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ELECTROREDUCTIVE CROSSED HYDROCOUPLING OF AROMATIC KETONES WITH ENOL ACETATES[1]

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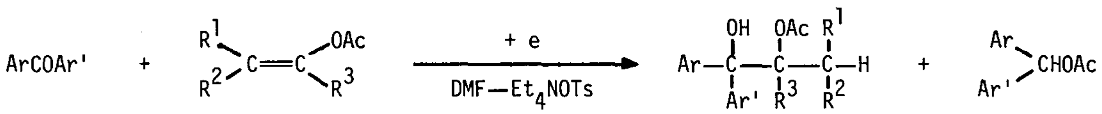
Cathodic reduction of aromatic ketones in the presence of enol acetates afforded crossed hydrocoupling products, that is, unsymmetrical pinacols, in which the new carbon-carbon bond formation took place between the carbonyl carbon of aromatic ketones and the carbon bearing acetoxyl group in enol acetates.

In our continuing study on the electroreductive carbon-carbon bond forming reaction, carbonyl group has played an important role as a key functional group.[2-5]

We report herein a new electroreductive crossed hydrocoupling of aromatic ketones with enol acetates yielding unsymmetrical pinacols in which the new carbon-carbon bond formation takes place between the carbonyl carbon of aromatic ketones and the carbon bearing the acetoxyl group in enol acetates (Scheme I).[6] The unsymmetrical pinacols I would be difficult to be synthesized by other conventional pinacol reduction.[8]

Scheme I



I

II

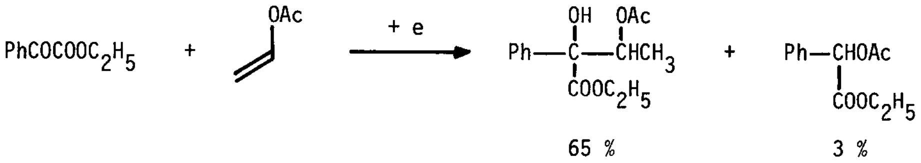
A typical procedure is described below. A solution of 10 g (0.033 mol, 0.36 M) of tetraethylammonium *p*-toluenesulfonate (Et_4NOTs) and 3 g (0.17 mol, 3.2 v%) of water[9] in 80 ml of *N,N*-dimethylformamide (DMF) was placed in cathodic (73 ml) and anodic (20 ml) chambers of a cell equipped with carbon rod electrodes[10] and a ceramic diaphragm. To the catholyte was added 1.82 g (0.01 mol) of benzophenone and 8.6 g (0.1 mol) of vinyl acetate.[11] The catholyte was stirred with a magnetic bar and electrochemically reduced at a constant current (200 mA, 0.015 A/cm^2) under external cooling with a water bath until 3 *F*/mol of electricity was passed. The catholyte was then poured into 200 ml of saturated aqueous solution of sodium chloride and extracted with three 100 ml portions of ether. The combined etherial solution was dried over anhydrous magnesium sulfate and evaporated. The product, 2-acetoxy-1,1-diphenyl-1-propanol, was isolated from the residue by column chromatography on silica gel, yield being 67 %. m.p. 142.4 °C; NMR (CCl_4) δ 1.10 (d, 3H, J = 6 Hz, CH_3-C-), 1.90 (s, 3H, CH_3COO), 2.50 (s, 1H, OH), 5.83 (q, 1H, J = 6 Hz, -CHOCO-), 6.95—7.50 (m, 10H, aromatic); ir (KBr), 3500 (OH), 1710 (C = O), 1600, 1500, 1265, 695 cm^{-1}; MS m/e 270; Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71; O, 17.76. Found: C, 75.49; H, 6.63; O, 17.69. Diphenylmethylacetate was obtained in a 18 % yield as a by-product. m.p. 41-42 °C; NMR (CCl_4) δ 2.10 (s, 3H, CH_3COO-), 6.83 (s, 1H, -CHO-), 7.10—7.53 (m, 10H, aromatic); ir (neat) 1730 (C=O), 1600, 1500, 1240, 695 cm^{-1}; MS m/e 226.

The scope of this electrochemical synthesis of crossed pinacols is illustrated in Table I.

Cathodic reduction of benzophenone and its derivatives in the presence of vinyl acetate gave the corresponding cross-coupled products in moderate yields (entry 1—3,8). Some electron donating substituents such as methyl or methoxyl group on benzophenone seem to increase the yield, whereas chloro or bromo substituent on benzophenone brought about very low yield (chloro; 19 %, bromo; 0 %) and the main product was benzophenone itself. In case of heterocyclic aromatic ketones, yields of the corresponding coupled products were slightly lower than benzophenone derivatives (entry 4—7).

Excepting isopropenyl acetate, enol acetates derived from ketones did not give the coupled compounds, but the products were the acetates of alcohols formed through simple reduction of ketones (entry 12—14). The steric hindrance at the carbon bearing acetoxyl group may be one of the factors controlling the reaction pathway.

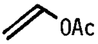
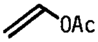
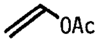
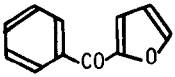
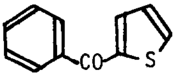
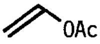
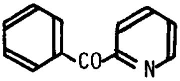
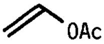
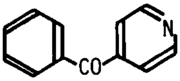
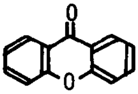
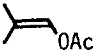
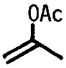
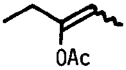
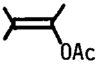
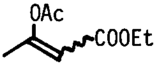
Cathodic reduction of ethyl benzoylformate gave the coupled product indicating that ketones substituted by anion stabilizing groups other than aromatic groups were also effective in this coupling reaction.



