Burg, R. W.; Miller, B. M.; Baker, E. E.; Birnbaum, J.; Currie, S. A.; Hartman, R.; Kong, Y.-L.; Monaghan, R. L.; Olson, G.; Putter, I.; Tunac, J. B.; Wallick, H.; Stapley, E. O.; Oiwa, R.; Omura, S. Avermectin, a New Family of Potent Anthelmintic Agents; Producing Organism and Fermentation. *Antimicrob. Agents Chemother.* **1979,** *15,* 361.

Campbell, W. C.; Fisher, M. H.; Stapley, E. O.; Albers-Schönberg, G.; Jacob, T. A. Ivermectin: a Potent new Antiparasitic Agent. *Science (Washington, D.C.)* **1983,** *221,* 823.

Chiu, S. H. L.; Buhs, R. P.; Sestokas, E.; Taub, R.; Jacob, T. A. Determination of Ivermectin Residues in Animal Tissues by High-Performance Liquid Chromatography–Reverse Isotope Dilution Assay. *J. Agric. Food Chem.* **1985,** *33,* 99.

Chiu, S. H. L.; Sestokas, E.; Taub, R.; Buhs, R. P.; Green, M.; Sestokas, R.; VandenHeuvel, W. J. A.; Arison, B. H.; Jacob, T. A. Metabolism of Ivermectin in Tissues of Cattle, Sheep, and Rats. *Drug Metab. Dispos.* **1986,** *14,* 590.

Kato, R. Characteristics and Differences in the Hepatic Mixed Function Oxidases of Different Species. *Pharmacol. Ther.* **1979,** *6,* 41.

Kline, W. F.; Maynard, M. S.; Feely, W. F.; Wislocki, P. G. The Isolation and Identification of Metabolites of Avermectin B_{1a} Utilizing High Performance Liquid Chromatography. *Abstracts of the Meeting,* 38th Pittsburgh Conference Exposition on Analytical Chemistry and Applied Spectroscopy, Atlantic City, NJ; The Pittsburgh Conference: Pittsburgh, PA, 1987; No. 875.

Ku, C. C.; Jacob, T. A.; Maynard, M. S.; Scimone, A. Photodegradation of Avermectin B_{1a} in Water and Soil. 185th National Meeting of the American Chemical Society, St. Louis, MO; American Chemical Society: Washington, DC, 1983; PEST 79.

Maynard, M. S.; Halley, B.; Green, M.; Hwang, S.; Alvaro, R.; Bennett, B.; Gruber, V. F.; Wislocki, P. G.; Jacob, T. A. The Fate of Avermectin B_{1a} in Rats. *Abstracts of Papers,* 190th National Meeting of the American Chemical Society, Chicago, IL; American Chemical Society: Washington, DC, 1985a; AGRO 59.

Maynard, M. S.; Gruber, V.; Ku, C. C.; Wislocki, P. G.; Jacob, T. A. The Fate of Avermectin B_{1a} in Lactating Goats. *Abstracts of Papers,* 190th National Meeting of the American Chemical Society, Chicago, IL; American Chemical Society: Washington, DC, 1985b; AGRO 60.

Maynard, M. S.; Iwata, Y.; Ku, C. C.; Wislocki, P. G.; Jacob, T. A. Fate of Avermectin B_{1a} on Citrus Fruit. 1. Distribution and Magnitude of the Avermectin B_{1a} and ^{14}C Residue on Citrus Fruits from a Field Study. *J. Agric. Food Chem.* **1989a,** *37,* 178.

Maynard, M. S.; Wislocki, P. G.; Ku, C. C. The Fate of Avermectin B_{1a} in Lactating Goats. *J. Agric. Food Chem.* **1989b,** *37,* 1491.

Maynard, M. S.; Gruber, V.; Feely, W. F.; Alvaro, R.; Wislocki, P. G. The Fate of the 8,9-Z Isomer of Avermectin B_{1a} in Rats. *J. Agric. Food Chem.* **1989c,** *37,* 1487.

