Highly Selective Palladium-Catalyzed Synthesis of Protected α,β-Unsaturated Methyl Ketones and 2-Alkoxy-1,3-butadienes. High-Speed Chemistry by Microwave Flash Heating

Karl S. A. Vallin, Mats Larhed, Katarina Johansson, and Anders Hallberg*

Department of Organic Pharmaceutical Chemistry, Uppsala Biomedical Centre, Uppsala University, Box 574, SE-751 23 Uppsala, Sweden

Received January 19, 2000

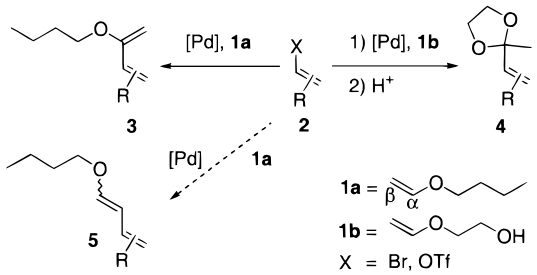
A selective and mild procedure is described for the direct synthesis of 2-alkene-2-methyl-1,3-dioxolanes via regiocontrolled Heck vinylation of commercially available 2-hydroxyethyl vinyl ether. The procedure permits chemoselective transformation of a vinylic triflate or bromide into a blocked α,β-unsaturated methyl ketone. Furthermore, a significantly improved and highly regioselective synthesis of 2-alkoxy-1,3-butadienes has been developed. Flash heating by microwave irradiation promotes the palladium-catalyzed reactions, and the starting materials are fully converted after reaction times of 5−7 min.

Introduction

Dioxolanation is one of the most widely used protective techniques for carbonyl compounds.[1−3] Frequently, the presence of sensitive groups might not permit the use of the standard conditions needed for acetal formation, and in systems with more than one carbonyl group, a selective acetalization is often not feasible.[1−4] Recently it was demonstrated that a direct chemoselective synthesis of cyclic acetals of acetophenones from aryl triflates or halides could be accomplished via internal palladium-catalyzed α-arylation of hydroxyalkyl vinyl ethers and successive ring-closing.[5] The preparation of nonprotected acetophenones by Heck[6−10] α-arylation of alkyl vinyl ethers followed by hydrolysis[11] has been known for almost two decades.[12−16] The related regioselective palladium-catalyzed α-vinylation of alkyl vinyl ethers affords 2-alkoxy-1,3-dienes.[17] After subsequent hydrolysis these dienes deliver α,β-unsaturated methyl ketones, or alternatively they may serve as dienes in Diels−Alder reactions.[18,19]

Unfortunately, with certain combinations of reactants the vinylic substitution is hampered with difficulties,[19] and an unsatisfactory regiocontrol in the Heck vinylation[19,20] often accounts for the low yields encountered. Cross-coupling methodologies, despite requiring preparation of, e.g., vinyl zinc,[20] tin,[21] and silicon[22] reactants, have therefore up to now attracted more attention when 2-alkoxy-1,3-dienes are desired.

We herein report, *first* a new bidentate ligand-controlled, highly regioselective synthesis of 2-alkoxy-1,3-dienes (**3**, eq 1) and, *second*, a mild chemo- and regio-



(1)

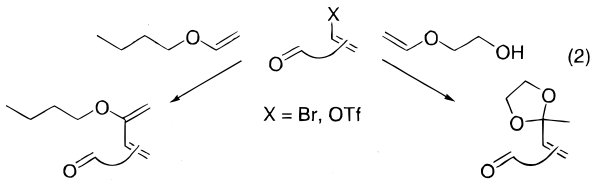
selective procedure for the direct synthesis of 2-alkene-2-methyl-1,3-dioxolanes (**4**, eq 1) via Heck vinylation of commercially available 2-hydroxyethyl vinyl ether (**1b**, eq 1). The latter one-pot procedure allows for the facile transformation of a vinyl triflate or bromide into a blocked α,β-unsaturated methyl ketone (**4**).[23] Flash heating by microwave irradiation, as a complement to the standard thermal heating, was employed to drastically reduce reaction times.

(1) Meskens, F. A. J. *Synthesis* **1981**, 501−502.
(2) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley & Sons, Inc.: New York, 1999; pp 297−329.
(3) Jarowicki, K.; Kocienski, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4005−4037.
(4) Hwu, J. R.; Wetzel, J. M. *J. Org. Chem.* **1985**, *50*, 3946−3948.
(5) Larhed, M.; Hallberg, A. *J. Org. Chem.* **1997**, *62*, 7858−7862.
(6) Larock, R. C. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press Inc.: Greenwich, CT, 1994; Vol. 3, pp 97−224.
(7) De Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379−2411.
(8) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2−7.
(9) Jeffery, T. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1996; Vol. 5, pp 153−260.
(10) Larhed, M.; Hallberg, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I., Ed.; Wiley-Interscience: New York, in preparation.
(11) DeVries, R. A. U.S. Patent 5248829, 1993.
(12) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1979**, *44*, 21−22.
(13) Hallberg, A.; Westfelt, L.; Holm, B. *J. Org. Chem.* **1981**, *46*, 5414−5415.
(14) Andersson, C.-M.; Hallberg, A.; Daves, G. D. *J. Org. Chem.* **1987**, *52*, 3529−3536.
(15) Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *J. Org. Chem.* **1990**, *55*, 3654−3655.
(16) Cabri, W.; Candiani, I.; Bedeschi, A.; Penco, S.; Santi, R. *J. Org. Chem.* **1992**, *57*, 1481−1486.
(17) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1989**, *54*, 1502−1505.
(18) Paquette, L. A.; Ra, C. S.; Edmonson, S. D. *J. Org. Chem.* **1990**, *55*, 2443−2445.
(19) Oh, J.; Cha, J. K. *Synlett* **1994**, 967−968.
(20) Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1990**, *31*, 1889−1892.
(21) Kwon, H. B.; Mckee, B. H.; Stille, J. K. *J. Org. Chem.* **1990**, *55*, 3114−3118.
(22) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918−920.
(23) Mcclelland, R. A.; Watada, B.; Lew, C. S. Q. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1723−1727.

