Synthesis and Herbicidal Activity of 2α,4α-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one Derivatives†

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The catalytic oxidation of 2α,4α-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one with osmium tetraoxide and excess hydrogen peroxide resulted in the formation of 2α,4α-dimethyl-6,7-*exo*-isopropylidenedioxy-8-oxabicyclo[3.2.1]octan-3-one (**2**), with 91% yield. Addition of aryllithium reagents to this compound resulted in the formation of the aromatic alcohols (**6a**−**h**) with 48−76% yield. These alcohols were treated with thionyl chloride in pyridine, and the corresponding alkenes (**7a**−**h**) were obtained with 46−80% yield. The effect of compounds **6a**−**h** and **7a**−**h** on the root growth of *Sorghum bicolor* was evaluated at a concentration of 6.6 μg g^{-1}. The alcohols **6a**−**h** caused an inhibitory effect (8−100%) on the *S. bicolor* radicle growth. The three most active compounds were **6e** (aryl = *p*-methylphenyl), **6g** (aryl = *p*-chlorophenyl), and **6h** (aryl = *p*-fluorophenyl) and caused 100% inhibition. The effect of alkenes **7a**−**h** was less pronounced and varied from 15% to 46% inhibition. Another experiment was carried out in a greenhouse to evaluate the effect of alcohols **6e**, **6g**, and **6h**, at a 6.6 μg g^{-1} dose, against *Cucumis sativus*, *S. bicolor* and the weeds *Bidens pilosa*, *Desmodium tortuosum*, and *Pennisetum setosum*. All three compounds showed an inhibitory effect on the development of the aerial parts (26−73%) and roots (13−79%) of the weeds and crops.

Keywords: *[3 + 4] cycloaddition; herbicides; plant growth regulators; weeds*

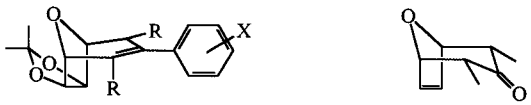
INTRODUCTION

Since the discovery, in 1946, of the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D), the agrochemical industry has successfully developed a wide array of selective herbicides (Tomlin, 1994). Despite the reported environmental and ecological problems caused by the herbicides and also by other crop protection agents, they continue to be used and are largely responsible for the increasing food production (Best and Ruthven, 1995; Klassen, 1995).

A major problem associated with the use of herbicides is the occurrence of herbicide-resistant weeds (Jasieniuk et al., 1996). The 1995−1996 *International Survey of Herbicide-Resistant Weeds* recorded 183 herbicide-resistant weed biotypes in 42 countries (Heap, 1997). As a consequence of this phenomenon, there is a continuous need for the development of new products with a new mode of action.

We have been involved in a research program directed toward the development of new herbicides and plant growth regulatory compounds, derived from the easily available 8-oxabicyclo[3.2.1]oct-6-en-3-one (**2**) (Barbosa et al.,1993; Barbosa et al.,1997; Demuner et al., 1998).

We have discovered that compounds having the general structure 3-aryl-6,7-*exo*-isopropylidenedioxy-8-oxabicyclo[3.2.1]oct-2-ene (**1**) (Figure 1) exibit a strong herbicidal activity against several crops and weeds. The substitution pattern of the aromatic ring was shown to influence the biological activity. For example, compound **1**, having X= *m*-methyl, at a dose of 6.6 μg g^{-1}, caused 100% mortality of the two important weeds *Desmodium tortuosum* and *Pennisetum setosum* (Conceição, 1995), while X=*p*-NMe_2 had no effect on the same plants.



1 R= H, X= H, alkyl, Cl, F, NMe_2, OCH_3
7 R= CH_3, X= H, alkyl, Cl, F, NMe_2, OCH_3

2

Figure 1. Generic structures for the new class of herbicidal heterocyclic compounds.

In this work, we describe the results of the preparation (Scheme 1) and biological activity of a new series of compounds, having the general structure (**7**), derived from the oxabicyclooctenone (**2**).

MATERIALS AND METHODS

Experimental Chemistry. All melting points were obtained with an Electrothermal digital apparatus and were corrected. Infrared spectra were measured on a FTIR 3000 Mattson Instruments using a potassium bromide disk or a sodium chloride liquid film cell, scanning from 625 to 4000 cm^{-1}. Mass spectra were recorded under electron-impact (70 eV) or chemical ionization (NH_3) conditions using a VG ANALYTICAL ZAB-IF high-resolution spectrometer. ^{1}H and ^{13}C NMR spectra, respectively, were recorded on a JEOL EX400 (400 and 100.53 MHz) spectrometer, using tetramethylsilane (TMS) as internal standard. Coupling constants (J) are given in Hertz. R_f's were determined by thin-layer chromatography on a 0.25 mm film of silica gel containing the UV_{254} fluorescent indicator supported on a plastic sheet (Camlab plc.). Chromatographic purification were carried out

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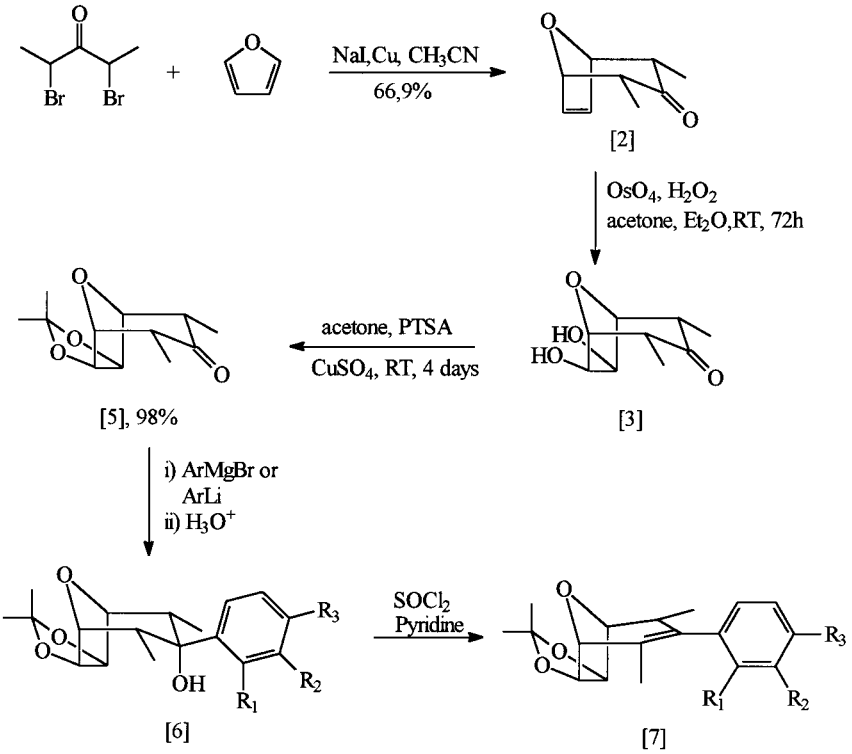
Scheme 1



using silica gel (63−230 μm). Reagents and the solvents used were purified according to the procedures described by Perrin and Armarego (1988).

Synthesis. 2,4-Dibromopentan-3-one. A two-necked, 250 mL flask was fitted with an overhead stirrer, a dropping funnel, and a condenser. Bromine (20 mL, 62.04 g, 338 mmol) was added dropwise to a stirred ice-cooled solution of pentan-3-one (20 mL, 198 mmol) and phosphorus tribromide (1 mL, 2.85 g, 10 mmol). After complete addition of bromine, the reaction was allowed to warm to 5−10 °C and stirred for an additional 16 h. The flask was then evacuated with a water pump to remove the dissolved hydrogen bromide, and the resultant blue solution formed was distilled under reduced pressure to yield (43.4 g, 178 mmol) 89.9% of the required bromopentanone as a pale yellow oil: IR (film, cm^{-1}) $\bar{\nu}_{max}$ 2980, 2900, 1725, 1464, 1340, 1190, 940, 850; ^{1}H NMR ($CDCl_3$) δ 1.90 (d, 6H, $J = 7.0$, 2 × CH_3), 5.10 (q, 2 H, $J = 7.0$, 2 × CHBr).

