ceric ammonium nitrate,<sup>3</sup> benzeneseleninic anhydride,<sup>4</sup> or peroxydisulfate/copper ion<sup>5</sup> have been reported for transformation of ring-substituted toluenes to aromatic aldehydes, their synthetic utility has been considerably limited owing to low yield, poor selectivity, serious pollution of environment, and troublesome procedure.

In this study, we present highly selective and versatile direct electrooxidation of para-substituted toluenes 1 followed by acid-catalyzed hydrolysis of the resulting product mixture to give the corresponding aromatic aldehydes 2 in good to excellent yields.



- 1a. X = OAc  
 1b. X = CH<sub>3</sub>  
 1c. X = CH(CH<sub>3</sub>)<sub>2</sub>  
 1d. X = C(CH<sub>3</sub>)<sub>3</sub>  
 1e. X = Cl  
 1f. X = OCH<sub>3</sub>  
 1g. X = CH(OCH<sub>3</sub>)<sub>2</sub>

(1) For part 3, see: Nishiguchi, I.; Hirashima, T.; Takumi, H.; Toda, M. *Nippon Kagaku Zasshi* 1984, 1838.

(2) (a) Rentea, C. N.; Rentea, M.; Necsoiu, I.; Necsoiu, C. D. *Tetrahedron* 1968, 24, 4667. (b) Puffin, H. C.; Tucker, R. B. *Tetrahedron* 1968, 24, 389, 6999, and others cited therein.

(3) Syper, L. *Tetrahedron Lett.* 1966, 4493.

(4) Barton, D. H. R.; Hui, R. A. H. F.; Lester, D. J.; Ley, S. V. *Tetrahedron Lett.* 1976, 3331.

(5) Perumal, P. T.; Bhatt, M. V. *Tetrahedron Lett.* 1981, 22, 2605.

Table I. Anodic Oxidation of *p*-Acetoxytoluene (1a)<sup>a</sup>

| run | solvent (volume ratio) | supporting electrolyte          | convn, % | yield, <sup>b</sup> % |    |
|-----|------------------------|---------------------------------|----------|-----------------------|----|
|     |                        |                                 |          | 2a                    | 3a |
| 1   | AcOH                   | Et <sub>4</sub> NOTs            | 0        | 0                     | 0  |
| 2   | MeOH                   | Et <sub>4</sub> NOTs            | 98       | 25                    | 12 |
| 3   | AcOH-MeOH (1:9)        | Et <sub>4</sub> NOTs            | 90       | 39                    | 25 |
| 4   | AcOH-MeOH (1:9)        | NaBF <sub>4</sub>               | 96       | 72                    | 1  |
| 5   | AcOH-MeOH (2:8)        | NaBF <sub>4</sub>               | 96       | 59                    | 12 |
| 6   | AcOH-MeOH (3:7)        | NaBF <sub>4</sub>               | 96       | 51                    | 3  |
| 7   | AcOH-MeOH (1:1)        | NaBF <sub>4</sub>               | 95       | 42                    | 6  |
| 8   | AcOH-MeOH (1:9)        | LiClO <sub>4</sub>              | 92       | 70                    | 0  |
| 9   | AcOH-MeOH (1:9)        | NH <sub>4</sub> BF <sub>4</sub> | 96       | 68                    | 1  |
| 10  | AcOH-MeOH (1:9)        | NaClO <sub>4</sub>              | 87       | 55                    | 1  |
| 11  | AcOH-MeOH (1:9)        | NEt <sub>3</sub>                | 27       | 2                     | 16 |
| 12  | AcOH-MeOH (1:9)        | NH <sub>4</sub> OAc             | 6        | 1                     | 3  |

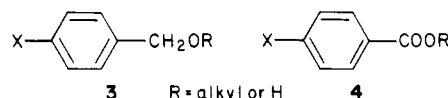
<sup>a</sup> Reaction was carried out in an undivided cell equipped with carbon rods as an anode and a cathode until 8.0 F/mol of electricity was passed through the reaction system. <sup>b</sup> Isolated.