10.1021/jo000070o CCC: $19.00
Published on Web 06/27/2000

Results

The preparative results after the reaction of a series of diverse vinyl triflates and bromides **2a**−**g** with butyl vinyl ether (**1a**) or 2-hydroxyethyl vinyl ether (**1b**) are summarized in Table 1. Two methods were devised (A and B). The vinylating agents were allowed to react either with 2.0 equiv of vinyl ether (**1a** or **1b**), palladium acetate (0.03 equiv), 1,3-bis(diphenylphosphino)propane (DPPP), and freshly distilled triethylamine (method A) or with a larger excess (5.0 equiv) of vinyl ether,[24] palladium acetate (0.03 equiv), (*R*)-(+)-2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl (tol-BINAP), and potassium carbonate as base (method B). Method A was applied in all dioxolanations and microwave-enhanced reactions. Utilizing vinyl bromides as starting materials required stoichiometric addition of thallium(I) acetate[25] to afford high internal regioselectivity.[16,26] The reactions were performed in dry DMSO under nitrogen and in the presence of molecular sieves to suppress the hydrolysis of products that otherwise were prevalent.[20] A very high α/β regioselectivity (>98/2) was achieved with conventional heating, and both the alkoxy dienes **3a**−**g** and the α,β-unsaturated acetals **4a**−**g** were isolated in fair to good yields in most cases after chromatography under basic conditions.[4,27−30] Notably, while the dienylacetal **4g** was smoothly formed from the organotriflate **2g**, addition of dry acetic acid was required to ensure full ring closure after complete consumption of the vinyl triflates **2a**−**c** (entries 2, 4, and 6, Table 1). The cyclic vinyl bromide **2f**, with a carbonyl group adjacent to the reaction center, underwent the most sluggish reactions. With this vinyl bromide a considerable reduction (dehalogenation) occurred, and high temperatures and long reactions times were needed to fully convert the starting material (entries 11 and 12). The low isolated yields encountered in the diene synthesis of **3e** from the aldehyde **2e** seem to be attributed mainly to a significant and concomitant polymerization (entry 9). The vinyl palladium precursors **2e**, **2f**, and **2g** with aldehyde or keto groups were selected as substrates to permit assessment of potential transacetalizations.[5,31] No products derived from transacetalization could be traced even after analysis of reactions conducted at high temperatures (entries 10, 12, and 14). Thus, the procedure seems to be completely chemoselective. Although only a few examples are given here (entries 9−14), we assume that the reactions should provide a facile route to monoprotected dicarbonyl compounds (eq 2).



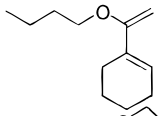
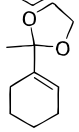
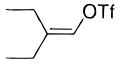
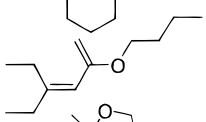
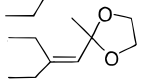
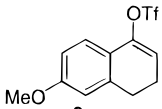
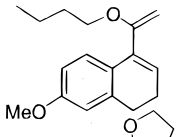
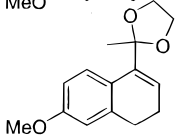
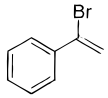
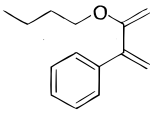
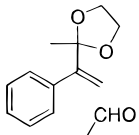
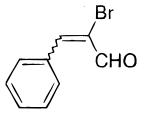
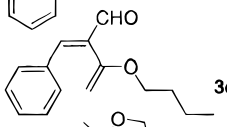
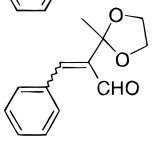
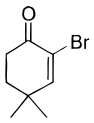
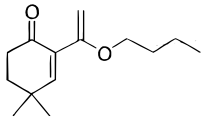
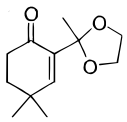
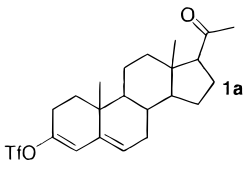
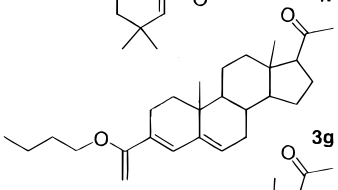
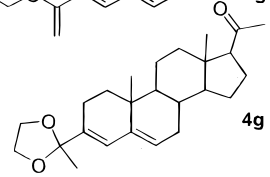
(2)

The long reaction times needed for the acetal and diene syntheses presented in Table 1 encouraged us to exploit microwaves as a nonconventional and energy-efficient heating source for promotion of the reactions. We have previously used flash heating by microwaves for the acceleration of various palladium-catalyzed transformations.[32−35] This in situ mode of energy conversion provides many benefits to the organic chemist since microwaves can heat the reaction mixture very rapidly, uniformly, and directly, without any problems of heat transfer through the walls of the reaction vessel.[36] The reactions were conducted with a commercially available single-mode microwave cavity in septum-sealed heavy-walled Pyrex tubes. To survey the scope of this heating methodology, the vinyl triflates **2a** and **2c**, the dienyl triflate **2g**, and the slowly reacting vinyl bromide **2f** were selected as representative vinylating agents. The experiments were performed without stirring in DMSO; a solvent that possesses a very high dissipation factor (tan $\delta = 0.825$ at rt).[37,38] Microwave treatment with 5−25 W magnetron input power for 5.0−7.0 min resulted in complete conversion and almost identical isolated yields to what was experienced under classical, thermal heating (entries 1, 2, 5, 6, and 11−14). To obtain full conversion of **2**, it was highly important to find the correct balance between microwave power and irradiation time. The preparations of **3c**, **3g**, **4a**, **4c**, **4f**, and **4g** were successfully accelerated, and high α/β ratios (>98/2) were encountered. The high α-selectivity (**3/5**) was partly lost in entries 1 and 11. The preparative results are shown in Table 1.