2α,4α-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (2). A 1 L two-necked round-bottom flask was fitted with a 100 mL dropping funnel, and dry acetonitrile (200 mL) was added. Dry NaI (90 g, 0.6 mol) was added with vigorous stirring under a slow stream of nitrogen. Then powdered copper (20 g, 0.314 mmol) was added, followed by furan (30 mL, 0.4 mol). A solution of 2,4-dibromopentan-3-one (29.04 g, 0.12 mol) in dry acetonitrile (50 mL) was added, by means of a dropping funnel, during 50 min, at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for an additional 12 h. After that time, the flask was cooled to 0 °C, and dichloromethane (150 mL) was added. The resultant mixture was then poured into a conical flask containing water (500 mL) and crushed ice (500 mL) and thoroughly stirred to allow the precipitation of copper salts. After filtration through a Celite pad, the mother liquor was washed with aqueous NH_3 solution (45% v/v, 3 × 20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated under reduced pressure to leave a pale yellow oil. Purification by flash chromatography (2:1 petroleum ether/ether) gave 66.9% (12.2 g, 80 mmol) overall yield of the required product **2** as a pale yellow oil: IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3080, 2960, 2910, 1710, 1450, 1340, 1170, 1050, 945; ^{1}H NMR ($CDCl_3$) δ 1.01 (d, 6H, $J = 7.0$, 2αMe), 2.85 (q, 2H, $J_{2,Me} = J_{4,Me} = 7.0$, H2 and H4), 4.80 (d, 2H, $J_{5,4} = J_{1,2} = 5.5$, H1 and H5), 6.40 (s, 2H, H6 and H7).

2α,4α-Dimethyl-6,7-*exo*-isopropylidenedioxy-8-oxabicyclo[3.2.1]octan-3-one (5). To a stirred solution of 2α,4α-dimethyl-8-oxabicyclo[3.2.1]octan-3-one **2** (14.0 g, 92.1 mmol) in acetone (60 mL) and diethyl ether (10 mL) was added a solution of osmium tetraoxide (2.5% w/w in *tert*-butyl alcohol, 3.0 mL, 0.24 mmol), followed by hydrogen peroxide (30%, 10 mL, 88 mmol). A cloudy brown suspension was produced, and this was stirred, in the dark, at room temperature for 72 h. After this period of time the mixture had changed to a chalky white appearance, and TLC analysis showed that all starting material had been consumed. In a few occasions when the reaction was repeated, a white solid was formed in variable amounts (0−9%), and it was then removed by filtration and identified as the dimer **4**. The reaction was then quenched by addition of $Na_2S_2O_3$(s) until complete decomposition of the excess of the hydrogen peroxide. After filtration, the solvent was removed under reduced pressure to yield a viscous clear oil. This oil was dissolved in dry acetone (70 mL), and to the resultant solution were added *p*-toluenesulfonic acid (0.08 g) and anhydrous $CuSO_4$ (5 g). After the solution was stirred at room temperature for 4 days, the solid material was removed by filtration and $NaHCO_3$ was added to the resultant solution to neutralize the acid. The solvent was then removed under reduced pressure, and the white solid obtained was purified by flash column chromatography (hexane/diethyl ether 2:1) to give 91% yield (18.9 g, 83.8 mmol) of the required product **3**: mp 86−88 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3400, 2990, 2930, 1710, 1390, 1275, 1230, 1205, 1175, 1080, 1050, 810, 680; ^{1}H NMR ($CDCl_3$) δ 1.01 (d, 6H, $J = 7.0$, 2αMe), 1.27 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 2.79 (dq, 2H, $J_{2,Me} = J_{4,Me} = 7.0$, $J_{2,1} = J_{4,5} = 5.5$, H2 and H4), 4.37 (d, 2H, $J_{1,2} = J_{5,4} = 5.5$, H1 and H5), 4.39 (s, 2H, H6 e H7); ^{13}C NMR ($CDCl_3$) δ 208.43 (C3), 111.72 (CMe_2), 85.34 (C6 and C7), 80.12 (C1 and C5), 48.32 (C2 and C4), 25.88 (Me), 24.47 (Me), 9.34 (Me).

Data for insoluble dimer byproduct **4**: mp 250−253 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3420, 3000, 2950, 2900, 1710, 1470, 1375, 1160, 1110, 1060, 1040, 950, 840, 810; ^{1}H NMR ($CDCl_3$) δ 1.03 (d, 3H, $J = 7.0$, Me), 1.05 (d, 3H, $J = 7.0$, Me), 2.72 (d, 1H, $J_{OH,7} = 9.1$, H8), 2.75−2.79 (m, 2H, H2 and H4), 3.69 (d, 1H, $J_{6,7} = 6.2$, H6), 4.04 (dd, 1H, $J_{7,6} = 6.2$, $J_{7,OH} = 9.1$, H7), 4.36 (d, 1H, $J_{1,2} = 4.7$, H1), 4.37 (d, 1H, $J_{5,4} = 5.1$, H5); ^{13}C NMR ($CDCl_3$) δ 208.00 (C3), 89.09 (C6), 86.06 (C5), 80.32 (C1), 71.45

Table 1. Synthesized 2α,4α-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one Derivatives

R_1	R_2	R_3	compd	yield (%)	compd	yield (%)
H	H	H	**6a**	68	**7a**	67
H	H	OMe	**6b**	60	**7b**	72
Me	H	H	**6c**	48	**7c**	56
H	Me	H	**6d**	55	**7d**	80
H	H	Me	**6e**	76	**7e**	63
H	H	NMe_2	**6f**	61	**7f**	46
H	H	Cl	**6g**	69	**7g**	64
H	H	F	**6h**	66	**7h**	64

(C7), 48.70 (C2), 48.26 (C4), 9.36 (CH_3), 9.21 (CH_3); MS *m/z* 354.1566 (M^+, $C_{18}H_{26}O_7$ requires 354.1678, 5), 337 (24), 239 (87), 197 (100), 169 (38), 152 (28), 137 (20), 125 (35), 111 (21), 96 (40), 81 (26), 69 (18), 55 (12), 41 (17).

Typical Procedure for the Preparation of the Alcohols 6a−h. To a round-bottom flask was added the aryl bromide (4.7 mmol) in dry THF (40 mL), and the system was kept under nitrogen atmosphere at −78 °C. To this solution was added butyllithium (1.6 M solution in hexane, 5 mmol), and the reaction mixture was stirred for 1 h before the addition of the acetonide **5** (2.2 mmol in 5 mL of dry THF). The resultant reaction mixture was allowed to warm to room temperature and stirred for a further 12 h when it was quenched by addition of water (20 mL). The product was extracted with ethyl acetate (5 × 30 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to give a white solid. This solid was purified by column chromatography (hexane/diethyl ether 2:1) to produce the required alcohols **6a−h**. The yields for the reactions are presented in Table 1.

