filtrate was evaporated, diluted with CH_2Cl_2, poured into H_2O, and extracted several times with CH_2Cl_2. The combined extracts were dried over anhydrous sodium sulfate, filtered, and evaporated from MeOH to afford pure bicyclic **2** (35.3 mg, 70%; crystallized from Et_2O/CH_2Cl_2). An additional 5.1 mg of **2** was recovered from the mother liquors (total yield 80%). The yields for this reaction reproducibly varied between 70% with 2 mequiv of **4** (96 h, 25 °C) to 86% with 7.3 mequiv (144 h, 25 °C).

Regeneration of Resin 4. The resin (1.3 gm) obtained after cyclization of **1** and washing was suspended in 1 N HCl in MeOH and stirred at 25 °C for 3 h. The polymer was filtered and washed successively with CH_2Cl_2, MeOH, THF, THF/H_2O (1:1), THF, MeOH, THF, THF/H_2O (1:1), THF, benzene, and MeOH and dried in vacuo to afford 1.30 g of resino mercury(II) chloride; IR (KBr, pellet) 1600, 1585, 1495, 1450, 750, 690, 525 cm^{-1}. This resin (1.08 g) was suspended in THF, and $AgClO_4$[7] (320 mg, 2.0 equiv) was added and the suspension stirred for 48 h at 25 °C. Successive agitative washing with THF (10 × 20 mL) afforded 1.3 g of **4**; IR (KBr) 1600, 1580, 1500, 1450, 1060, 1020, 900, 750, 690, 605, 525 cm^{-1}. The regenerated resin obtained above effected the deprotection/cyclization of **1** → **2** (R = CH_2Ph-*p*-OMe; R′ = H) in 80–85.6% yields.

Acknowledgment. We gratefully acknowledge financial support for this work from the National Institutes of Health, Grants 1R01AIGM18957-02 and 1R01HL30888-01. NMR measurements at 360 MHz were obtained at the Colorado State University Regional NMR Center, funded by the National Science Foundation Grant CHE78-18581.

Registry No. **1** (R = *p*-$MeOC_6H_4CH_2$; R′ = H), 91238-03-8; **1** (R = CH_3; R′ = H), 91238-04-9; **1** (R = $PhCH_2$: R′ = CH_2OMs), 91238-05-0; **1** (R = *p*-$MeOC_6H_4$; R′ = H), 91238-06-1; **1** (R = *p*-$MeOC_6H_4CH_2$; R′ = CH_2OMs), 91238-07-2; **1** (R = $PhCH_2$; R′ = H), 91238-08-3; **2** (R = MeO-*p*-$C_6H_4CH_2$; R′ = H), 91238-09-4; **2** (R = Me; R′ = H), 78877-97-1; **2** (R = $PhCH_2$; R′ = CH_2OMs), 90301-46-5; **2** (R = *p*-$MeOC_6H_4$; R′ = H), 91238-10-7; **2** (R = *p*-$MeOC_6H_4CH_2$; R′ = CHOMs), 91238-11-8; **2** (R = $PhCH_2$; R′ = H), 91238-12-9; iii, 29182-87-4; iv, 21535-05-7; v, 91238-13-0; $Cu(ClO_4)_2$, 13770-18-8; $AgClO_4$, 7783-93-9; $Hg(ClO_4)_2$, 7616-83-3; $Fe(ClO_4)_3$, 13537-24-1; $Ni(ClO_4)_2$, 13637-71-3; $Pb(ClO_4)_2$, 13637-76-8; $PhHgClO_4$, 49804-95-7; AgOTf, 2923-28-6; $AgSbF_6$, 26042-64-8; *t*-$BuMe_2SiO(CH_2)_3I$, 78878-05-4; *p*-anisidine, 104-94-9; bromoacetyl bromide, 598-21-0; 2,2′-dipyridyl disulfide, 2127-03-9.

Supplementary Material Available: Detailed experimental procedure for the preparation of 8,10-bis(*p*-methoxyphenyl)-8,10-diaza-2-oxabicyclo[4.2.2]decane-7,9-dione (**2**, R = Ph-*p*-OCH_3; R′ = H) and spectral data for compounds **2** (R = CH_2Ph, R′ = CH_2OMs; R = CH_2Ph-*p*-OCH_3, R′ = CH_2OMs); complete table of reagents examined for the conversion of **1** → **2** (27 entries) (6 pages). Ordering information is given on any current masthead page.