Miwa, G. T.; Walsh, J. S.; VandenHeuvel, W. J. A.; Arison, B. H.; Sestokas, E.; Buhs, R.; Rosegay, A.; Avermitilis, S.; Lu, A. Y. H.; Walsh, M. A. R.; Walker, R. W.; Taub, R.; Jacob, T. A. The Metabolism of Avermectins B_{1a}, H_2B_{1a}, and H_2B_{1b} by Liver Microsomes. *Drug Metab. Dispos.* **1982,** *10,* 268.

Studies into the Mode of Action of Herbicides Derived from 4-[(Benzyloxy)methyl]-1,3-dioxolanes and Benzyl Methyl Ethers of Poly(ethylene glycols)

Ewan J. T. Chrystal,[†] Alan H. Haines,[*,‡] and Rajnikant Patel[‡]

Jealott's Hill Research Station, ICI Agrochemicals, Bracknell, Berkshire RG12 6EY, and School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ, England

The known herbicidal activity of 4-[(benzyloxy)methyl]-2,2,4-trimethyl-1,3-dioxolanes and the similar activity of certain benzyl methyl ethers of some poly(ethylene glycols), $ArCH_2O(CH_2CH_2O)_nMe$ ($n = 1$–3), described in this paper, cannot be explained in terms of efficient complexation of the herbicide with the alkali metal ions lithium, sodium, or potassium or with the alkaline-earth metal ions magnesium and calcium. A study of the extraction of metal picrates from aqueous solution into dichloromethane solutions of the herbicides gave little evidence for effective complexation of the type observed with cyclic polyethers, and there was no correlation between metal ion induced chemical shifts in the ^1H NMR spectra of members of the two series of compounds and their herbicidal activity.

The potent herbicidal activity of the 2,6-dichlorobenzyl ether of 4-(hydroxymethyl)-2,2,4-trimethyl-1,3-diox-

olane (1) (Barker et al., 1975), of the 2-methylbenzyl ether of r-2-ethyl-5-methyl-cis-5-hydroxy-1,3-dioxane (3) (Young and Hill, 1973), and of related compounds in controlling grass species invites speculation on how such structurally simple compounds, with seemingly benign functionality, can exert their influence on plant growth. Biolog-

---

[†] ICI Agrochemicals.

[‡] University of East Anglia.

Dioxolane and PEG-Derived Herbicides

J. Agric. Food Chem., Vol. 38, No. 3, 1990 **871**

ical studies (Jeffcoat, 1977) demonstrated that activity of the 2,6-dichlorobenzyl ether of 4-(hydroxymethyl)-4-ethyl-2,2-dimethyl-1,3-dioxolane (2) depends on its efficient uptake and movement to the site of action in the meristematic tissue of the root. Further studies (Burrows, 1978) demonstrated that compound 2 inhibited both DNA and RNA synthesis; protein synthesis and root growth were also subsequently inhibited. Our interest (Haines et al., 1975; Haines and Karntiang, 1980) in the interaction of polyoxygenated compounds with alkali metal ions, coupled with the growing general awareness of the importance of carbohydrate/metal ion interaction (Angyal, 1980), led us to consider the possibility that the geometrical arrangement of oxygen atoms in 1 and 3 might be particularly favorable for chelation with biologically important metal ions such as Na$^+$, K$^+$, Mg^{2+}, or Ca^{2+} and that such interaction might be the cause of their herbicidal activity. In seeking support for this conjecture, we were encouraged by the presence in both 1 and 3 of the O–C–C–O spacing, so favorable for interaction with alkali metal ions (Pedersen, 1967), and by the observation (Sammes et al., 1983) that in the pairs of stereoisomeric benzyl ethers 5/6 and 7/8 herbicidal activity was only observed in those isomers, 5 and 7, possessing a syn relationship between the benzyloxy group and the bridgehead oxygen atom.