Data for **6a**: mp 198−200 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3490, 2985, 2850, 1500, 1440, 1400, 1360, 1280, 1200, 1160, 1100; ^{1}H NMR ($CDCl_3$) δ 0.73 (d, 6H, J = 7.3, 2 × Me), 1.39 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.66 (s, 1H, OH), 2.39 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$ = 7.3, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 4.13 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4.0, H1 and H5), 5.09 (s, 2H, H6 and H7), 7.28−7.37 (m, 5H-aromatic); ^{13}C NMR ($CDCl_3$) δ 144.88 (C1′), 128.23 (C3′ and C5′), 126.95 (C4′), 124.87 (C2′ and C6′), 111.06 (CMe_2), 84.25 (C6 and C7), 80.63 (C1 and C5), 76.7 (C3), 42.65 (C2 and C4), 26.18 (Me), 24.63 (Me), 9.60 (Me); MS *m/z* 289 ([M − 15]$^+$, 100), 229 (10), 211 (8), 176 (8), 159 (6), 134 (13), 105 (72), 77 (18), 43 (26).

Data for **6b**: mp 211−213 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3495, 3010, 2970, 2950, 2800, 1600, 1500, 1450, 1320, 1250, 1200, 1100, 1050, 820, 760, 700; ^{1}H NMR ($CDCl_3$) δ 0.71 (d, 6H, J = 7.2, 2xMe), 1.36 (s, 3H, Me), 1.51 (s, 3H, Me), 1.86 (s, 1H, OH), 2.32 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$=7.2, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 3.78 (s, 3H, OMe), 4.09 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4.0, H1 and H5), 5.06 (s, 2H, H6 and H7), 6.86 (d, 2H, J = 8.9, H3′ and H5′), 7.26 (d, 2H, J = 8.9, H2′and H6′); ^{13}C NMR ($CDCl_3$) δ 158.18 (C4′), 136.83 (C1′), 126.21 (C2′ and C6′), 113.41 (C3′and C5′), 110.87 (CMe_2), 84.30 (C6 and C7), 80.42 (C1 and C5), 76.76 (C3), 55.19 (OMe), 42.77 (C2 and C4), 26.12 (Me), 29.65 (Me), 9.67 (Me); MS *m/z* 335 ([M + 1], 3), 334 (M^+; 11), 276 (9), 259 (8), 206 (27), 193 (100), 181 (24), 164 (66), 147 (24), 135 (68), 123 (16), 112 (80), 97 (31), 83 (39), 69 (6), 55 (11), 43 (47).

Data for **6c**: mp 195−197 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3490, 3010, 2980, 2950, 2890, 1480, 1370, 1220, 1080, 1050, 950, 680, 740; ^{1}H NMR ($CDCl_3$) δ 0.73 (d, 6H, J = 7.4, 2x Me), 1.39 (s, 3H, Me), 1.52 (s, 3H, Me), 1.65 (s, 1H, OH), 2.38 (s, 3H, Ar-Me), 2.41 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$ = 7.2, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 4.11 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4.7, H1 and H5), 5.09 (s, 2H, H6 and H7), 7,15−7,46 (m, 4H, H-aromatic); ^{13}C NMR ($CDCl_3$) δ 145.02 (C1′), 135.10 (C2′), 133.48 (C3′), 127.52 (C4′), 125.79 (C5′), 123.82 (C6′), 111.03 (CMe_2), 84.25 (C6 and C7), 80.63 (C1 and C5), 76.70 (C3), 39.01 (C2 and C4), 26.29 (M), 24.68 (Me), 21.68 (Me-Ar), 9,63 (Me); MS *m/z* 303 ([M − 15]$^+$,100), 269 (11), 243 (7), 197 (6), 173 (7), 148 (12), 133 (6), 119 (60), 112 (17), 91 (18), 43 (7).

Data for **6d**: mp 188−190 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3450, 3000, 2990, 2950, 2850, 1590,1500 1440, 1320, 1260, 1200, 1100, 1050, 900, 800, 760, 700; ^{1}H NMR ($CDCl_3$) δ 0.74 (d, 6H, J = 7.3, 2 × Me), 1.38 (s, 3H, Me), 1.54 (s, 3H, Me), 1.68 (s, 1H, OH), 2.35 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$ = 7.2, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 2.35 (s, 3H, Ar-Me), 2.39 (m, 2H, H2 and H4), 4.12 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4.5, H1 and H5), 5.07 (s, 2H, H6 and H7), 7.07−7.23 (m, 4H, H-aromatic); ^{13}C NMR ($CDCl_3$) δ 144.88 (C1′), 137.80 (C3′), 128.05 (C5′), 125.52 (C4′), 125.52 (C2′), 121.96 (C6′), 111.03 (CMe_2), 84,25 (C6 and C7), 80.63 (C1 and C5), 76.70 (C3), 42.65 (C2 and 4), 26.19 (M), 24.64 (Me), 21.67 (Me-Ar), 962 (Me); MS *m/z* 303 ([M − 15]$^+$,100), 243 (10), 225 (7), 197 (6), 173 (7), 148 (12), 133 (6), 119 (60), 112 (17), 105 (7), 91 (18), 83 (11), 43 (7).

Data for **6e**: mp 230−232 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3490, 2950, 2900,1580, 1490, 1400, 1340, 1200, 1080, 1050, 950, 850, 810, 750, 680; ^{1}H NMR ($CDCl_3$) δ 0.72 (d, 6H, J = 7.3, 2xMe), 1.37 (s, 3H, Me), 1.52 (s, 3H, Me), 1.57 (s, 1H, OH), 2.33 (s, 3H, Ar-Me), 2.35 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$ = 7.3, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 4.10 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4,0; H1 and H5), 5.06 (s, 2H, H6 and H7), 7.15 (d, 2H, J = 8,0, H3′and H5′), 7.25 (d, 2H, J = 8.0, H2′and H6′); ^{13}C NMR ($CDCl_3$) δ 141.89 (C1′), 136.54 (C4′), 128.93 (C3′ and C5′), 124.08 (C2′ and C6′), 111.01 (CMe_2), 84.49 (C6 and C7), 84.27 (C1 and C5), 76.7 (C3), 42.65-(C2 and C4), 26.18 (Me), 24.64 (Me), 20.90 (Ar-Me), 9.54 (Me); MS, *m/z* 303 ([M − 15]$^+$,57), 269 (13), 243 (8), 177 (23), 148 (17), 112 (28), 91 (24), 59 (6), 43 (33).

Data for **6f**: mp 227−229 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3510, 3400, 3010, 2990, 2950, 2880, 1640, 1610, 1450, 1370, 1090, 1050, 800, 860, 700; ^{1}H NMR ($CDCl_3$) δ 0.73 (d, 6H, J = 7.2, 2 × Me), 1.37 (s, 3H, Me), 1.52 (s, 3H, Me), 1.62 (s, 1H, OH), 2.32 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$ = 7.2, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 2.94 (s, 6H, NMe_2), 4.09 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4.4, H5 and H1), 5.06 (s, 2H, H6 and H7), 6.69 (d, 2H, J = 8.9, H3′and H5′), 7.2 (d, 2H, J = 8.9, H2′and H6′); ^{13}C NMR ($CDCl_3$) δ 149.29 (C4′), 132.47 (C2′ and C6′), 125,61 (C1′), 111.99 (C3′ and C5′), (CM_2), 110.91, 84.34 (C6 and C7), 80.66 (C1 and C5), 76,70 (C3), 42.67 (C2 and C4), 40.47 (NMe_2), 26.17 (Me), 24.61 (Me), 9.62 (Me); MS, *m/z* 348 ([M + 1], 6), 347 (M^+, 20), 329 (87), 271 (13), 242 (18), 214 (13), 177 (52), 148 (100), 121 (39), 69 (8), 43 (14).