The combination of acetophenone and vinyl acetate, however, gave the coupled product only in a 6 % yield, and aliphatic ketones were not effective in this reaction.

This reductive coupling may be explained by an anion mechanism (Scheme II, route A), in which the initiation step involves two electron transfer to benzophenone[12] and one protonation followed by addition of the resulting anion (a) to the carbon atom bearing the acetoxyl group to yield the more stable anion intermediate (b). Another possible first active species (d), that is, a radical generated from benzophenone by one electron transfer and one protonation may not yield the pinacol type product, since according to the theory of radical polymerization of vinyl acetate, the radical (d) has to add to vinyl acetate in head to tail manner giving the different type product (f) (route B).

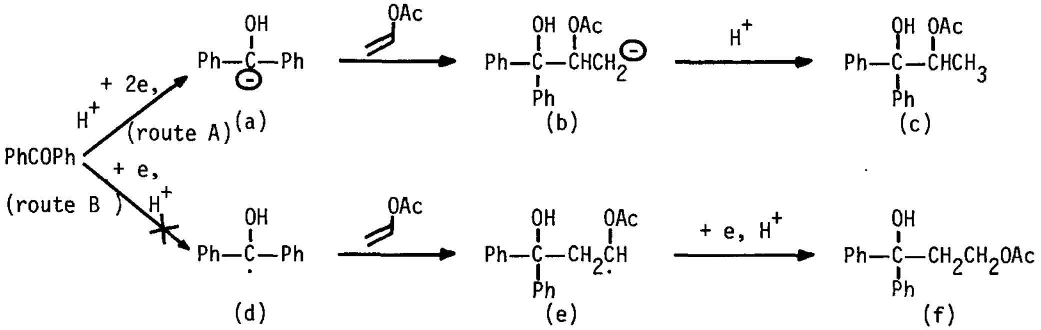
Table I

Entry	Aromatic Ketone	Enol Acetate	Isolated Yield (%)	
			(I)	(II)
1	PhCOPh		67	18
2	PhCOPh—Me—P		71a)	15
3	PhCOPh—OMe—P		76a)	8
4			50	25
5			48	19
6			54	19
7			46	—
8			59	—
9	PhCOPh		54b)	42
10	PhCOPh		53b)	34
11	PhCOPh		45b)	38
12	PhCOPh		0	63
13	PhCOPh		0	72
14	PhCOPh		0	59

a) Diol was contained by 15 %.

b) Coupled product was diol.

Scheme II



References and Notes

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2. (a) T. Shono and M. Mitani, *J. Am. Chem. Soc.*, **93**, 5284 (1971); (b) T. Shono, I. Nishiguchi, H. Ohmizu, and M. Mitani, *J. Am. Chem. Soc.*, **100**, 545 (1978).
3. T. Shono, I. Nishiguchi, and H. Ohmizu, *Chem. Lett.*, **1976**, 1233.
4. T. Shono and M. Mitani, *Nippon Kagaku Kaishi*, **1973**, 975.
5. T. Shono, I. Nishiguchi, and H. Ohmizu, *J. Am. Chem. Soc.*, **99**, 7396 (1977).
6. It has been reported that an anion generated from bromoform, chloroform, or phenylacetonitriles under basic or phase transfer conditions adds to vinyl acetate at the carbon bearing an acetoxyl group.[7]
7. M. Fedorynski, I. Gorzkowska, and M. Makosza, *Synthesis*, **1977**, 120.
8. For example, D. G. Botteron, and G. Wood, *J. Org. Chem.*, **30**, 3871 (1965). Recently E. J. Corey and his co-workers have reported an improved method for preparation of unsymmetrical pinacols; E. J. Corey, R. L. Danheiser, and S. Chandrasekara, *J. Org. Chem.*, **41**, 260 (1976).
9. The yield of the cross-coupled product remarkably depends on amount of a proton source in the reaction system. When water was not added to the solvent, the yield of the coupled product decreased (45 %) and a large amount of polymeric products were formed. Addition of a small amount of water to solvent, however, improved the yield and the best result was obtained when 3 g (0.17 mol, 3.2 v%) of water was added. Other proton sources such as phenol, acetic acid, and methanesulfonic acid did not give so good result as water.
10. The yield of the cross-coupled product seems not to depend on the cathode material. However, the best result was obtained with carbon cathode. Carbon (67 %), Pb (64 %), Pt (61 %), Cu (57 %), Zn (59 %).
11. The best result was obtained when the ratio of vinyl acetate to benzophenone was ten.
12. Reduction peak potential of benzophenone was found at -1.85 V *vs.* SCE, while vinyl acetate did not show any reduction peak between 0—-2.5 V *vs.* SCE [DMF-Et_4NOTs (0.36 M), scanning rate 100 mV/sec, concentration of substrate 4.8×10^{-3} M]. Electroreduction was carried out at the constant potential of -2.0 V *vs.* SCE, and the coupled product was obtained in a 48 % yield suggesting that the initiation step of this reaction was the electron transfer to not vinyl acetate but benzophenone.

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