Further support for our hypothesis of activation by metal ion complexation was provided by ^{1}H NMR spectroscopic studies on the interaction of the *cis*- and *trans*-1,3-dioxanes, 3 and 4, respectively, with sodium ions (Chrystal et al., 1989). The induced ^{1}H chemical shifts for the acetal proton (H-2) of the cis compound on addition of aliquots of sodium iodide to a solution in acetone-d_6 were considerably greater than those observed for the related proton in the trans isomer. This observation is consistent with more effective Na$^+$ binding to the oxygen atoms in 3, which are suitably arranged to interact cooperatively with cations, than to the less favorably disposed oxygen atoms in 4. For optimum herbicidal activity, the cis arrangement of substituents in the 2- and 5-positions of these 1,3-dioxanes and their ring-substituted analogues is preferred to the trans arrangement (Young and Hill, 1973; Konz, 1977; 1980).

To rationalize how metal ion complexation might promote the herbicidal activity of compounds such as 1, we considered the possibility that formation of a polydentate complex such as 9 might increase the electrophilic nature of the benzylic carbon atom and generate, thereby, a species capable of transferring a benzyl group to a suitable nucleophilic receptor, possibly an enzyme important for plant growth regulation. Although benzyl ether cleavage is known to be brought about by Lewis acids [for example BBr$_3$ (Benton and Dillon, 1942; Kutney et al., 1966)], carbenium ions (Barton et al., 1972; Bartlett and Rychnovsky, 1981), or incipient carbenium ions (Verheyden et al., 1978; Shotorbani et al., 1981), and with sodium thiocresolate under forcing conditions (Hansson and Wickberg, 1976), there seem to be no reports of cleavage occurring with alkali or alkaline-earth metal halides. Nevertheless, the possible involvement of metal complexation in herbicidal action receives some support from the fact that dioxolane 1 shows much higher herbicidal activity than the 4-desmethyl analogue 10, since in studies (Nakatsuji et al., 1983, 1984) of complexation phenomena in crown ether compounds 11–14 containing an electron-donating side arm it has been found that for compounds 12 and 14, which contain methyl groups at the pivotal positions, stability constants for complexation with

sodium ion are over 10 times greater than those for the corresponding compounds, 11 and 13, having hydrogen atoms at those positions.

Although our complexation hypothesis has not been supported by subsequent study, we report our results in order to encourage alternative investigations into the mode of action of this class of herbicides.

EXPERIMENTAL SECTION

^{1}H NMR spectra were measured on a Jeol PMX60SI spectrometer at 60 MHz, and ^{13}C NMR spectra were measured on a Jeol FX-100 spectrometer at 25.05 MHz in deuteriochloroform, with TMS as an internal standard, unless stated otherwise. Adsorption chromatography was performed in glass columns on Merck Kieselgel 60 (70–230 mesh).

2-Methyl-1,2,3-propanetriol was prepared from 2-methylpropen-1-ol as already described (Isaac and Barker, 1971) and converted to 4-(hydroxymethyl)-2,2,4-trimethyl-1,3-dioxolane by acid-catalyzed reaction with acetone by the literature procedure (Isaac and Barker, 1971). 4-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolane (Solketal) was obtained from Aldrich Chemical Co. 2-Methoxyethanol, 2-(2-methoxyethoxy)ethanol, and 2-[2-(2-methoxyethoxy)ethoxy]ethanol were commercial samples.