Data for **6g**: mp 228−230 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3520, 3410, 3350, 3010, 2980, 2870, 1500, 1370, 1200, 1080, 1050, 950, 850, 800, 750, 680; ^{1}H NMR ($CDCl_3$) δ 0.74 (d, 6H, J = 7.2, 2 × Me), 1.39 (s, 3H, Me), 1.54 (s, 3H, Me), 1.61 (s, 1H, OH), 2.34 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$ = 7.2, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 4.12 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4.1, H1 and H5), 5.06 (s, 2H, H6 and H7), 7.28−7.34 (m, 4H, H-aromatic); ^{13}C NMR ($CDCl_3$) δ 143.56 (C1′), 132.93 (C4′), 128.40 (C3′and C5′), 126.47 (C2′ and C6′), 111.20 (CMe_2), 84.17 (C6 and C7), 80.57 (C1 and C5), 76.71 (C3), 42.65(C2 and C4), 26.21 (Me), 24.68 (Me), 9.51 (Me); MS *m/z* 324 ([M+1], 17), 323 (M^+; 100), 263 (13), 245 (6), 217 (7), 193 (8), 181 (11), 139 (60), 123 (13), 111 (17), 95 (10), 83 (14), 55 (6), 43 (33).

Data for **6h**: mp 222−224 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3490, 2950, 2920, 1500, 1370, 1220, 1090, 1050, 800, 860, 960, 670; ^{1}H NMR ($CDCl_3$) δ 0.76 (d, 6H, J = 7.0, 2xMe), 1.38 (s, 3H, Me), 1.53 (s, 3H, Me), 1.67 (s, 1H, OH), 2.76 (dq, 2H, $J_{2,Me}$ = $J_{4,Me}$ = 7.0, $J_{2,1}$ = $J_{4,5}$ = 4.0, H2 and H4), 4.10 (d, 2H, $J_{1,2}$ = $J_{5,4}$ = 4.1, H1 and H5), 5.04 (s, 2H, H6 and H7), 6.92−6.96 (m, 4H, H-aromatic); ^{13}C NMR ($CDCl_3$) δ 163.20 (C4′), 143.50 (C1′), 125.90 (C2′ and C6′), 116.96 (C3′ and C5′), 111.34 (CMe_2), 84.15 (C6 and C7), 80.60 (C1 and C5), 76.70 (C3), 39.45(C2 and C4), 26.23 (Me), 24.70 (Me), 9.95 (Me); MS *m/z* 307 ([M − 15]$^+$, 100), 247 (11), 205 (10), 201 (9), 163 (13), 152 (12), 123 (76), 111 (14), 109 (12), 83 (11), 43 (37), 41 (9).

Typical Procedure for the Dehydration Reaction and Preparation of Alkenes 7a−h. To a stirred solution of the alcohol **6a−h** (4 mmol) in dry pyridine (2 mL), kept at 0 °C, was added thionyl chloride (1 mL), and the resultant solution was stirred at 0 °C until TLC analysis revealed the complete consumption of the starting material (this time varied from 2 to 12 h). The reaction was quenched by addition of aqueous HCl solution (2 M) until complete neutralization of the pyridine. The product was extracted with diethyl ether (3 × 20 mL). The organic extracts were combined, washed with brine (2 × 20 mL), dried over $MgSO_4$, and concentrated under reduced pressure to give the crude product as pale yellow solid.

This solid was purified by column chromatography (hexane/diethyl ether 5:1) to yield the required alkenes (**7a**−**h**) as a white solids. The products were recrystalized with a mixture of dichloromethane and hexane. The yields for these reactions are presented in Table 1.

Data for **7a**: mp 157−159 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 2980, 2970, 2670, 1580, 1490, 1440, 1370, 1270, 1200, 1080, 1050, 810, 720, 680; ^{1}H NMR ($CDCl_3$) δ 0.75 (d, 3H, $J_{Me,4} = 7.4$, Me), 1.38 (s, 3H, Me), 1.57 (s, 3H, Me), 1.58 (d,3H, $J_{Me,4} = 2.3$, Me), 3.07 (m, 1H, H4), 4.27 (s, 1H, H1), 4.33 (d, 1H, $J_{5,4} = 5.4$, H5), 4.69 (d, 1H, $J_{6,7} = 5.7$, H6), 4.86 (d, 1H, $J_{7,6} = 5.7$, H7), 7.05 (d, 2H, $J = 7.9$, H2′and H6′), 7.25 (t, H, $J = 7.9$, H4′), 7.33 (t, 2H, $J = 7.9$, H3′and H5′); ^{13}C NMR ($CDCl_3$) δ 138.64 (C1′), 135.46 (C3), 129.28 (C3′ and C5′), 128.47 (C4′), 128.13 (C2′ and C6′), 126.66 (C2), 112.10 (CMe_2), 84.73 (C7), 84.28 (C6), 81.80 (C5), 80.57(C1), 35.53 (C4), 26.26 (Me), 24.94 (Me), 16.71 (Me), 13.95 (Me); MS *m*/*z* 287 ([M + 1], 16), 286 (M^+, 98), 271 (35), 228 (11), 213 (16), 199 (100), 185 (35), 171 (29), 158 (10), 143 (18), 128 (18), 115 (24), 105 (8), 91 (16), 82 (9), 69 (6), 43 (23). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.47; H, 7.70.

Data for **7b**: mp 163−165 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 2990, 2880, 1610, 1500, 1320, 1250, 1080, 1050, 810, 760, 650; ^{1}H NMR ($CDCl_3$) δ 0.74 (d, 3H, $J_{Me,4} = 7.4$, Me), 1.35 (s, 3H, Me), 1.55 (s, 3H, Me), 1.57 (d,3H, $J_{Me,4} = 2.3$, Me), 3.01 (m, 1H, H4), 3.79 (s, 3H, OCH_3), 4.24 (s, 1H, H1), 4.30 (d, 1H, $J_{5,4} = 5.4$, H5), 4.66 (d, 1H, $J_{6,7} = 5.7$, H6), 4.83 (d, 1H, $J_{7,6} = 5.7$, H7), 6.85 (dm, 2H, H3′and H5′), 6.95 (dm, 2H, H2′and H6′); ^{13}C NMR ($CDCl_3$) δ 158.23 (C4′), 135.00 (C3), 130.90 (C1′), 129.53 (C2′ and C6′), 129.19 (C2), 113.50 (C3′ and C5′), 112.05 (CMe), 84.61 (C7), 81.53 (C6), 81.67 (C5), 80.40 (C1), 55.2 (OMe), 35.57 (C4), 26.24 (Me), 24.93 (Me), 16.77 (Me), 14.045 (Me); MS *m*/*z* 317 ([M + 1], 22), 316 (M^+, 100), 301 (12), 258 (12), 243 (11), 229 (86), 215 (24), 201 (36), 175 (8), 158 (9), 135 (10), 128 (6), 121 (14), 91 (5), 43 (13). Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 71.91; H, 7.55.