The important issue of the actual reaction temperature under microwave irradiation has previously not been addressed in context with palladium-catalyses in closed reaction vessels, as no suitable equipment for temperature measurements was available.[39] However, the use of fluoroptic probes[40] has now allowed the determination of temperature/time/power profiles.[41] Figure 1 describes the temperature profiles for septum-sealed Heck reactions (entries 2, 5, 11, and 12) in DMSO medium under 5−7 min of irradiation at various power inputs. A microwave power of 20−25 W for 5−7 min rapidlyproduced high temperatures (192−216 °C), which apparently had a negative impact on the regiocontrol in one of the

(24) To ensure full conversion of the vinyl bromide or vinyl triflate and to suppress homocoupling, 5 equiv of **1a** was utilized.
(25) *Caution! Thallium acetate is a very toxic salt.*
(26) Grigg, R.; Loganathan, V.; Santhakumar, V.; Sridharan, V.; Teasdale, A. *Tetrahedron Lett.* **1991**, *32*, 687−690.
(27) α,β-Unsaturated dioxolanes are very sensitive to hydrolysis, even that occurring on silica gel or on alumina columns. See refs 28−30.
(28) Huet, F.; Pellet, M.; Conia, J. M. *Tetrahedron Lett.* **1977**, 3505−3508.
(29) Brown, J. J.; Lenhard, R. H.; Bernstein, S. *J. Am. Chem. Soc.* **1964**, *86*, 2183-2187.
(30) Becker, D.; Brodsky, N. C.; Kalo, J. *J. Org. Chem.* **1978**, *43*, 2557−2562.
(31) Kim, S.; Kim, Y. G.; Kim, D.-I. *Tetrahedron Lett.* **1992**, *33*, 2565−2566.
(32) Larhed, M.; Hallberg, A. *J. Org. Chem.* **1996**, *61*, 9582−9584.
(33) Bremberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *J. Org. Chem.* **1999**, *64*, 1082−1083.
(34) Olofsson, K.; Kim, S.-Y.; Larhed, M.; Curran, D. P.; Hallberg, A. *J. Org. Chem.* **1999**, *64*, 4539−4541.
(35) Alterman, M.; Andersson, H. O.; Garg, N.; Ahlsen, G.; Lövgren, S.; Classon, B.; Danielson, U. H.; Kvarnström, I.; Vrang, L.; Unge, T.; Samuelsson, B.; Hallberg, A. *J. Med. Chem.* **1999**, *42*, 3835−3844.
(36) Cundy, C. S. *Collect. Czech. Chem. Commun.* **1998**, *63*, 1699−1723.
(37) Generally, solvents with tan δ greater than 0.1 are effective in microwave flash heating. See ref 38.
(38) Gabriel, C.; Gabriel, S.; Grant, E. H.; Halstead, B. S. J.; Mingos, D. M. P. *Chem. Soc. Rev.* **1998**, *27*, 213−223.
(39) Clearly, in the absence of a correct temperature profile, a reaction may not be reproducible when different microwave heating systems are used.
(40) Mingos, D. M. P.; Whittaker, A. G. In *Chemistry Under Extreme or Non-Classical Conditions*; Van Eldik, R., Hubbard, C. D., Eds.; John Wiley & Sons and Spektrum Akademischer Verlag: New York, 1997; pp 479−514.
(41) Kaiser, N.-F. K.; Bremberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *J. Organomet. Chem.*, in press.

Table 1. Thermal and Microwave-Heated Synthesis of Alkoxy Dienes 3 and Cyclic Acetals 4[i]

entry	vinyl triflate or vinyl bromide	vinyl ether	reaction conditions: additive	method	thermal/microwave[a]	product		α/β[b]	isolated yield[c] (%)
1	 **2a**	**1a**[d]	-	A A	20 h 40 °C 5 min 10 W		**3a**	98/2 90/10	86 66[e]
2		**1b**	-	A A	20 h 40 °C 5 min 10 W		**4a**	>99/1 >99/1	68[f] 67
3	 **2b**	**1a**	-	B	20 h 60 °C		**3b**	>99/1	73
4		**1b**	-	A	20 h 40 °C		**4b**	>99/1	51[f]
5	 **2c**	**1a**	- -	A A	20 h 40 °C 5 min 5 W		**3c**	>99/1 >99/1	87 73
6		**1b**	- -	A A	20 h 40 °C 5 min 5 W		**4c**	>99/1 >99/1	69[f] 89
7	 **2d**	**1a**	TlOAc	B	30 h 60 °C		**3d**	>99/1	55
8		**1b**	TlOAc	A	68 h 40 °C		**4d**	>99/1	67
9	 **2e**	**1a**	TlOAc	A	168 h 60 °C		**3e**	>99/1	10[g]
10		**1b**	TlOAc	A	20 h 60 °C		**4e**	>99/1	56[h]
11	 **2f**	**1a**	TlOAc TlOAc	B A	144 h 80 °C 5 min 25 W		**3f**	98/2 80/20	41 57[e]
12		**1b**	TlOAc TlOAc	A A	240 h 100 °C 7 min 20 W		**4f**	>99/1 >99/1	32 45
13	 **2g**	**1a**	- -	A A	6 h 60 °C 5 min 5 W		**3g**	>99/1 >99/1	79 64
14		**1b**	- -	A A	20 h 40 °C 7 min 5 W		**4g**	>99/1 >99/1	59 53

[a] Continuous irradiation (2450 MHz, Microwell 10, magnetron input power 5−25 W). [b] Determined by GC/MS and NMR. [c] Greater than 95% purity by GC/MS. [d] A 10.0 equiv sample of vinyl ether was utilized to suppress homocoupling. [e] Isolated as a mixture of α- and β-regioisomers (**3** + **5**). [f] Dry HOAc was added for ring-closure. [g] *E*/*Z* > 97/3, determined by NOE. [h] *E*/*Z* = 90/10, was determined by NOE. [i] Reaction conditions: (method A) 1.0 equiv of **2a**−**g**, 2.0 equiv of vinyl ether, 3 mol % $Pd(OAc)_2$, 6 mol % DPPP, 1.5 equiv of Et_3N, molecular sieves (4 Å) in DMSO under N_2; (method B) 1.0 equiv of **2b**,**d**,**f**, 2.0 equiv, 5.0 equiv of vinyl ether, 3 mol % $Pd(OAc)_2$, 6 mol % tol-BINAP, 1.5 equiv of K_2CO_3, molecular sieves (4 Å) in DMSO under N_2. Reactions were conducted in Pyrex tubes sealed with a silicon septum.