General Procedure for Benzylations. To a stirred solution of the alcohol (50 mmol) in dry 1,2-dimethoxyethane (80 mL) was added sodium hydride (2.4 g = 4.8 g of a 50% dispersion in oil, 100 mmol) in portions, and the mixture was stirred for 15 min. The benzyl halide (50 mmol) was then added, and the resulting mixture was stirred vigorously for 12 h at room temperature. Excess sodium hydride was destroyed by addition of methanol until effervescence ceased, and water (2 mL) was then added slowly followed by a few pieces of solid carbon dioxide. The mixture was concentrated to a thick slurry, which was partitioned between water and dichloromethane. The organic layer was separated, and the aqueous layer was extracted with several portions of dichloromethane (7 × 60 mL). The combined organic solutions were washed with water, dried, filtered, and concentrated, to give a crude product that was purified by distillation, with prior column chromatography if necessary. The benzyl ethers so prepared, compounds 1, 10, 15–17, and 19–25, gave satisfactory elemental analysis, and their ^{1}H and ^{13}C NMR were in agreement with their structure. Boiling points of the series of ethers are as follows [compound, bp (°C)/pressure (mmHg)]: 1, 107/0.1; 10, 151/1; 15, 103/0.2; 16, 108/0.8; 17, 101/0.05; 19, 78/0.05; 20, 118/0.15; 21, 164/0.15; 22, 83/0.2; 23, 96/0.25; 24, 93/0.15; 25, 83/2.

4-[(Triphenylmethoxy)methyl]-2,2,4-trimethyl-1,3-dioxane (18). Treatment of 4-(hydroxymethyl)-2,2,4-trimethyl-1,3-dioxolane with chlorotriphenylmethane in pyridine gave, from light petroleum ethyl acetate, the trityl ether, mp 84–85 °C. A satisfactory elemental analysis was obtained, and its ^{1}H and ^{13}C NMR spectra were in accord with its structure.

Extraction Measurements on Metal Picrates. The method was essentially that described by Pedersen (1968) with slight modifications (Haines and Karntiang, 1980).

The required picrate solutions were prepared as follows. Picric acid (approximately 0.016 g, 7 × 10^{-5} mol) was dissolved in 0.1 M aqueous solutions of ammonium, lithium, sodium, and potassium hydroxide (1 L). Barium picrate was prepared in the same way, but with twice as much picric acid (approximately 0.032 g, 1.4 × 10^{-4} mol) per liter of 0.1 M aqueous barium hydroxide to account for the divalency of barium. Because of the low solubility of calcium and magnesium hydroxide in water at room temperature (saturated solutions are approximately 1.54 × 10^{-4} and 0.025 M, respectively), picric acid (1.4 × 10^{-4} mol) was added to saturated solutions (1 L) of the two hydroxides and sufficient magnesium or calcium nitrate was added to the appropriate solutions to bring their concentration with respect to the metal ion to 0.1 M.

Solutions of the benzyl ethers (7 × 10^{-4} M) were prepared in dichloromethane. Equal volumes (50 mL) of the organic solution and an aqueous 7 × 10^{-5} M metal picrate solution were placed in a separatory funnel, and the contents were shaken vigorously 100 times. The absorbance, *A*, of the aqueous layer
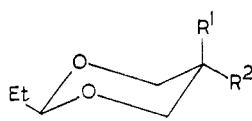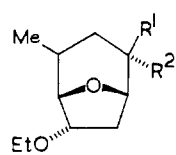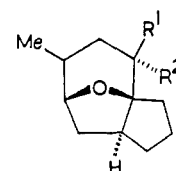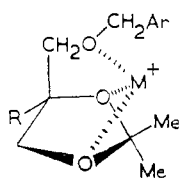
Chart I
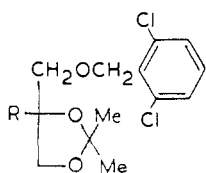
$\underline{1}$ R = Me
$\underline{2}$ R = Et
$\underline{10}$ R = H

$\underline{3}$ R^1 = 2-MeC$_6$H$_4$CH$_2$O; R^2 = Me
$\underline{4}$ R^1 = Me; R^2 = 2-MeC$_6$H$_4$CH$_2$O