Data for **7c**: mp 118−120 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 2950, 2820, 1480, 1370, 1210, 1040, 1080, 950, 870, 760; ^{1}H NMR ($CDCl_3$) δ 0.75(d, 3H, $J_{Me,4} = 7.4$, Me), 1.39 (s, 3H, Me), 1.57 (s, 3H, Me), 1.58 (d,3H, $J_{Me,4} = 2.3$, Me), 2.25 (s, 3H, Ar-Me), 3.05 (m, 1H, H4), 4.29 (s, 1H, H1), 4.32 (d, 1H, $J_{5,4} = 5.4$, H5), 4.67 (d, 2H, $J_{6,7} = 5.7$, H6), 4.89 (d, 2H, $J_{7,6} = 5.7$, H7), 6.75 (d, 1H, $J = 7.3$, H6′), 7.19 (d, 1H, $J = 6.22$, H4′), 7.12−7.73 (m, 3H, H-aromatic); ^{13}C NMR ($CDCl_3$) δ 138.59 (C1′), 137.65 (C3′), 135.50 (C3), 132.26 (C4), 127.98 (C5′), 127.38 (C2′), 122.08 (C2), 120.01 (C6′), 112.07 (CMe_2), 84.75 (C7), 84.71 (C6), 81.78 (C5), 80.60 (C1), 35.54 (C4), 26.26 (Me), 24.94 (Me), 19.70 (Me), 16.75 (Me), 13.99 (Me); MS *m*/*z* 301 ([M + 1], 12), 300 (M^+, 70), 285 (15), 242 (8), 213 (100), 199 (30), 141 (12), 128 (20), 91 (25), 43 (37). Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.93; H, 7.95.

Data for **7d**: mp 138−140 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 2980, 2850, 1600, 1480, 1370, 1260, 1080, 1050, 850, 760, 700.; ^{1}H NMR ($CDCl_3$) δ 0.70 (d, 3H, $J_{Me,4} = 7.4$, Me), 1.29 (s, 3H, Me), 1.47 (s, 3H, Me), 1.48 (d,3H, $J_{Me,4} = 2.3$, Me), 2.26 (s, 3H, Ar-Me), 2.99 (m, 1H, H4), 4.18 (s, 1H, H1), 4.24 (d, 1H, $J_{5,4} = 5.0$, H5), 4.60 (d, 2H, $J_{6,7} = 5.8$, H6), 4.78 (d, 2H, $J_{7,6} = 5.8$, H7), 6.75 (d, 1H, $J = 7.3$, H6′), 7.12 (d, 1H, $J = 7.8$, H4′), 7.14 (s, 1H, H2′), 7.22 (t, 1H, $J = 7.5$, H5′); ^{13}C NMR ($CDCl_3$) δ 138.58 (C1′), 137.65 (C3′), 135.55 (C3), 129.05 (C4), 127.98 (C5′), 127.38 (C2′), 125.55 (C2), 123.32 (C6′), 112.07 (CMe_2), 84.72 (C7), 84.71 (C6), 81.78 (C5), 80.56 (C1), 35.44 (C4), 26.26 (Me), 24.95 (Me), 21.45 (Me), 16.75 (Me), 13.99 (Me); MS *m*/*z* 301 ([M + 1], 17), 300 (M^+, 74), 285 (19), 242 (10), 213 (100), 199 (40), 128 (26), 91 (28), 43 (41). Anal. Calcd for $C_{19}H_{24}O_3$: C. 75.97; H, 8.05. Found: C, 75.90; H, 8.01.

Data for **7e**: mp 180−183 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3100, 2990, 1600, 1450, 1370, 1200, 1100, 850; ^{1}H NMR ($CDCl_3$) δ 0.75 (d, 3H, $J_{Me,4} = 7.4$, Me), 1.36 (s, 3H, Me), 1.55 (s, 3H, Me), 1.58 (d,3H, $J_{Me,4} = 2.3$, Me), 2.33 (s, 3H, Ar-Me), 3.04 (m, 1H, H4), 4.25 (s, 1H, H1), 4.30 (d, 1H, $J_{5,4} = 5.4$, H5), 4.66 (d, 1H, $J_{6,7} = 5.5$, H6), 4.84 (d, 1H, $J_{7,6} = 5.5$, H7), 6.91 (d, 2H, $J = 8.0$, H3′ and H5′), 7.21 (d, 2H, $J = 8,0$, H2′ and H6′); ^{13}C NMR ($CDCl_3$) δ 136.23 (C4′), 135.58 (C1′), 134.35 (C3), 128.80 (C3′ and C5′), 124.70 (C2′ and C6′), 122.24 (C2), 112.05 (CMe_2), 84.76 (C7), 84.71 (C6), 81.82 (C5), 80.57(C1), 35.50 (C4), 26.24 (Me), 24.93 (Me), 21.16 (Ar-Me), 16.75 (Me), 14.01 (Me); MS *m*/*z* 301 ([M + 1], 16), 300 (M^+, 80), 285 (25), 242 (13), 227 (24), 213 (100), 199 (35), 185 (55), 141 (16), 115 (22), 91 (23), 43 (34). Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.89; H, 7.98.

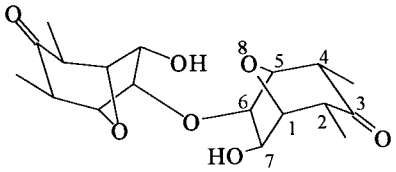
Data for **7f**: mp 191−193 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 2970, 2920, 2870, 1460, 1370, 1200, 1070, 1040, 850, 950, 680; ^{1}H NMR ($CDCl_3$) δ 0.73 (d, 3H, $J_{Me,4} = 7.4$, Me), 1.36 (s, 3H, Me), 1.59 (s, 3H, Me), 1.60 (d, 3H, $J_{Me,4} = 2.3$, Me), 2.95 (s, 6H, NMe_2), 3.01 (m, 1H, H4), 4.26 (s, 1H, H1), 4.33 (d, 1H, $J_{5,4} = 5.40$, H5), 4.66 (d, 1H, $J_{6,7} = 5.7$, H6), 4.85 (d, 1H, $J_{7,6} = 5.7$, H7), 6.68 (dm, 2H, $J = 8.7$, H3′and H5′), 7,25 (dm, 2H, $J = 8.7$, H2′and H6′); ^{13}C NMR ($CDCl_3$) δ 150.10 (C4′), 129.32 (C3), 126.54 (C1′), 125.20 (C2′ and C6′), 120.02 (C2), 113.40 (C3′and C5′), 111.29 (CMe), 84.73 (C7), 84.61 (C6), 81.67 (C5), 80.31 (C1), 40.4 (NMe_2), 30.30 (C4), 26.02 (Me), 24.70 (Me), 16.65 (Me), 13.93 (Me); MS *m*/*z* 330 ([M + 1], 30), 329 (M^+, 100), 314 (5), 271 (8), 254 (6), 243 (9), 242 (30), 228 (35), 213 (11), 174 (13), 148 (12), 82 (16), 57 (17), 43 (41). Anal. Calcd for $C_{20}H_{27}NO_3$: C, 72.92; H, 8.26; N, 3.98. Found: C, 72.87; H, 8.23; N, 4.03.

Data for **7g**: mp 165−167 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3050, 2970, 2830, 1480, 1370, 1260, 1080, 1050, 880, 860; ^{1}H NMR ($CDCl_3$) δ 0.74 (d, 3H, $J_{Me,4} = 7.4$, Me), 1.36 (s, 3H, Me), 1.56 (s, 3H, Me), 1.57 (d, 3H, $J_{Me,4} = 2.3$, Me), 3.03 (m, 1H, H4), 4.26 (s, 1H, H1), 4.32 (d, 1H, $J_{5,4} = 5.5$, H5), 4.66 (d, 2H, $J_{6,7} = 5.7$, H6), 4.84 (d, 2H, $J_{7,6} = 5.7$, H7), 6.97 (dd, 2H, $J = 8.4$, H3′ and H5′), 7,30 (dd, 2H, $J = 8.4$, H2′ and H6′); ^{13}C NMR ($CDCl_3$) δ 137.03 (C1′), 134.44 (C4′), 132.57 (C3), 130.10 (C2), 129.87 (C3′ and C5′), 128.43 (C2′and C6′), 122.90 (C2), 111.30 (CMe_2), 84.67 (C7), 84.59 (C6), 81.64 (C5), 80.55 (C1), 35.47 (C4), 26.26 (Me), 25.02 (Me), 16.60 (Me), 13.91 (Me); MS *m*/*z* 321 ([M + 1], 21), 320 (M^+, 95), 305 (71), 262 (17), 247 (27), 233 (100), 205 (46), 181 (14), 141 (19), 115 (29), 82 (14), 57 (9), 43 (47). Anal. Calcd for $C_{18}H_{21}ClO_3$: C, 67.39; H, 6.60. Found: C, 67.05; H, 6.56.