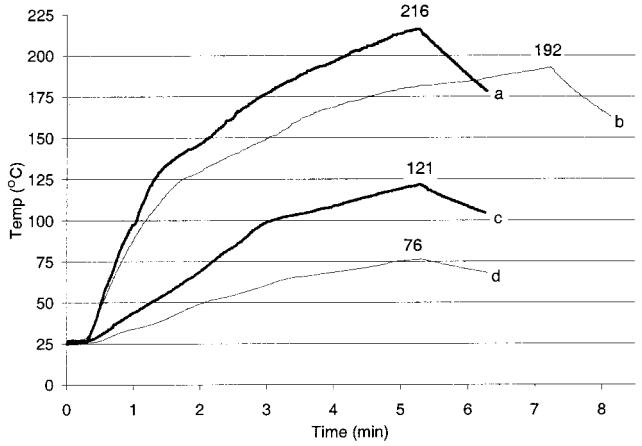


Figure 1. Temperature profiles for Heck reactions in DMSO: (a) 5 min and 25 W (entry 11); (b) 7 min and 20 W (entry 12); (c) 5 min and 10 W (entry 2); (d) 5 min and 5 W (entry 5). Different organohalides or organotriflates did not change the temperature profiles. The data collection time started 20 s before and finished 60 s after the irradiation time of 5 min. Temperature profiles were recorded using fluoroptic probes.

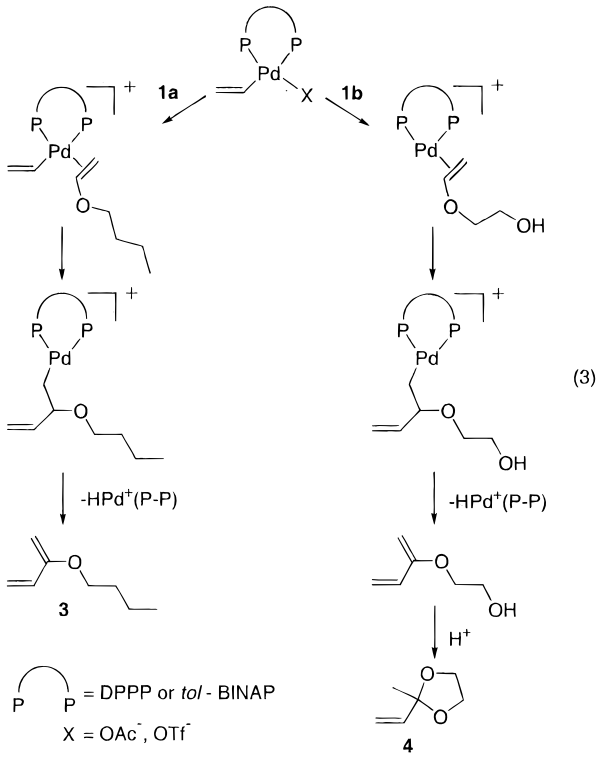
insertions (entry 11). With the highest power (25 W) considerable superheating is noted (bp(DMSO) = 189 °C).

Since the energy carried by microwaves at the output frequency of 2450 MHz is too small (~1 J/mol) to induce any noteworthy direct molecular activation,[36] the overall advantage of microwave heating lies in the direct rapid in situ heating and in the bulk superheating that easily can be achieved.[42,43] We believe these factors alone can account for the accelerated reaction rates.

Discussion

Intermolecular Heck vinylations generally proceed with more unpredictable regio- and stereochemical outcome as compared to the corresponding Heck arylations.[9] The selectivity is often low, but with certain alkenes, e.g., acrylates, acrylonitriles, or vinylglycine, a range of successful terminal β-vinylation procedures have been reported.[44−46] Furthermore, examples of α-vinylations of alkyl vinyl ethers have previously been disclosed by us.[17] The synthesis of the vinyl acetals and alkoxy dienes reported herein relies on a highly regioselective vinyl group insertion encountered with cationic π-complexes (eq 3).[8] These cationic intermediates are created by spontaneous dissociation of the weakly coordinating triflate anion[47] or, when vinyl bromides are utilized, by addition of thallium acetate.[16] The bidentate ligands introduced by Cabri et al.[16] to promote internal arylation of electron-rich olefins ensure that the reaction follows the cationic route.[48] Importantly, the same α/β ratio was regularly found with **1a** and **1b**, and the only deviation from this general observation was noted in the microwave-accelerated vinylation of **2a** and **2f** (entries 1 and 11, Table 1). This new ligand-controlled and highly selective procedure for internal Heck vinylation of **1a** is superior to the previously reported methodology.[17]

The cyclization of the α-vinylated **1b** to the corresponding acetal is probably not catalyzed by palladium.[5] The ring closure most likely occurs via an initial protonation at the terminal β-position[49−52] (by $HNEt_3^+$ or HOAc) of the α-vinyl-substituted vinyl ether followed by an intramolecular nucleophilic attack by the hydroxyl group at the oxygen-stabilized cation (eq 3).[23,53]



(3)

Conclusion

In conclusion, the palladium-catalyzed 2-alkoxy-1,3-diene synthesis provides a facile and experimentally very simple alternative to other more elaborate cross-coupling methodologies. In view of the known difficulties in preparing selectively monoblocked dicarbonyl compounds, we also believe that the direct preparation of 2-alkene-2-methyl-1,3-dioxolanes from vinyl triflates or bromides constitutes a valuable new method. The procedure also provides a mild synthetic method for the transformation of ketones, via their vinyl triflates, into protected α,β-unsaturated methyl ketones, a class of compounds that are not easily acquired by other methods.[29,54−58] Finally,