$\underline{5}$ R^1 = OCH$_2$Ph; R^2 = H
$\underline{6}$ R^1 = H; R^2 = OCH$_2$Ph

$\underline{7}$ R^1 = OCH$_2$Ph; R^2 = H
$\underline{8}$ R^1 = H; R^2 = OCH$_2$Ph

$\underline{9}$
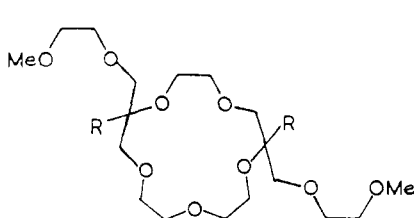
$\underline{11}$ R = H
$\underline{12}$ R = Me
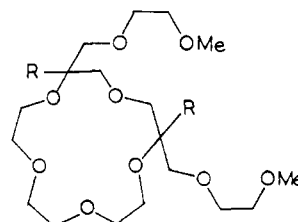
$\underline{13}$ R = H
$\underline{14}$ R = Me
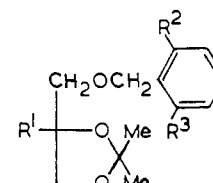
$\underline{15}$ R^1 = Me; R^2 = Cl; R^3 = H
$\underline{16}$ R^1 = Me; R^2 = R^3 = H
$\underline{17}$ R^1 = R^2 = R^3 = H
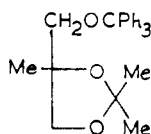
$\underline{18}$
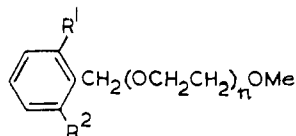
$\underline{19}$ n = 1; R^1 = R^2 = Cl
$\underline{20}$ n = 2; R^1 = R^2 = Cl
$\underline{21}$ n = 3; R^1 = R^2 = Cl
$\underline{22}$ n = 2; R^1 = R^2 = H
$\underline{23}$ n = 2; R^1 = Cl; R^2 = H
$\underline{24}$ n = 2; R^1 = Me; R^2 = H
$\underline{25}$ n = 0; R^1 = R^2 = Cl

before and after the extraction experiment, A_0 and A_e, respectively, were measured at the position of maximum absorption near 357 nm, and the percent extraction of metal picrate into the organic layer was calculated by the expression $100(A_0 - A_e)/A_0$. The experiments were repeated for the ethers at a concentration of 7×10^{-3} M. For no compound was an extraction of >2% observed. Control experiments conducted with dibenzo-18-crown-6 and benzo-15-crown-5 for sodium and potassium picrate at a polyether concentration of 7×10^{-4} M gave the following percentages of metal picrate extracted [literature values (Haines, 1980) in parentheses]: dibenzo-18-crown-6, Na$^+$ 7 (7), K$^+$ 79 (78); benzo-15-crown-5, Na$^+$ 27 (26), K$^+$ 51 (45).

Measurement of Induced Chemical Shifts. The procedure is essentially that previously described (Haines et al., 1975) with small modifications.

The ^{1}H NMR spectrum of the compound (20–110 mg) in acetone-d_6 (0.50 mL) was recorded at 60 MHz with a TMS–cyclooctatetraene mixture in a sealed capillary tube as external standards; the chemical shift of cyclooctatetraene as the neat liquid is δ 5.68. The NMR tube was weighed, a small, roughly weighed portion of the metal iodide (10–40 mg), previously dried at 10 mmHg over P$_2$O$_5$, was added to the solution in the NMR tube, and the tube and contents were reweighed in order to determine the accurate weight of metal iodide added. The tube and contents were shaken to ensure complete dissolution of the salt, and the spectrum was remeasured. Further additions of known weights of the iodide were made, and the

spectrum was remeasured after each addition. In all cases, the scale of the spectrum was calibrated with the aid of the external standards, and chemical shifts were calculated accordingly. Changes in the chemical shift (Δδ) of the signal for the benzylic hydrogen with respect to the shift of this signal with no salt added were measured, a graph of Δδ against the molar ratios of salt/compound was plotted for each compound, and the gradient of the line was determined by linear regression analysis. Values of the gradients are given in Table II.