Electrolytic Side-Chain Oxidation of Alkylbenzenes Using Polymeric Electron Carrier

Jun-ichi Yoshida, Keiji Ogura, and Nariyoshi Kawabata*

Department of Chemistry, Faculty of Polytechnic Science, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan

Received December 29, 1983

The utility of indirect electrochemical reactions using a catalytic electron carrier (mediator) has been recognized by synthetic organic chemists in the last decade (Scheme I).[1] Use of electron carrier makes it possible to perform electrochemical oxidations at lower potentials than those required for direct anodic reactions. Although various inorganic and organic carriers have been employed so far, recent development of polymeric electron carriers[2] opens an intriguing aspect of indirect electrochemical reactions. Such polymeric electron carriers enable simple workup of the reaction as well as easy recovery and repeated use of the reagent. Previously we have reported polymer-mediated oxidation of alcohols[2a] and sulfides[2c] and epoxidation of olefins.[2b] In this paper we describe the use of a polymeric electron carrier to effect electrochemical side-chain oxidation of alkylbenzenes[3] (eq 1).

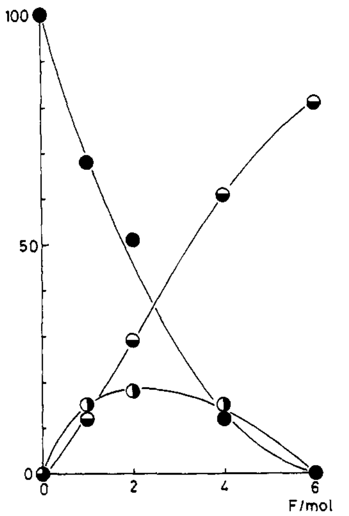
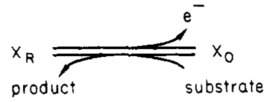


Figure 1. Electrolytic oxidation of diphenylmethane using PVP·HBr (0.50 g) and PVP·H_2SO_4 (0.50 g) in a mixture of acetonitrile (2.7 mL) and acetic acid (0.3 mL). Dependence of yields of benzophenone (◒), diphenylmethanol (◑), and unchanged diphenylmethane (●) on the passed electricity.

Scheme I



X_R : reduced form of electron carrier
X_O : oxidized form of electron carrier

$$\mathrm{ArCH_2R} + \mathrm{H_2O} \xrightarrow[\substack{\mathrm{PVP\cdot HBr} \\ \mathrm{PVP\cdot H_2SO_4}}]{-e^-} \mathrm{ArC(O)R} \qquad (1)$$

Diphenylmethane was chosen as a simple model to explore reaction conditions. Constant electric current was passed through a cell containing platinum electrodes, polymer beads, diphenylmethane, water, and solvent with slow stirring, and the reaction was monitored by GLC analysis. The initial question of what kind of polymer best effects the side-chain oxidation of alkylbenzenes was answered by the observation that a 1:1 mixture of cross-linked poly(vinylpyridinium bromide) (hereafter abbreviated as PVP·HBr) and cross-linked poly(vinylpyridinium sulfate) (PVP·H_2SO_4) efficiently catalyzed the reaction to give benzophenone in 81% yield (6.0 F/mol) (eq 2). In the early stage of the reaction both benzophenone and

---

[1] For example: (a) Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4492. (b) Masui, M.; Ueshima, T.; Ozaki, S. *J. Chem. Soc., Chem. Commun.* **1983**, 479. (c) Moyer, B. A.; Thompson, M. S.; Meyer, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 2310. (d) Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. *Tetrahedron Lett.* **1980**, *21*, 1867. (e) Shono, T.; Matsumura, Y.; Mizoguchi, M.; Hayashi, J. *Ibid.* **1979**, 3861.

[2] (a) Yoshida, J.; Nakai, R.; Kawabata, N. *J. Org. Chem.* **1980**, *45*, 5269. (b) Yoshida, J.; Hashimoto, J.; Kawabata, N. *Ibid.* **1982**, *47*, 3575. (c) Yoshida, J.; Sofuku, H.; Kawabata, N. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1243.