(42) Organic solvents superheat under microwave irradiation even at atmospheric pressure; see ref 43.
(43) Mingos, D. M. P. *Res. Chem. Intermed.* **1994**, *20*, 85−91.
(44) Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1991**, *32*, 1579−1582.
(45) Crisp, G. T.; Glink, P. T. *Tetrahedron* **1992**, *48*, 3541−3556.
(46) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427−436.
(47) Amatore, C.; Jutand, A. *J. Organomet. Chem.* **1999**, *576*, 254−278.
(48) The bidentate ligand DPPP (method A) or tol-BINAP (method B) delivered a higher α/β ratio than the monodentate PPh_3, which was employed in the initial studies.
(49) Jones, D. M.; Wood, N. F. *J. Chem. Soc.* **1964**, 5400−5403.
(50) Salomaa, P.; Kankaanperä, A.; Lajunen, M. *Acta Chem. Scand.* **1966**, *20*, 1790−1801.
(51) Kresge, A. J.; Chen, H. J. *J. Am. Chem. Soc.* **1972**, *94*, 2818−2822.
(52) Burt, R. A.; Chiang, Y.; Kresge, A. J.; Szilagyi, S. *Can. J. Chem.* **1984**, *62*, 74−76.
(53) Deslongchamps, P.; Dory, Y. L.; Li, S. G. *Helv. Chim. Acta* **1996**, *79*, 41−50.
(54) Acetal formation from α,β-unsaturated ketones using ethylene glycol and strong protic acids typically requires a large amount of acid and often leads to formation of undesirable side products (e.g., β,γ-unsaturated acetals). See refs 1, 2, 28−30, and 55−58.

application of microwave irradiation as the energy source resulted in dramatically shortened reaction times, from hours to a few minutes.

Experimental Section

General Procedure. All reactions were conducted under nitrogen in heavy-walled Pyrex tubes[59] sealed with a screwcap fitted with a Teflon gasket silicon septum. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ at 270 and 67.8 MHz. Mass spectra were recorded at an ionizing voltage of 70 eV (EI). The GC/MS was equipped with a HP-1 (25 m × 0.20 mm) capillary column. Isomers were assumed to have the same response factor. Column chromatography was performed using commercially available silica gel 60 (particle size 0.040−0.063 mm, Merck) or on basic alumina (aluminum oxide 90, 0.063−0.200 mm, Merck). Microwave heating was performed in a MicroWell 10 single-mode microwave cavity[60] from Personal Chemistry AB, producing continuous irradiation at 2450 MHz. Temperature profiles were recorded using a NoEMI-TS Reflex (NortechFibronic, Inc.) utilizing temperature-sensitive fluoroptic probes (TPP-01-M2.5-A; Nortech Fibronic). The probe was positioned 2 cm above the bottom of the reaction tube. The sampling rate was 3 Hz. After irradiation the samples were allowed to cool in the cavity for 1 min before being handled. The inner diameter of the Pyrex tubes was 11 mm, and the height of the reaction mixture in the tube was 22 mm. Contrary to conventional conductive heating, the rise in temperature is dependent on both the volume and the geometry of the reaction mixture. The reactions were performed without stirring. *Caution! Great care should be taken when pressurized microwave reactions are performed.*[61] Elemental analyses were performed by Micro Kemi AB, or Analytische Laboratories, Prof. Dr. H. Malissa and G. Reuter GmbH. High-resolution mass spectral (HRMS) data were performed by E. Nilsson, University of Lund. The isolated products **3a,b,d** have previously been characterized and the data obtained corresponded satisfactorily with MS and NMR literature data.[17]

Materials. Butyl vinyl ether (**1a**) (Aldrich), 2-hydroxyethyl vinyl ether (**1b**) (ethylene glycol vinyl ether, Aldrich) and DMSO (H_2O <0.01%, Fluka) were used as received. The vinyl triflates **2a**−**c,g** and the α-bromoketone **2f** are known compounds and were prepared by literature procedures.[62−64] α-Bromostyrene (**2d**) was purchased from Aldrich in >95% purity, and (*Z*)-α-bromocinnamaldehyde[65] (**2e**) was purchased from Acros. Triethylamine was distilled over potassium hydroxide, and acetic acid was dried with P_2O_5 prior to use. Palladium(II) acetate, thallium(I) acetate,[25] 1,3-bis(diphenylphosphino)propane (DPPP), oven-dried (300 °C for 48 h) molecular sieves (4 Å), (*R*)-(+)-2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl [(*R*)-(+)-*tol*-BINAP], and K_2CO_3 (oven-dried at 300 °C for 48 h) were purchased from commercial suppliers and were used directly as received. All reactions were performed until complete consumption of the starting vinyl halide or vinyl triflate was obtained, utilizing an appropriate choice of thermal heating time and temperature, or microwave power and irradiation time.

Synthesis of 2-Alkoxy-1,3-Dienes. General Method. Method A (3a,c,e,g). A mixture of the corresponding vinyl triflate or bromide (0.50 mmol), butyl vinyl ether (0.10 g, 1.0 mmol), $Pd(OAc)_2$ (0.0034 g, 0.0150 mmol), DPPP (0.012 g, 0.030 mmol), triethylamine (0.076 g, 0.750 mmol), molecular sieves (0.50 g/mmol, 0.25 g), and, if present, TlOAc (0.16 g, 0.60 mmol)[25] in 2.0 mL of dry DMSO was stirred under N_2 in a screwcap-sealed tube (for the reaction time and temperature see Table 1).

Method B (3b,d,f). A mixture of the corresponding vinyl triflate or bromide (0.50 mmol), butyl vinyl ether (0.100 g, 1.0 mmol), $Pd(OAc)_2$ (0.0034 g, 0.015 mmol), tol-BINAP (0.020 g, 0.030 mmol), K_2CO_3 (0.102 g, 0.750 mmol), molecular sieves (0.50 g/mmol, 0.25 g), and, if present, TlOAc (0.16 g, 0.60 mmol)[25] in 2.0 mL of dry DMSO was stirred under N_2 in a screwcap-sealed tube (for the reaction time and temperature see Table 1).

After complete conversion of the starting vinyl triflate or bromide as analyzed by GC/MS, the reaction mixture was allowed to cool. The reaction mixture was thereafter poured into 1 M NaOH and was extracted with diethyl ether. The combined organic layers were washed with brine and concentrated at reduced pressure. The product was purified by column chromatography or filtration (basic systems, >95% pure by GC/MS).

1-(1-Butoxyethenyl)cyclohexene (3a; entry 1, method A):[17] colorless oil; eluent diethyl ether, alumina; ^{1}H NMR ($CDCl_3$) δ 6.28−6.34 (m, 1H), 4.14 (d, 1H, J = 2.0 Hz), 3.98 (d, 1H, J = 2.0 Hz), 3.72 (t, 2H, J = 6.5 Hz), 2.09−2.21 (m, 4H), 1.36−1.79 (m, 8H), 0.95 (t, 3H, J = 7.3 Hz); ^{13}C NMR δ 160.6, 132.1, 124.8, 80.5, 66.8, 31.2, 25.4, 25.1, 22.7, 22.1, 19.5, 13.9; MS (70 ev) *m*/*z* (relative intensity) 180 (6, M^+), 165 (50), 109 (100).