RESULTS AND DISCUSSION

The series of compounds **1, 10,** and **15–18** was prepared in order to study structure/herbicidal activity relationships in the dioxolane-type herbicides and to relate the herbicidal activity of these compounds with their ability to complex the biologically important ions Na$^+$, K$^+$, Mg^{2+}, Ca^{2+} and other related species. In addition, working on the assumption that benzyl ethers containing O–C–C–O subunits would be likely to show herbicidal activity similar to that of **1** and **3**, we prepared and tested a series of simple acyclic ethers, **19–24,** with the general formula ArCH$_2$O(CH$_2$CH$_2$)$_n$OMe (n = 1–3) and methyl 2,6-dichlorobenzyl ether (**25**) for comparative purposes.

The syntheses of compounds **1, 15, 16,** and **10** and **17** simply involved treatment of 4-(hydroxymethyl)-2,2,4-

Dioxolane and PEG-Derived Herbicides

J. Agric. Food Chem., Vol. 38, No. 3, 1990 873

Table I. Herbicidal Activity of Benzyl Ether Derivatives

compd	rate[c]	preemergence[a] crop[d]	dicot weeds	monocot weeds	CYPRO	postemergence[b] crop[e]	dicot weeds	monocot weeds	CYPRO
1	1	1	3	3	2	0	0	0	0
10	5	1	1	0	1	1	1	0	0
15	5	2	1	4	5	0	1	1	0
16	5	1	0	3	4	2	0	2	0
19	5	3	3	3	3	0	1	0	0
20	5	2	3	3	4	0	1	0	0
21	5	1	2	3	3	—[f]	—	—	—
23	4	1	1	2	3	1	1	0	0
24	4	1	1	2	3	1	1	0	0

[a] Degree of damage assessed 20 days after treatment. Chemical effects were assessed visually against controls on all species, averaged as appropriate, and expressed on a 0–5 scale of damage: 0 = 0–10%; 1 = 11–25%; 2 = 26–50%; 3 = 51–80%; 4 = 81–95%; 5 = 96–100% kill. [b] Degree of damage assessed 13 days after treatment. Chemical effects were assessed visually against controls and processed according to footnote a. [c] Kilograms per hectare. [d] The groups of species were as follows. Crops: sugarbeet, rape, cotton, soya, maize, winter wheat, rice. Dicotyledonous weeds: *Senecio vulgaris, Ipomea purpurea, Amaranthus retroflexus, Polygonum aviculare, Chenopodium album, Galium aparine, Xanthium spinosum, Abutilon theophrasti, Cassia obtusifolia*. Monocotyledonous weeds: *Avena sativa, Digitaria sanguinalis, Alopecurus myosuroides, Setaria viridis, Echinochloa crus-galli, Sorghum halepense, Elymus repens*. CYPRO: *Cyperus rotundus*. [e] The groups of species were as listed in footnote d, except in monocotyledonous weeds *Avena fatua* replaced *Avena sativa*. [f] Not tested on a broad range of plants postemergence at lower rates. At a rate of 10 kg ha⁻¹ it caused scorch damage (effect 1) in *Setaria viridis* and *Lolium perenne*.

trimethyl-1,3-dioxolane (Isaac and Barker, 1971) and 4-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane (Solketal; Aldrich Chemical Co.), respectively, with sodium hydride and the appropriate benzyl halide in 1,2-dimethoxyethane. All chiral compounds were prepared as racemic mixtures. Compounds 19–24 and 25 were prepared from the commercially available mono-*O*-methyl ethers of the poly-(ethylene glycols) and methanol, respectively, by a similar benzylation procedure. Compound 18 was obtained by conventional tritylation of the parent alcohol.