[3] (a) Matsue, T.; Fujihira, M.; Osa, T. *J. Electrochem. Soc.* **1981**, *128*, 2565. (b) Torii, S.; Tanaka, H.; Siroi, T.; Akada, M. *J. Org. Chem.* **1979**, *44*, 3305. (c) Ramaswamy, R.; Venkatachalapathy, M. S.; Udupa, H. V. K. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1751. (d) Ramaswamy, R.; Venkatachalapathy, M. S.; Udupa, H. V. K. *J. Electrochem. Soc.* **1963**, *110*, 202.

0022-3263/84/1949-3419$01.50/0 © 1984 American Chemical Society

$$\underset{1}{\mathrm{PhCH_2Ph}} \rightarrow \underset{2}{\mathrm{PhCOPh}} + \underset{3}{\mathrm{PhCH(OH)Ph}} + \underset{4}{\mathrm{PhCH(OAc)Ph}} \quad (2)$$

diphenylmethanol were formed, and as the reaction proceeded the latter was gradually consumed with an increase in the amount of the former (Figure 1). This indicates that the initial oxidation product is diphenylmethanol which is further oxidized to benzophenone under the reaction conditions. As a matter of fact, PVP·HBr is known to mediate the oxidation of alcohols to ketones as reported previously.[2a]

Lower conversions and yields of benzophenone by individual use of either PVP·HBr or PVP·H_2SO_4 demonstrated the cooperative function of the two polymers (Table I). Although mechanistic details are not clear at present, such cooperation suggests the possibility of various electrolytic reactions which may be mediated by the combination of two different types of polymers.[4]

The reaction was proved to be quite sensitive to the nature of the solvent (Table II). When acetonitrile was used as solvent, the current did not flow smoothly and hence the reaction was very slow. The addition of a small amount of acetic acid gave rise to smooth reaction, but further addition or use of acetic acid as solvent resulted in the formation of diphenylmethyl acetate. A 9:1 mixture of acetonitrile and acetic acid was found to be the best solvent among those examined. Dimethylformamide (DMF) was also suitable as a solvent in some cases.

Recovery of the polymer beads was accomplished by simple filtration. After being washed with organic solvents, the polymer beads can be reused for the reaction with minor loss of the reactivity (67% yield, 6.0 F/mol). A slight decrease in the yield of benzophenone is presumably attributed to the partial mechanical destruction of the polymer beads during the reaction. Fine powder of the polymer was formed which adhered to the electrode and seemed to retard the reaction.

Table III summarizes the results obtained with several alkylbenzenes. The methylene group adjacent to the aromatic ring was oxidized to afford the corresponding phenyl ketones in good yields. On the other hand, the yields of aldehyde from oxidation of a side methyl group were low probably because of susceptibility of the product toward further oxidation under the conditions.[5] As for chemoselectivity, ethers and esters are compatible (i.e., inert toward the oxidation).

The use of much less than a stoichiometric amount of chemical oxidizing agent,[6] reusability of the polymer, and easy workup, as well as mild reaction conditions make this method a useful tool for oxidizing the methylene group adjacent to an aromatic ring to the corresponding carbonyl group.

Table I. Electrolytic Oxidation of Diphenylmethane Using Polymeric Electron Carrier. Effect of Polymer[a]

polymer	product,[b] %			unchanged 1,[b] %
	2	3	4	
PVP·HBr/PVP·H_2SO_4 (1:1)[c]	81	trace	trace	0
PVP·HBr	59	16	trace	7
PVP·H_2SO_4	23	17	trace	25

[a] Reactions were carried out with diphenylmethane (5.0 mmol), water (50 mmol), and the polymer beads (1.0 g) in a mixture of acetonitrile (2.7 mL) and acetic acid (0.3 mL). The passed electricity was 6.0 F/mol based on diphenylmethane. [b] Determined by GLC analysis. [c] Ratio by weight.