Data for **7h**: mp 161−162 °C; IR (KBr, cm^{-1}) $\bar{\nu}_{max}$ 3020, 2950, 2920, 2850, 1580, 1500, 1360, 1230, 1070, 1040, 800, 850, 750; ^{1}H NMR ($CDCl_3$) δ 0.73(d, 3H, $J_{Me,4} = 7.4$, Me), 1.36 (s, 3H, Me), 1.54 (s, 3H, Me), 1.55 (d, 3H, $J_{Me,4} = 2.3$, Me), 3.01 (m, 1H, H4), 4.25 (s, 1H, H1), 4.31 (d, 1H, $J_{5,4} = 5.5$, H5), 4.65 (d, 2H, $J_{6,7} = 5.9$, H6), 4.83 (d, 2H, $J_{7,6} = 5.9$, H7), 6.98−7.26 (m, 4H, H-aromatic); ^{13}C NMR ($CDCl_3$) δ 163.40 (C4′), 134.53 (C1′), 133.42 (C3), 129.50 (C2′ and C6′), 123.15 (C2), 115.30 (C3′ and C5′), 112.42 (CMe_2), 84.65 (C7), 84.47 (C6), 81.75 (C5), 80.52 (C1), 35.57 (C4), 26.22 (Me), 24.93 (Me), 16.70 (Me), 13.94 (Me); MS, *m*/*z* 305 ([M + 1], 14), 304 (M^+, 65), 289 (61), 246 (15), 217 (100), 203 (39), 189 (67), 133 (24), 109 (28), 82 (16), 57 (17), 43 (41). Anal. Calcd for $C_{18}H_{21}FO_3$: C, 71.03; H, 6.95. Found: C, 70.80; H, 6.85.

Bioassays. Two different bioassays were carried out to evaluate the plant growth regulatory activity of the synthesized compounds. In all cases, a stock solution was prepared dissolving each compound (50 mg) in xylene (3 mL). To this solution were added sodium dodecyl sulfate (0.12 g), the surfactant Tween 40 (0.7 mL), and water (10 mL). The resultant suspension was sonicated for 3 min and then transferred to a volumetric flask (1 L), and the volumewas completed with water. A solution with the same composition described above, but without the compound to be tested, was used as a control.

Assay of Root Elongation in Petri Dishes. Groups of eight pregerminated *Sorghum bicolor* L. cv. BR007B were placed in Petri dishes (i.d. = 9 cm) containing washed sand (150 g) and the solution (20 mL) containing the compound to be tested. The Petri dishes were sealed with Parafilm and incubated at 28 °C, in darkness, and at 75 °C. After 48 h, the root length was measured to the nearest millimeter. All treatments were replicated six times in a completely randomized design. The percentage of root growth inhibition was calculated in relation to the root length of the control that was 5.98 cm. The data were analyzed using Tukey's test at 0.05 probability level (Gomes, 1990).



4

Figure 2. Structure of the diol isolated from the oxidation reaction of compound (**2**).

Greenhouse Experiments with *S. bicolor, Cucumis sativus,* and Weeds *Bidens pilosa, Desmodium tortuosum,* and *Pennisetum setosum*. To each 0.35 L plastic pot was added washed sand, which was then saturated with the solution of the test compound (60 mL/450 g of sand, corresponding to 6.6 μg at a.i./g substrate). Six seeds of each test plant were placed in each pot. The pots were kept in a greenhouse, watered regularly to mantain the humidity at 13.3% w/w, and three times a week, a solution containing the required nutrients was applied. Fourteen days after sowing the plants were harvested and the roots and aerial parts separated and weighed. They were then dried at 72 °C, until constant weight and the mass of the dried matter determined. The percentage of root and aerial part growth inhibition was calculated in relation to the mass of the control, respectively.

For *S. bicolor* and *C. sativus*, an experiment using soil as substrate was carried out, and the results presented in Table 5.

The data were analyzed using Tukey's test at 0.05 probability level (Gomes, 1990).

RESULTS AND DISCUSSION

Synthesis. The [3 + 4] cycloaddition between the oxyallyl cation generated from the ketone 2,4-dibromopentan-3-one and furan resulted in the formation of the required cycloadduct **2** in 66.9% yield (Aschroft and Hoffmann, 1978). This reaction was carried out on a 0.1 mol scale and allowed for the preparation of several grams (~30 g) of the required starting material **2** (Scheme 1).

The oxidation of alkene **2** was carried out, at room temperature, using excess hydrogen peroxide and a catalytic amount of osmium tetraoxide (Schröder, 1980). The end of the oxidation was visualized when the reaction mixture changed to colorless. This oxidation was repeated several times, and in a few cases, a formation of a white solid was observed. This solid **(4)** (Figure 2) was removed by filtration and the crude diol **3** was then converted in 90−98% yield into the acetonide **5**.

The IR spectrum of compound **5** showed a strong absorption at 1710 cm^{-1} (ν C═O). Special features in the ^1H NMR spectrum are the singlets at δ 1.27 and 1.50, due to the *gem*-dimethyl groups. The ^{13}C NMR spectrum showed eight signals, and the presence of the isopropylidenedioxy group was confirmed by the signals at δ 111.72, 25.8 (CH_3) and 9.34 (CH_3).

The side product **4**, formed with 0−9% yield, and had its structure deduced by spectroscopic means. The IR spectrum showed a very strong absorption at 3420 cm^{-1} due to a OH group, and another band at 1710 cm^{-1} for the ketone. The molecular formula $C_{18}H_{26}O_7$ was derived from HRMS (*m*/*z* 354.1566). The ^{13}C NMR spectrum showed eight signals, all in accordance with the dimer structure. As far as we are aware, the formation of this type of dimer during the oxidation of alkenes has not been previously reported.

The ketone **5** was subsequently converted into several aromatic alcohols (**6a**−**h**). Initially, ketone **5** was treated with the Grignard reagent phenylmagnesium bromide, but the required product **6a** was obtained in only 30% yield. The same Grignard methodology (Baker et al., 1991) was used for the preparation of **6b**, which was isolated with only 24% yield. In both cases, a TLC analysis of the reaction mixture revealed the formation of several side products, as observed by Conceição (1995) in a similar reaction. An alternative methodology involving the use of aryllithium, prepared in situ from butyllithium and aryl bromide, was used and a much better yield of compounds **6a** (68%) and **6b** (60%) was resulted. This methodology was then applied for the preparation of the aromatic alcohols **6c**−**h**, with good yield (48−76%). All compounds (**6a**−**h**) were purified by column chromatography and recrystallized using a mixture of dichloromethane and hexane.