Table II. Anodic Oxidation of Para-Substituted Toluenes 1

| 1  | X                                  | supporting electrolyte | amount of current (F/mol) | isolated yield, % |                |                 |
|----|------------------------------------|------------------------|---------------------------|-------------------|----------------|-----------------|
|    |                                    |                        |                           | 2                 | 3 <sup>a</sup> | 4 <sup>b</sup>  |
| 1a | OAc                                | NaBF <sub>4</sub>      | 8.0                       | 72                | 1              | 0               |
| 1a | OAc                                | LiClO <sub>4</sub>     | 8.0                       | 70                | 0              | 0               |
| 1b | CH <sub>3</sub>                    | NaBF <sub>4</sub>      | 5.6                       | 86                | 0              | 0               |
| 1b | CH <sub>3</sub>                    | Et <sub>4</sub> NOTs   | 5.6                       | 82                | 0              | 0               |
| 1c | CH(CH <sub>3</sub> ) <sub>2</sub>  | NaBF <sub>4</sub>      | 6.0                       | 74                | 0              | 8               |
| 1c | CH(CH <sub>3</sub> ) <sub>2</sub>  | Et <sub>4</sub> NOTs   | 6.0                       | 87                | 0              | 4               |
| 1d | C(CH <sub>3</sub> ) <sub>3</sub>   | NaBF <sub>4</sub>      | 7.0                       | 80                | 0              | 6               |
| 1d | C(CH <sub>3</sub> ) <sub>3</sub>   | Et <sub>4</sub> NOTs   | 7.0                       | 89                | 0              | 2               |
| 1e | Cl                                 | NaBF <sub>4</sub>      | 8.0                       | 78                | 5              | 0               |
| 1e | Cl                                 | Et <sub>4</sub> NOTs   | 8.0                       | 46                | 19             | 0               |
| 1f | OCH <sub>3</sub>                   | Et <sub>4</sub> NOTs   | 4.0                       | 78                | 0              | 2               |
| 1f | OCH <sub>3</sub>                   | KF                     | 6.0                       | 3                 | 0              | 80              |
| 1g | CH(OCH <sub>3</sub> ) <sub>2</sub> | NaBF <sub>4</sub>      | 8.0                       | 81 <sup>c</sup>   | 3 <sup>d</sup> | 10 <sup>e</sup> |
| 1g | CH(OCH <sub>3</sub> ) <sub>2</sub> | LiClO <sub>4</sub>     | 8.0                       | 74 <sup>c</sup>   | 4 <sup>d</sup> | 10 <sup>e</sup> |

<sup>a</sup> Para-substituted benzyl methyl ethers. <sup>b</sup> Methyl para-substituted benzoates. <sup>c</sup> Terephthalaldehyde. <sup>d</sup> 4-Formylbenzyl methyl ether. <sup>e</sup> Methyl 4-formylbenzoate.

Hitherto reported methods for direct anodic oxidation<sup>6,7</sup> of para-substituted toluenes 1 followed by hydrolysis have generally resulted in nonselective formation of three types of products, namely, the corresponding benzaldehyde 2, benzylic ethers (or benzylic alcohols) 3, and benzoates (or benzoic acids) 4.



The yield of the desired aldehydes 2 was substantially influenced by the character of the solvent or the supporting electrolyte employed in the electrochemical oxidation of 1. For example, *p*-acetoxybenzaldehyde (2a) was isolated in 70-72% yield as an almost sole product under the optimum conditions where the reaction was carried out in a mixed solvent of methanol and acetic acid (volume ratio 9:1) containing sodium tetrafluoroborate or lithium perchlorate as a supporting electrolyte in an undivided cell equipped with carbon rods as an anode and a cathode, as shown in Table I.

Similar anodic oxidation of some other para-substituted toluenes (1b-g) in the same mixed solvent containing an

(6) Torii, S.; Shiroy, T. *J. Synth. Org. Chem., Jpn.* 1979, 37, 914.

(7) For direct anodic oxidation of benzylic alcohols or ethers, see: Garwood, R. F.; Naser-ud-Din; Weedon, B. C. L. *J. Chem. Soc., Perkin Trans. 1* 1975, 2471. Weinreb, S. M.; Epling, G. A.; Comi, R.; Reitaro, M. *J. Org. Chem.* 1975, 40, 1356.