Table II. Electrolytic Oxidation of Diphenylmethane Using Polymeric Electron Carrier. Solvent Effect[a]

solvent	product,[b] %			unchanged 1,[b] %
	2	3	4	
AcOH	20	10	11	48
MeCN	22	21	0	54
MeCN/AcOH (4:1)[c]	30	16	5	43
MeCN/AcOH (9:1)[c]	29	18	trace	51

[a] Reactions were carried out with diphenylmethane (5.0 mmol), water (50 mmol), and a mixture of PVP·HBr (0.50 g) and PVP·H_2SO_4 (0.50 g) in 3.0 mL of solvent. Passed electricity was 2.0 F/mol based on diphenylmethane. [b] Determined by GLC analysis. [c] Ratio by volume.

Table III. Electrolytic Side-Chain Oxidation of Alkylbenzenes Using Polymeric Electron Carrier[a]

substrate	electricity (F/mol)	product	yield,[b] %
$C_6H_5CH_2C_6H_5$	6.0	$C_6H_5COC_6H_5$	78 (81)
$C_6H_5CH_2CH_3$	4.0	$C_6H_5COCH_3$	(72)
$C_6H_5CH_2CH_2CH_2$-CH_3	6.0	$C_6H_5COCH_2CH_2CH_3$	(74)
p-$CH_3OC_6H_4$-CH_2CH_3	4.0[c]	*p*-$CH_3OC_6H_4COCH_3$	54 (73)
p-$CH_3COOC_6H_4$-CH_2CH_3	6.0	*p*-$CH_3COOC_6H_4COCH_3$	60 (76)
$C_6H_5CH_3$	4.0	C_6H_5CHO	(13)
p-$CH_3OC_6H_4$-CH_3	6.0	*p*-$CH_3OC_6H_4CHO$	(15)

[a] The reactions were normally carried out with alkylbenzene (5.0 mmol), water (50 mmol), and a mixture of PVP·HBr (0.50 g) and PVP·H_2SO_4 (0.50 g) in a mixture of acetonitrile (2.7 mL) and acetic acid (0.3 mL) unless otherwise stated. [b] Yields are given for isolated pure material. Yields in parentheses are GLC determined. [c] Carried out in DMF.

Experimental Section

All electrolyses were conducted at constant current with a Kikusui Model PAB-32-0.5 regulated power supply or a Trio Model PR-653 regulated DC power supply. Infrared spectra were measured with a Hitachi Model 215 grating spectrometer. ^1H NMR spectra were measured with a Varian Model T-60A spectrometer in CCl_4 using Me_4Si as internal standard. Analytical and preparative GLC were performed on a Shimadzu GC-4B or GC-4C gas chromatograph. Elemental analyses were performed by the Elementary Analyses Center of Kyoto University. Cross-linked poly(vinylpyridinium bromide) (PVP·HBr) (containing 3.04 mmol/g of HBr) was prepared in an identical manner with that reported previously.[2a] Cross-linked poly(vinylpyridinium sulfate) (PVP·H_2SO_4) (containing 2.58 mmol/g of H_2SO_4) was prepared in a similar fashion. The polymer beads were dried under vacuum before use.

Electrolytic Oxidation of Alkylbenzenes. General Procedure. The reactions were carried out in 10-mL, two-necked glass cell[2a] equipped with a mechanical stirrer and calcium chloride drying tube. Platinum electrodes (10 × 10 × 0.5 mm) were placed in the cell parallel to each other with about 7 mm of space between them. Alkylbenzene (5.0 mmol), water (50 mmol), and 9:1 mixture of acetonitrile (2.7 mL) and acetic acid (0.3 mL) were placed in the cell, and then a mixture of PVP·HBr (0.50 g) and PVP·H_2SO_4 (0.50 g) was added. The electric current (20 mA) was passed through the layer of polymer beads with slow stirring (30 rpm) at 40 °C. (With higher current density the yields of the ketones were lower; therefore, the current density must be carefully controlled.) After the reaction was complete (monitored by GLC analysis), the reaction mixture was filtered, the polymer beads were washed with ether (3 × 5 mL), and the combined filtrate

---

(4) A double mediatory system using two types of electron carriers has been reported. See: Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. *Tetrahedron Lett.* **1980**, *21*, 1867.

(5) PVP·HBr is known to oxidize primary alcohols to a mixture of carboxylic acid and ester probably via an aldehyde. See ref 2a.