The characterization of the alcohols **6a**−**h** was carried out by spectroscopic means. In all cases, the IR spectra showed a strong absorption around 3450−3520 cm^{-1} due to the OH group stretching and also strong bands at approximately 1600, 1580 and 1500 cm^{-1} due to the C═C stretching of the aromatic ring. Special features in the ^1H NMR spectra were the presence of the signals at around δ 6.8−7.4, due to the aromatic rings. The absorptions due to the aliphatic part of the molecules were similar, as can be observed from the data presented in Materials and Methods. It should be pointed out that for all alcohols (**6a**−**h**) the resonances due to H6 and H7 appeared as a singlet at δ 5.04−5.09. These hydrogens were deshielded by approximately 0.6 ppm when compared with the same hydrogens in ketone **5**. This deshilding effect is attributed to the presence of the hydroxyl group at the endo face of the molecule, and the formation of only this isomer is a consequence of

Table 2. Effect of the Alcohols 6a−h, at 6.6 μg g^{-1}, on the Radicle Growth of *S. bicolor* L. after 2 Days Incubation at 25 °C

compd	radicle length[a] (cm)	inhibition (%)
control	5.98a	0
6b	5.48a,b	8
6f	5.58a,b	7
6c	5.51a,b	8
6d	5.51a,b	8
6a	4.66b	22
6e	0.00c	100
6g	0.00c	100
6h	0.00c	100
CV (%)	11.41	

[a] Means, in the same column, with the same letter are not significantly different at $P = 0.05\%$ by Tukey's test.

Table 3. Effect of the Alkenes 7a−h, at 6.6 μg g^{-1}, on the Radicle Growth of *S. bicolor* L. after 2 Days Incubation at 25 °C

compd	radicle length[a] (cm)	inhibition (%)
control	5.00a	0
7h	4.25a,b	15
7b	3.60b,c	28
7e	3.40b,c	32
7c	3.25c	35
7f	3.25c	35
7a	3.18c	36
7g	3.15c	37
7d	2.71c	46
CV (%)	13.29	

[a] Means, in the same column, with the same letter are not significantly different at $P = 0.05\%$ by Tukey's test.

Table 4. Effect of the Alcohols 6e,g,h at 6.6 μg g^{-1}, on the Development of *C. sativus* L. and *S. bicolor* L. after 14 Days at 25 °C, Using Sand as Substrate

	C. sativus L.				*S. bicolor* L.			
compd	aerial part (g)	inhibition (%)	roots (g)	inhibition (%)	aerial part (g)	inhibition (%)	roots (g)	inhibition (%)
control	0.18a[a]		0.038a		0.180a		0.700a	
6e	0.15b	21	0.028b	26	0.040b	78	0.050a,b	29
6g	0.12b,c	37	0.015b	60	0.020b	89	0.040b	43
6h	0.08d	58	0.015c	61	0.010c	94	0.010c	86
CV (%)	15.76		20.54		11.15		20.16	

[a] Means, in the same column, with the same letter are not significantly different at $P = 0.05\%$ by Tukey's test.

Table 5. Effect of the Alcohols 6e,g,h at 6.6 μg g^{-1}, on the Development of *C. sativus* L. and *S. bicolor* L. after 14 Days at 25 °C, Using Soil as Substrate

	C. sativus L.				*S. bicolor* L.			
compd	aerial part (g)	inhibition (%)	roots (g)	inhibition (%)	aerial part (g)	inhibition (%)	roots (g)	inhibition (%)
control	0.46a[a]		0.12a		0.29a		0.14a	
6g	0.45a,b	2	0.14a	−17	0.28a	3	0.12a	14
6e	0.31c	35	0.90a	9	0.27a	7	0.13a	7
6h	0.35b,c	24	0.09b	18	0.04b	86	0.01b	86
CV (%)	11.30		13.99		9.38		18.11	

[a] Means, in the same column, with the same letter are not significantly different at $P = 0.05\%$ by Tukey's test.

Table 6. Percentage of Inhibition on the Development of the Aerial Part (AP) and Roots (R) of *D. tortuosum*, *B. pilosa*, and *P. setosum* Caused by Compounds 6e,g,h after 14 Days at 25 °C, Calculated in Comparison with the Control

	inhibition (%)					
compd	*D. tortuosum*		*B. pilosa*		*P. setosum*	
	AP	R	AP	R	AP	R
6e	63	73	41	64	26	13
6h	73	67	55	61	30	19
6g	73	75	57	79	40	51

the preferential attack of the nucleophile from the less hindered face of the carbonyl group (Deslongchamps, 1989).

The dehydration of the alcohols was initially carried out with concentrated HCl in acetone under reflux, but the alkenes were obtained in very low yield (ex. **7a**, 24%). The low yield for these reaction could be associated with the partial hydrolysis of the acetonide (Madhavan and Martin, 1986) moiety and also to the formation of the compounds result from the substitution of the OH group by chlorine (Ferreira, 1998).

Another dehydration procedure, using $SOCl_2$ in pyridine (Bernstein and Allen, 1954), was used, and the alkenes **7a**−**h** were obtained in good yields (46−80%).

All compounds, after purification by column chromatography, were recrystalized and obtained in a very pure form for the biological assays.

The structure of the alkenes **7a**−**h** were confirmed by spectroscopic analysis.

The synthetic route developed allowed for the preparation of gram quantities of eight new alkenes derived from the 2α,4α-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**2**), in good yields.

Biological Activity. In the process of discovery of new agrochemicals, the strategy that involves a random screening of new chemicals is still used (Cobb, 1992; Copping and Hewitt, 1998).

In this work, we initially planed to prepare several aromatic alkenes to evaluate the influence of the aromatic portion and also the presence of the methyl groups at the 2 and 4 positions on the biological activity. Although we do not know the mode of action of the compounds (**1**), prepared by Conceição (1995), we decided to evaluate the biological activity of the synthetic intermediate alcohols **6a**−**h**.

In a preliminary in vivo screening carried out on Petri dishes the effect of compounds **6a**−**h** and **7a**−**h**, at 6.6 μg g^{-1}, on the radicle growth of *S. bicolor* was evaluated, according to the methodology proposed by Parker (1965). The results are shown in Tables 2 and 3. The most active alcohols were **6e** (*p*-methyl), **6g** (*p*-chloro), and **6h** (*p*-fluoro) that caused 100% inhibition on the Sorghum root development. The compounds having a methyl group on the ortho position (**6c**) and meta position (**6d**) had no significant effect (8% inhibition) on the sorghum development, indicating that the position of the substituents is important, in this case, for the biological activity.