2-Butoxy-4-ethyl-1,3-hexadiene (3b, entry 3, method B):[17] colorless oil; eluent diethyl ether, filtration through Celite and dry K_2CO_3: ^{1}H NMR ($CDCl_3$) δ 5.57 (s, 1H), 4.04 (d, 1H, J = 1.6 Hz), 3.98 (d, 1H, J = 1.6 Hz), 3.69 (t, 2H, J = 6.4 Hz), 2.35 (q, 2H, J = 7.5 Hz), 2.08 (dq, 2H, J = 1.3, 7.5 Hz), 1.64−1.75 (m, 2H), 1.28−1,53 (m, 2H), 1.03 (t, 3H, J = 7.5 Hz), 1.02 (t, 3H, J = 7.6 Hz), 0.95 (t, 3H, J = 7.5 Hz); ^{13}C NMR δ 160.2, 148.6, 119.3, 84.6, 67.0, 31.2, 30.3, 24.9, 19.5, 13.9, 13.5, 12.7; MS (70 ev) *m*/*z* (relative intensity) 182 (8, M^+), 125 (17), 111 (100).

4-(1-Butoxyvinyl)-7-methoxy-1,2-dihydronaphthalene (3c; entry 5, method A): white crystals; eluent pentane/diethyl ether (19/1, v/v) with 1% (v) triethylamine, silica gel; ^{1}H NMR ($CDCl_3$) δ 7.22 (d, 1H, J = 9.3 Hz), 6.69−6.72 (m, 2H), 6.16 (t, 1H, J = 4.6 Hz), 4.29 (d, 1H, J = 1.7 Hz), 4.22 (d, 1H, J = 1.7 Hz), 3.81 (s, 3H), 3.80 (t, 2H, J = 6.5 Hz), 2.76 (t, 2H, J = 8.0 Hz), 2.30 (dt, 2H, J = 8.0, 4.6 Hz), 1.72 (tt, 2H, J = 6.5, 7.4 Hz), 1.45 (sext, 2H, J = 7.4 Hz), 0.96 (t, 3H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 161.4, 158.4, 138.1, 136.1, 126.5, 126.4, 125.9, 113.4, 110.9, 84.9, 67.3, 55.2, 31.1, 28.4, 23.0, 19.4, 13.8; MS (70 ev) *m*/*z* (relative intensity) 258 (45, M^+), 186 (100), 115 (99). Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.97; H, 8.71.

2-Butoxy-3-phenyl-1,3-butadiene (3d; entry 7, method B):[17] pale yellow oil; eluent hexane with 3% (v) dimethylethylamine, silica gel; ^{1}H NMR ($CDCl_3$) δ 7.29−7.39 (m, 5H), 5.72 (s, 1H), 5.22 (s, 1H) 4.27−4.29 (m, 1H), 4.12 (d, 1H, J = 2.0 Hz), 3.81 (t, 2H, J = 6.3 Hz), 1.72−1.79 (m, 2H), 1.45−1.60 (m, 2H), 0.98 (t, 3H, J = 7.3 Hz); ^{13}C NMR δ 160.2, 145.9, 140.4, 128.7, 127.8, 127.4, 114.7, 87.4, 67.4, 31.1, 19.4, 13.9; MS (70 ev) *m*/*z* (relative intensity) 202 (21, M^+), 131 (91), 103 (100).

(55) de Leeuw, J. W.; de Waard, E. R.; Beetz, T.; Huisman, H. O. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 1047−1052.
(56) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357−1358.
(57) Otera, J.; Dan-oh, N.; Nozaki, H. *Tetrahedron* **1992**, *48*, 1449−1456.
(58) Torok, D. S.; Figueroa, J. J.; Scott, W. J. *J. Org. Chem.* **1993**, *58*, 7274−7276.
(59) Baghurst, D. R.; Mingos, D. M. P. *J. Chem. Soc., Dalton Trans 1* **1992**, 1151−1155.
(60) Stone-Elander, D. P.; Elander, N.; Thorell, J. O.; Solås, G.; Svennebrink, J. *J. Labeled Compd. Radiopharm.* **1994**, *34*, 949−960.
(61) Kingston, H. M.; Walter, P. J.; Engelhart, W. G.; Parsons, P. J. In *Microwave-Enhanced Chemistry*; Kingston, H. M., Haswell, S. J., Eds.; American Chemical Society: Washington, DC, 1997; pp 697−745.
(62) BordWell, F. G.; Wellman, K. M. *J. Org. Chem.* **1963**, *28*, 2544−2547.
(63) Pal, K. *Synthesis* **1995**, *12*, 1485−1487.
(64) Cacchi, S.; Morera, E.; Ortar, G. *Org. Synth.* **1990**, *68*, 138−147.
(65) The assignment of the stereochemistry for (*Z*)-α-bromocinnamaldehyde (**2e**) (Acros) is supported by NOE data, confirming the proximity of the vinylic proton to the formyl group. Similarly, the geometrical arrangement of the major product (*E*)-2-(1-formyl-2-phenylethenyl)-2-methyl-1,3-dioxolane (**4e**) is confirmed by NOE between the aldehyde proton and one of the aromatic protons and, to a lesser extent, between the vinylic proton and the methyl group. The assignment of the major product (3*E*)-2-butoxy-3-formyl-4-phenyl-1,3-butadiene (**3e**) is confirmed by NOE data between the aldehyde proton and the vinylic proton.