(6) For example: (a) Bhatt, V.; Perumal, P. T. *Tetrahedron Lett.* **1981**, *22*, 2605. (b) Ho, T.-L. *Synthesis* **1973**, 347.

and washings were dried over anhydrous Na_2SO_4. After removal of the solvent the crude product was purified by distillation or flash chromatography. All products were identified by comparison of their ^1H NMR and IR spectra with those of authentic samples.

The polymer beads were recovered by filtration as described above, washed with ether (3 × 5 mL), acetonitrile (3 × 3 mL), and ether (3 × 3 mL), dried under vacuum, and reused for the next cycle of the reaction.

Electrolytic Oxidation of Diphenylmethane. Typical Procedure. Diphenylmethane (830 mg, 4.93 mmol), water (894 mg, 49.6 mmol), acetic acid (0.30 mL), and acetonitrile (2.70 mL), were placed in the cell, and then a mixture of PVP·HBr (522 mg) and PVP·H_2SO_4 (496 mg) was added. The electric current (20 mA) was passed with slow stirring at 40 °C. After 40 h the reaction mixture was filtered, the polymer beads were washed with ether (3 × 5 mL), and the combined filtrate and washings were dried over Na_2SO_4. After removal of the solvent, the crude product was purified by flash chromatography (hexane/ethyl acetate, 10:1) followed by bulb-to-bulb distillation to give 702 mg (78% yield) of benzophenone. The ^1H NMR and IR spectra were identical with those of an authentic material.

Acknowledgment. We thank the Ministry of Education for the Grant-in-Aid for Scientific Research (No. 58750689) for support of this work.

Registry No. 1, 101-81-5; 2, 119-61-9; 3, 91-01-0; 4, 954-67-6; PVP·HBr, 82444-38-0; PVP·H_2SO_4, 91110-42-8; $C_6H_5CH_2CH_3$, 100-41-4; $C_6H_5CH_2CH_2CH_2CH_3$, 104-51-8; p-$CH_3OC_6H_4CH_2CH_3$, 1515-95-3; p-$CH_3COOC_6H_4CH_2CH_3$, 3245-23-6; $C_6H_5CH_3$, 108-88-3; p-$CH_3OC_6H_4CH_3$, 104-93-8; $C_6H_5COCH_3$, 98-86-2; $C_6H_5COCH_2CH_2CH_3$, 495-40-9; p-$CH_3OC_6H_4COCH_3$, 100-06-1; p-$CH_3COOC_6H_4COCH_3$, 13031-43-1; C_6H_5CHO, 100-52-7; p-$CH_3OC_6H_4CHO$, 123-11-5.

Nitrone Cycloadditions. An Efficient Method for the Homologation of Aldehydes to α,β-Unsaturated Aldehydes

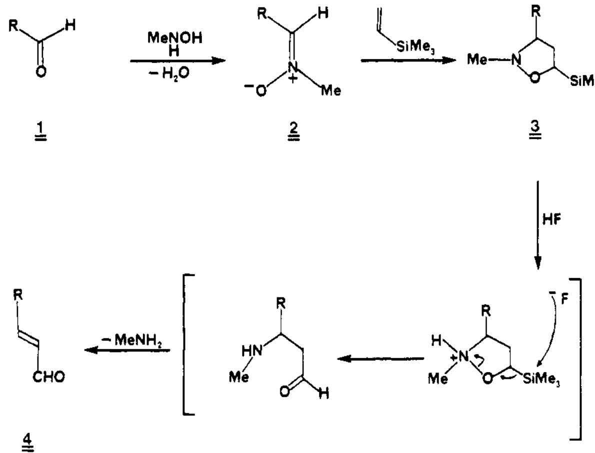
Philip DeShong* and Joseph M. Leginus

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

Received February 28, 1984

Homologation of an aldehyde into an α,β-unsaturated carbonyl compound with the introduction of two additional carbon atoms in the resulting chain is an important reaction in organic synthesis since the products are useful intermediates for further synthetic elaboration.[1] The Wittig reaction or the Emmons-Wadsworth-Horner modification of the Wittig reaction is most often employed to effect the transformation of an aldehyde into an olefinic ketone or ester derivative.[2] However, the direct conversion of an aldehyde to an α,β-unsaturated aldehyde cannot be performed by using Wittig methodology; therefore, alternative strategies have been developed to perform this conversion. Generally this involves the homologation of the aldehyde to the unsaturated ester followed by reduction with Dibal.