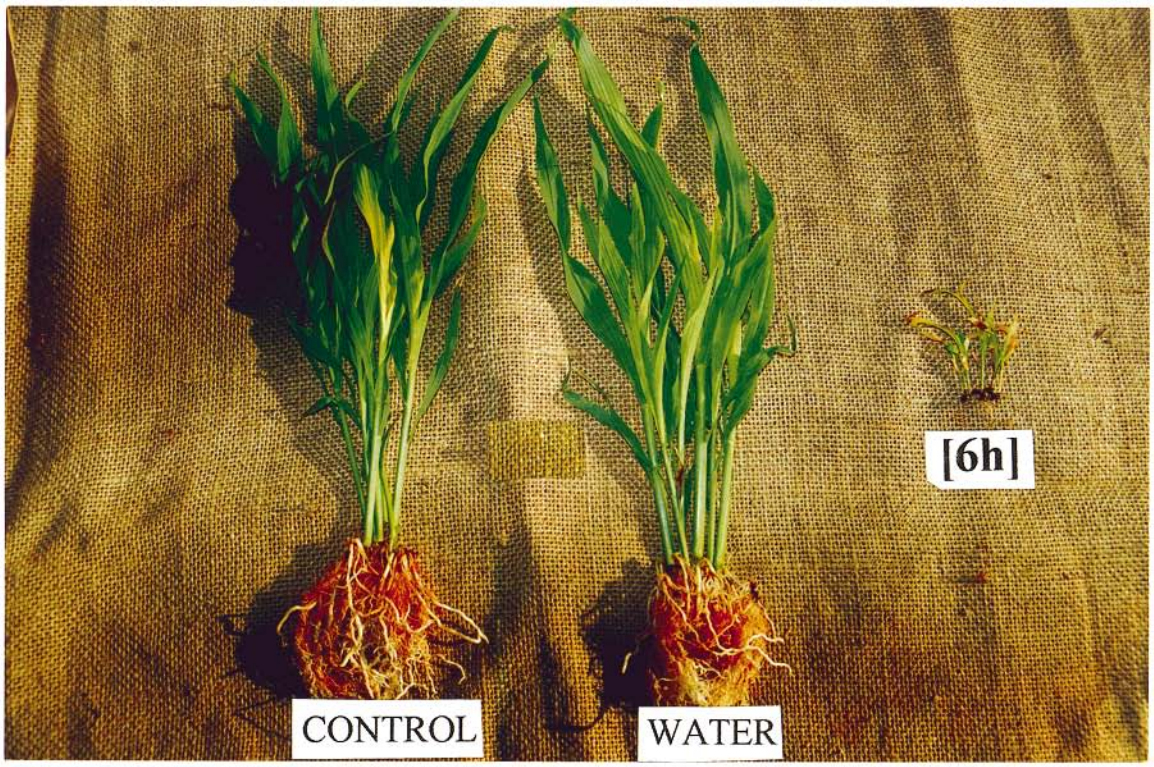
The only alkene that did not cause any significant effect on the development of *S. bicolor* was **7h** (15% inhibition). Although all the other alkenes caused a significant inhibition on the sorghum root development, this effect was small (28−46%) compared with the alcohols **6e**,**g**,**h**.

Considering the results obtained, the three most prominent compounds (**6e**,**g**,**h**) were submitted to a greenhouse experiment, employing plastic flower pots containing sand or soil as substrate.

The compounds were tested at the concentration of 6.6 μg g^{-1}, initially against *S. bicolor* and *C. sativus* L. From the results presented in Table 4 (sand as substrate) all compounds had a significant inhibitory effect on the development of the aerial part (21 to 58%) and roots (26 to 61%) of *C. sativus*.

The compounds caused a greater inhibition on the development of *S. bicolor* (aerial part 78−94%) and roots 29−86%), confirming the results previously obtained from the assays carried out on Petri dishes (Table 2).

When soil was used as substrate, compounds **6e** and **6g** caused a small effect or had no influence at all on the development of *S. bicolor* and *C. sativus*. On the other hand, **6h** caused 24% and 18% inhibition on the aerial parts and roots, respectively, of *C. sativus*, but was very active against *S. bicolor* (86% inhibition on the aerial parts and roots (Table 5).



a)

b)

Figure 3. Comparison of aerial parts and root growth in *S. bicolor*. (a) From left to right: control, water, and plant treated with 6.6 μg g^{-1} of compound **6h**, after 14 days at 25 °C using soil as substrate. (b) Detail showing the symptoms caused by compound **6h**.

Although we have no information about the mode of action of these compounds, a general reduction of the plant growth was observed, and in all cases chlorosis, followed by necrosis occurred as exemplified in Figure 3.

The alcohols **6e**, **6g**, and **6h** were also active against the important weeds *D. tortuosum*, *B. pilosa*, and *P. setosum* (Table 6). The less pronounced effect was observed in the case of *P. setosum* (13−51% inhibition on the aerial parts and roots).

In conclusion, we have demonstrated that the new compound derivatives of 2α,4α-dimethyl-8-oxabicyclo-[3.2.1]oct-6-en-3-one present relative herbicidal activity. These compounds can be further modified in order to increase the biological activity.

Future structural modification and biological evalu-

ation should be carried out in order to explore the full potential of this new class of herbicidal molecules.

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LITERATURE CITED

Aschroft, M. R.; Hoffmann, H. M. R. *Org. Synth*. **1978**, *55*, 17−23.

Baker, K. Y.; Brown, J. M.; Hughs, N.; Skarnulis, A. J.; Sexton, A. Mechanical action of magnesium turnings for the preparation of reactive Grignard reagent. *J. Org. Chem*. **1991**, *56*(*2*), 698−703.

Barbosa, L. C. A.; Demuner, A. J.; Borges, E. E. L.; Mann, J. Synthesis and evaluation of the plant growth regulatory activity of 8-oxabicyclo[3.2.1]oct-6-en-3-one derivatives. *J. Braz. Chem. Soc.* **1997**, *8*, 19−27.

Barbosa, L. C. A.; Demuner, A. J.; Mann, J.; Pilo-Veloso, D. Novel rearrangement of 2α-isopropyl-8-oxabicyclo[3.2.1]oct-6-ene producing the monoterpene 3-hydroxyphellandral. *J. Chem. Soc., Perkin Trans. 1* **1993**, 585−587.

Bernstein, S.; Allen,W. S. Steroidal cyclic ketals. *J. Org. Chem*. **1954**, *77*, 1028−1033.

Best, G. A.; Ruthven, A. D. *Pesticides: Development, impacts and control*; RSC: Cambridge, U.K., 1995.

Cobb, A. *Herbicides and plant physiology*; Chapman & Hall: London, U.K., 1992.

Conceição, G. A. Síntese e avaliação da atividade herbicida de compostos do tipo 3-aril-6,7-*exo*-isopropilidenodioxi-8-oxabiciclo[3.2.1]oct-2-eno (Synthesis and evaluation of the herbicidal activity of 3-aryl-6,7-*exo*-isopropylidenedioxy-8-oxabicyclo[3.2.1]oct-2-ene compounds). MS Thesis, University of Viçosa, 1995.

Copping, L. G.; Hewitt H. G. *Chemistry and mode of action of crop protection agents*; RSC: London, 1998.

Demuner, A. J.; Barbosa, L. C. A.; Veloso D. P., New 8-oxabicyclo[3.2.1]oct-6-en-3-one Derivatives with Plant Growth Regulatory Activity. *J. Agric. Food Chem*. **1998**, *46*, 1173−1176.

Deslongchamps, P. *Stereoeletronics effects in organic chemistry*; Pergamon Press: Oxford, U.K. 1989.

Ferreira, M. L. Síntese e avaliação da atividade herbicida de quinonas. MS Thesis, University of Viçosa, 1998.

Gomes, F. P. *Curso de estatística experimental*; 13th ed.; Nobel: Piracicaba, 1990.

Heap, T. M. The occurrence of herbicide resistant weeds worldwide. *Pestic. Sci*. **1997**, *51*, 235−243.

Jasieniuk, M.; Brûlé-Babel, A. L. and Morrison, I. N. The evolution and genetics of herbicide resistance in weeds. *Weed Sci.* **1996**, *44*, 176−193.

Klassen, W. In *World food security up to 2010 and global pesticide situation*; Ragsdak, N. M., Kearney, P. C., Plimmer, J. R. Fifth international congress of pesticide chemistry; ACS: Washington, DC, 1995.

Madhavan, G. V. B.; Martin, J. C. A Novel and Stereospecific Synthesis of (±)- and (−)-Aristeromycin. *J. Org. Chem* **1986**, *51*, 1287−1293.

Parker, C. A. Rapid bioassay method for the detection of herbicides which inhibit photosynthesis. *Weed Sci.* **1965**, *5*, 181−184.

Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; Pergamon Press: Oxford, U.K., 1988.

Schröder, M. Osmium Tetroxide *cis*-Hydroxylation of Unsaturated Substrates. *Chem. Rev*. **1980**, *80*, 187−213.

Tomlin, C. *The pesticide manual*; RSC: Cambridge, U.K., 1994.

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