(3*E*)-2-Butoxy-3-formyl-4-phenyl-1,3-butadiene (3e; entry 9, method A):[65] colorless oil (mixture of geometrical isomers, *E*/*Z* = 97/3); eluent pentane/diethyl ether (1/1, v/v), alumina. Spectroscopic data are given for the major *E*-isomer: ^{1}H NMR ($CDCl_3$) δ 9.59 (s, 1H), 7.59−7.64 (m, 2H), 7.35−7.42 (m, 3H), 7.29 (s, 1H), 4.48 (d, 1H, *J* = 2.7 Hz), 4.22 (d, 1H, *J* = 2.7 Hz), 3.81 (t, 2H, *J* = 6.3 Hz), 1.55−1.67 (m, 2H), 1.24−1.38 (m, 2H), 0.88 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR δ 192.5, 153.9, 150.1, 137.7, 133.8, 130.7, 130.6, 128.5, 87.9, 67.4, 30.8, 19.2, 13.7; MS (70 ev) *m*/*z* (relative intensity) 230 (17, M^+), 173 (100), 145 (91). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.2; H, 7.9. Found: C, 78.2; H, 7.9.

2-(1-Butoxyvinyl)-4,4-dimethyl-2-cyclohexen-1-one (3f; entry 11, method B): colorless oil; eluent isohexane with 3% (v) dimethylethylamine, alumina; ^{1}H NMR ($CDCl_3$) δ 6.93 (s, 1H), 4.79 (d, 1H, *J* = 1.8 Hz), 3.98 (d, 1H, *J* = 1.8 Hz), 3.71 (t, 2H, *J* = 7.9 Hz, 2.49−2.54 (m, 2H), 1.82−1.88 (m, 2H), 1.64−1.75 (m, 2H), 1.36−1.50 (m, 2H), 1.30−1.12 (m, 6H), 0.92−1.98 (m, 3H); ^{13}C NMR δ 197.1, 156.2, 154.9, 132.1, 87.2, 66.9, 35.9, 35.7, 33.0, 31.0, 27.9, 19.4, 13.9; MS (70 eV) *m*/*z* (relative intensity) 222 (24, M^+), 207 (17), 165 (100), 151 (91); high-resolution MS (EI) calcd for $C_{14}H_{22}O_2$ (M^+) 222.1620, found 222.1619. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.6; H, 10.0. Found: C, 75.2; H, 10.2.

3-(1-Butoxyvinyl)pregna-3,5-dien-20-one (3g; entry 13, method A): white solid; eluent hexane/ethyl acetate (19/1, v/v), alumina, with 3% (v) triethylamine, alumina; ^{1}H NMR ($CDCl_3$) δ 6.49 (s, 1H), 5.54−5.57 (m, 1H) 4.22 (d, 1H, *J* = 2.1 Hz), 4.06 (d, 1H, *J* = 2.1 Hz), 3.72 (t, 2H, *J* = 6.2 Hz), 2.49−2.57 (m, 1H), 2.11 (s, 3H), 0.89−1.97 (m, 3H), 0.92 (s, 3H), 0.66 (s, 3H); ^{13}C NMR δ 209.4, 160.2, 141.6, 129.1, 125.6, 125.4, 81.8, 66.9, 57.0, 48.1, 46.2, 44.1, 38.8, 34.8, 33.9, 31.9, 31.7, 31.4, 31.2, 24.4, 22.8, 22.6, 21.1, 19.5, 18.9, 13.9, 13.3; high-resolution MS (EI) calcd for $C_{27}H_{40}O_2$ (M^+) 396.3028, found 396.3029. Anal. Calcd for $C_{27}H_{40}O_2$: C, 81.8; H, 10.2. Found: C, 80.9; H, 10.0.

Synthesis of 2-Alkenyl-2-methyl-1,3-dioxolanes (4a−g). General Method. A mixture of the corresponding vinyl triflate or bromide (2.0 mmol), 2-hydroxyethyl vinyl ether (0.35 g, 4.0 mmol), $Pd(OAc)_2$ (0.013 g, 0.060 mmol), DPPP (0.049 g, 0.120 mmol), triethylamine (0.30 g, 3.0 mmol), molecular sieves (0.5 g/mmol, 1.0 g), and, if present, TlOAc (0.63 g, 2.4 mmol)[25] in 6.0 mL of dry DMSO was stirred under N_2 in a screwcap-sealed tube (for the reaction time and temperature see Table 1). After complete conversion of the starting vinyl triflate or bromide (GC/MS), the reaction mixture was allowed to cool (entries 8, 10, 12, and 14), or alternatively, the reaction mixture was stirred with 2.0 mL of dry acetic acid for an additional 30 min at 40 °C (accomplishing complete ring-closure, entries 2, 4, and 6). The reaction mixture was thereafter poured into 1 M NaOH and was extracted with diethyl ether. The combined organic layers were washed with brine and concentrated at reduced pressure. The product was purified by column chromatography (basic systems, >95% pure by GC/MS).

2-(1-Cyclohexen-1-yl)-2-methyl-1,3-dioxolane (4a; entry 2): colorless oil; eluent pentane/diethyl ether (29/1, v/v) with 4% (v) dimethylethylamine, silica gel; ^{1}H NMR ($CDCl_3$) δ 5.86−5.83 (m, 1H), 3.89−3.78 (m, 4H), 2.06−1.96 (m, 4H), 1.66−1.49 (m, 4H), 1.43 (s, 3H); ^{13}C NMR δ 137.7, 122.6, 109.6, 64.5, 24.9, 24.0, 23.9, 22.9, 22.4; MS (70 eV) *m*/*z* (relative intensity) 168 (1, M^+), 153 (100), 87 (53); high-resolution MS (CI, CH_4) calcd for $C_{10}H_{17}O_2$ (M^+ + 1) 169.1229, found 169.1229. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.4; H, 9.6. Found: C, 71.7; H, 10.6.

2-(2-Ethyl-1-butenyl)-2-methyl-1,3-dioxolane (4b; entry 4): pale yellow oil; eluent pentane with 2% (v) dimethylethylamine, silica gel; ^{1}H NMR ($CDCl_3$) δ 5.18 (s, 1H), 3.96−3.83 (m, 4H), 2.27 (q, *J* = 7.5 Hz, 2H), 2.00 (dq, *J* = 7.5, 1.3 Hz, 2H), 1.48 (s, 3H), 0.99 (t, *J* = 7.5 Hz, 3H), 0.98 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR δ 148.6, 124.8, 108.5, 64.2, 28.9, 26.0, 23.6, 13.3, 12.9; MS (70 eV) *m*/*z* (relative intensity) 155 (100), 111 (14), 87 (34); high-resolution MS (CI, CH_4) calcd for $C_{10}H_{19}O_2$ (M^+ + 1) 171.1385, found 171.1383. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.5; H, 10.7. Found: C, 69.9; H, 10.6.