Herbicidal Evaluation. After preliminary testing at higher rates, active compounds were tested on a broad range of crop and monocotyledonous and dicotyledonous weed species. The chemicals were applied with a traveling boom track sprayer at a volume equivalent to 1000 L ha⁻¹ with 0.1% mixed wetters and Span 80 and Tween 20 in a ratio of 1 to 4, at varying concentrations corresponding to application rates of 5.0, 4.0, or 1.0 kg ha⁻¹. In the preemergence tests the compounds were sprayed directly onto the seeds, which were then covered with a layer of sterile loam-based compost. Assessments for preemergence activity were made 20 days after treatment. Assessments were also made for postemergence activity 13 days after spraying onto the plant at the two-leaf growth stage. The results, together with the assessment scale and test species, are listed in Table I. Compounds 17, 18, 22, and 25, which were inactive in the preliminary testing at rates of 10 kg ha⁻¹, were not tested on the broad range of plant species at lower rates and, therefore, data on these compounds are absent from Table I.

In the series of 1,3-dioxolane derivatives 1, 10, and 15–18 compound 1 is the most effective herbicide in preemergent screens, in agreement with the published data on this and related compounds (Barker et al., 1975). The importance of a 4-alkyl group for herbicidal activity in this class of compounds is apparent from the low or nonexistent activities of 10 and 17 compared to 1 and 16, respectively, and this structure/activity relationship has been noted in earlier work (Kirby and Turner, 1974). Replacement of the benzyl moiety in 1, 15, or 16 by the triphenylmethyl group to give 18 leads to loss of activity. Of the 1,3-dioxolanes, only 16 showed any significant postemergence activity.

In the series of acyclic 2,6-dichlorobenzyl ethers, 19 and 20 were active as preemergence herbicides but, somewhat surprisingly, the longer chain compound 21 was somewhat less active. Compounds 19–21 showed relatively little postemergence activity. Compound 25, which lacks the O-C-C-O moiety, was, essentially, inactive on both pre- and postemergence screens. In the series of benzyl ethers derived from 2-(2-methoxyethoxy)ethanol, benzyl ether 22 was inactive in both pre- and postemergent screens, and neither the 2-chloro- nor the 2-methylbenzyl compound, 23 and 24, respectively, was as active as the 2,6-dichlorobenzyl compound, 20, in preemergence screens.

Picrate Extraction Studies. Experimental evidence for interaction of compounds prepared in this study with metal ions was sought in two ways: first, by the picrate extraction technique (Pedersen, 1968; Haines and Karntiang, 1980); second, by the metal ion induced shift procedure (Haines et al., 1975). Values for the percent extraction of ammonium, lithium, sodium, potassium, magnesium, calcium, and barium picrate from aqueous solution into dichloromethane containing a given benzyl ether were measured under standard conditions for a representative group of the compounds, comprised of 1, 10, 16, 17, 20, and 21, which contains compounds having varying degrees of herbicidal activity. Extraction values for dibenzo-18-crown-6 and benzo-15-crown-5 were also measured as a check, and good agreement was obtained with those reported (Haines, 1980). With none of the benzyl ethers was an extraction value of greater than 2% observed. Under these conditions with potassium as the metal ion, dibenzo-18-crown-6 and benzo-15-crown-5 afforded extraction values of 79% and 51%, respectively. Clearly, complexing ability of this order is not a necessary requirement for a compound to possess herbicidal activity. Attempts to make solid sodium or potassium salt complexes with dioxolane 1 and linear ethers 19–21 proved fruitless.