Scheme I



During the course of a study in our laboratory we required a method to homologate an aldehyde to an α,β-unsaturated aldehyde utilizing conditions which avoided basic or reducing reagents. Based upon earlier findings,[3] we decided to investigate the nitrone route shown in Scheme I to accomplish our objective. A nitrone route was especially appealing since we had previously demonstrated that the nitrones of aldehydes are readily prepared by the reaction of a *N*-methylhydroxylamine and the respective aldehyde. Cycloaddition of nitrones **2** with a variety of electron-rich,[3] as well as electron-deficient, dipolarophiles[3,4] was documented and the reaction with vinyltrimethylsilane was expected to produce the 5-(trimethylsilyl)-substituted isoxazolidine **3** on the basis of the results of Cunico[5] and Padwa.[6] Treatment of the (trimethylsilyl)isoxazolidine with HF would result in the protonation-fragmentation of the isoxazolidine followed by elimination of the β-amino substituent to produce the desired unsaturated aldehyde. In this paper, we report the first example of a nitrone cycloaddition to a vinylsilane and that the resulting cycloadducts **3** serve as precursors of α,β-unsaturated aldehydes as outlined in Scheme I. This methodology is especially significant because it allows for the homologation of aldehydes by two carbons while avoiding strongly basic reaction conditions.

The results summarized in Table I show that the nitrone route in Scheme I is an excellent alternative to Wittig chemistry for the preparation of unsaturated aldehydes. Aldehydes are readily converted into the corresponding nitrones in excellent yield (see Experimental Section). In all but one instance, only the (*Z*)-nitrone was obtained.[7] The crude nitrones could be utilized in subsequent reactions without a decrease in the yield of cycloadduct. Cycloaddition of the nitrones and vinyltrimethylsilane in a benzene solution resulted in the formation of the 5-(trimethylsilyl)-substituted isoxazolidine in good yield. A mixture of stereoisomers was formed in the cycloaddition;

---

[1] Fonza, G.; Fuganti, C.; Grasselli, P.; Marinoni, G. *Tetrahedron Lett.* **1979**, 3883. Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873. Hanessian, S.; Pongny, J. R.; Boessenkool, I. K. *J. Am. Chem. Soc.* **1982**, *104*, 6164. Minami, N.; Ko, S. S.; Kishi, Y. *Ibid.* **1982**, *104*, 1109. Lewis, M. D.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2343 and references cited therein. Lee, A. W. M.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Walker, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 3515. Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1378. Williams, D. R.; Barner, B. A.; Nishitani, K.; Phillips, J. G. *J. Am. Chem. Soc.* **1982**, *104*, 4708.

[2] Reviews: Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87. Wadsworth, W. S. *Org. React.* (*N. Y.*) **1977**, *25*, 73. See also: Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405 and references cited therein. Schmid, G.; Fukuyama, T.; Akasaka, K.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 259.

[3] Dicken, C. M.; DeShong, P. *J. Org. Chem.* **1982**, *47*, 2047. Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 633. Huisgen, R.; Grashey, R.; Sauer, J. "The Chemistry of Alkenes"; Patai, S., Ed.; Interscience: London, 1964; pp 806-878. Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396.

[4] Padwa, A.; Fisera, L.; Koehler, K. F.; Rodriguez, A.; Wong, G. S. K. *J. Org. Chem.* **1984**, *49*, 276. Joucla, M.; Tonnard, F.; Gree, D.; Hamelin, J. *J. Chem. Res. Synop.* **1978**, 240. Sims, J.; Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 5798. Ali, S. A.; Sevaratore, A.; Illig, C. R.; Meckler, H.; Tufariello, J. J. *Tetrahedron Lett.* **1979**, 4167.

[5] Cunico, R. F. *J. Organomet. Chem.* **1981**, *212*, C51.

[6] Padwa, A.; MacDonald, J. G. *J. Org. Chem.* **1983**, *48*, 3189.

[7] DeShong, P.; Dicken, C. M.; Staib, R. R.; Freyer, A. J.; Weinreb, S. M. *J. Org. Chem.* **1982**, *47*, 4397.

0022-3263/84/1949-3421$01.50/0