2-(3,4-Dihydro-6-methoxy-1-naphthyl)-2-methyl-1,3-dioxolane (4c; entry 6): white crystals; eluent pentane/triethylamine (5/1, v/v), silica gel; ^{1}H NMR ($CDCl_3$) δ 7.77−7.73 (m, 1H), 6.75−6.71 (m, 2H), 6.25 (t, *J* = 4.6 Hz, 1H), 4.05−3.85 (m, 4H), 3.81 (s, 3H), 2.70 (t, *J* = 7.6 Hz, 2H), 2.29−2.22 (m, 2H), 1.66 (s, 3H); ^{13}C NMR δ 158.3, 139.5, 136.7, 126.9, 125.7, 123.9, 113.8, 110.9, 109.2, 64.3, 55.4, 29.3, 26.1, 22.8; MS (70 eV) *m*/*z* (relative intensity) 246 (65, M^+), 231 (100), 159 (28), 87 (84). Anal. Calcd for $C_{15}H_{18}O_2$: C, 73.1; H, 7.4. Found: C, 73.1; H, 7.4.

2-Methyl-2-(1-phenylvinyl)-1,3-dioxolane (4d; entry 8): yellow oil; eluent pentane/diethyl ether (19/1, v/v), alumina; ^{1}H NMR ($CDCl_3$) δ 7.54−7.49 (m, 2H), 7.37−7.29 (m, 3H), 5.57 (d, *J* = 1.6 Hz, 1H), 5.27 (d, *J* = 1.6 Hz, 1H), 4.09−3.96 (m, 4H), 1.50 (s, 3H); ^{13}C NMR δ 149.2, 139.7, 128.4, 128.1, 127.5, 115.0, 109.2, 64.6, 25.2; MS (70 eV) *m*/*z* (relative intensity) 190 (2, M^+), 87 (100), 43 (27). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.8; H, 7.4. Found: C, 76.0; H, 7.6.

2-(1-Formyl-2-phenylethen-1-yl)-2-methyl-1,3-dioxolane (4e; entry 10): yellow solid (mixture of geometrical isomers, *E*/*Z* = 90/10);[65] eluent pentane/diethyl ether (1/1, v/v), alumina. Spectroscopic data are given for the major *E*-isomer: ^{1}H ($CDCl_3$) NMR δ 9.86 (s, 1H), 7.93 (s, 1H), 7.43−7.31 (m, 5H), 4.10−4.00 (m, 2H), 3.98−3.89 (m, 2H), 1.72 (s, 3H); ^{13}C NMR δ 191.8, 145.0, 140.5, 133.3, 130.3, 129.7, 128.6, 107.8, 64.8, 25.5; MS (70 eV) *m*/*z* (relative intensity) 218 (13, M^+), 203 (49), 87 (100). Anal. Calcd for $C_{13}H_{14}O_2$: C, 71.5; H, 6.5. Found: C, 71.6; H, 6.5.

2-(2-(4,4-Dimethyl-2-cyclohexene-1-one))-2-methyl-1,3-dioxolane (4f; entry 12): pale yellow oil; eluent pentane/diethyl ether (2.5/1, v/v), alumina; ^{1}H NMR ($CDCl_3$) δ 6.80 (s, 1H), 3.99−3.89 (m, 2H), 3.85−3.72 (m, 2H), 2.48−2.42 (m, 2H), 1.84−1.78 (m, 2H) 1.78 (s, 3H) 1.33−1.12 (m, 6H); ^{13}C NMR δ 197.8, 155.0, 135.7, 107.3, 64.5, 35.9, 35.8, 32.6, 29.7, 25.1; MS (70 eV) *m*/*z* (relative intensity) 210 (2, M^+), 195 (28), 87 (100). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.5; H, 8.6. Found: C, 68.3; H, 8.7.

2-(17β-Acetylandrosta-3,5-diene-3-yl)-2-methyl-1,3-dioxolane (4g; entry 14): white solid; eluent hexane with 3% (v) triethylamine, alumina; ^{1}H NMR ($CDCl_3$) δ 6.10 (s, 1H), 5.48−5.45 (m, 1H), 4.01−3.77 (m, 4H), 2.58−2.51 (m, 1H), 2.13 (s, 3H), 1.49 (s, 3H), 0.91 (s, 3H), 0.66 (s, 3H); ^{13}C NMR δ 209.7, 141.2, 135.9, 124.5, 109.3, 64.7, 64.4, 63.9, 57.3, 48.3, 44.3, 39.0, 35.0, 34.2, 32.0, 31.8, 24.6, 24.1, 23.0, 21.8, 19.1, 13.6; MS (70 eV) *m*/*z* (relative intensity) 384 (4, M^+), 369 (100), 87 (20); high-resolution MS (CI, CH_4) calcd for $C_{25}H_{37}O_3$ (M^+ + 1) 385.2743. Found: 385.2726. Anal. Calcd for $C_{25}H_{36}O_3$: C, 78.1; H, 9.4. Found: C, 77.2; H, 9.4.

Synthesis of Alkoxy Dienes (3a,c,f,g) and 2-Alkene-2-Methyl-1,3-Dioxolanes (4a,c,f,g) Using Microwave Irradiation. General Method. Dry nitrogen gas was for 90 s passed through a reaction mixture prepared exactly as in the thermal synthesis of 2-alkoxy-1,3-dienes or synthesis of 2-alkene-2-ethyl-1,3-dioxolanes (method A) on a 0.5 mmol scale. The reaction tube was sealed (finger-tight) before the contents were mixed with a Whirlimixer. Heating was therafter applied by means of microwave irradiation (see Table 1 for details). After irradiation, the reaction tube was allowed to cool in the microwave cavity for 1 min before any handling of the mixture took place. When the reaction tube had reached rt, the purification was performed as previously presented for the thermal reactions.

Acknowledgment. We gratefully acknowledge the support from the Swedish Natural Science Research Council. We also thank Dr. Adolf Gogoll for the determination of the stereochemistry of (*Z*)-α-bromocinnamaldehyde and (*E*)-2-(1-formyl-2-phenylethen-1-yl)-2-methyl-1,3-dioxolane.

JO000070O