Metal Ion Induced Shifts in ¹H NMR Spectra. In the ¹H NMR spectra of benzyl ethers prepared in this work, resonances of benzylic protons are readily identified and invariably appear as singlets. If metal ion complexation at benzylic oxygen occurs, significant shifts to low field are to be expected for this resonance (Haines

Table II. Gradients from Plots of Induced Shifts ($\Delta\delta$) in Benzylic Resonances of Benzyl Ethers vs Molar Ratios of Salt to Benzylic Ether

	salt[a]		
compd	LiI	NaI	CaI$_2$
1	7.2[b]	5.5	7.0
10	7.0	6.7	7.6
16	9.7	8.6	11.0
17	9.6	9.6	12.4
19	8.4	7.8	10.0
25	11.0	6.0	14.0

[a] Molar ratio of salt to substrate varied between 0.2 and 3. [b] In hertz. Estimated accuracy ±0.05 Hz.

et al., 1975). A series of experiments were conducted, therefore, on a representative group of the ethers in which increasing amounts of lithium, sodium, and calcium iodide were added to a solution of the benzyl ether in acetone-d_6. The choice of the metal iodide is limited by its solubility in acetone-d_6. The slope of a plot of induced shift for benzylic protons against the molar ratio of salt to compound affords a measure of the extent of interaction between the metal ion and the substrate, and results are recorded in Table II for compounds 1, 10, 16, 17, 19, and 25. The most significant finding is that despite the fact that the group contains compounds of varying herbicidal activity, the induced shifts are all of the same order of magnitude; indeed, the poor herbicide 17 shows a greater induced shift than the active compound 1. Further, introduction of chlorine substituents at the 2,6-positions of the aromatic ring in place of hydrogen reduces the shift induced by addition of the metal ion (compare 1 and 10 with 16 and 17, respectively), and replacement of H-4 on the 1,3-dioxolane ring by methyl, which has an important effect on herbicidal activity, produces only minor changes in the induced shift.

In summary, we have found no evidence from this study that herbicidal activity in this class of compounds is associated with their general complexing ability toward alkali or alkaline-earth metal ions. These results contrast with our observations (Chrystal et al., 1989) for the two 1,3-dioxanes 3 and 4.

ACKNOWLEDGMENT

LITERATURE CITED

Angyal, S. J. Sugar-Cation Complexes-Structure and Applications. *Chem. Soc. Rev.* **1980**, 415–428.

Barker, M. D.; Isaac, E. R.; Kirby, P.; Smith, G. C. (Shell Oil Co.). 2,6-Dihalobenzyl Ethers. U.S. Patent 3 919 252, 1975; *Chem. Abstr.* **1976**, *84*, 44012u. See also (Shell Internationale Research, Maataschappi, N.V.): 2,6-Dihalobenzyl Ethers. Brit. Patent 1 470 509, 1977. Method of Treating Rice. Brit. Patent 1 542 399, 1979. Herbicidal Dioxanes and Dioxolanes. Ger. Offen. 2 428 694, 1975; *Chem. Abstr.* **1975**, *82*, 170973e.

Bartlett, P. A.; Rychnovsky, S. D. Stereocontrolled Synthesis of cis-2,5-Disubstituted Tetrahydrofurans and cis- and trans-Linalyl Oxides. *J. Am. Chem. Soc.* **1981**, *103*, 3963–3964.

Barton, D. H. R.; Magnus, P. D.; Smith, G.; Streckert, G.; Zurr, D. Experiments on the Synthesis of Tetracyclines. Part XI. Oxidation of Ketone Acetals and Ethers by Hydride Transfer. *J. Chem. Soc., Perkin Trans. 1* **1972**, 542–552.

Benton, F. L.; Dillon, T. E. The Cleavage of Ethers with Boron Bromide. I. Some Common Ethers. *J. Am. Chem. Soc.* **1942**, *64*, 1128–1129.

Burrows, W. J. Effects of Glycerol Ethers on Monocotyledon Nucleic Acid and Protein Biosynthesis. *Pestic. Biochem. Physiol.* **1978**, *8*, 137–145.

Chrystal, E. J. T.; Haines, A. H.; Patel, R. Sodium-Ion Induced ^{1}H-n.m.r. Shifts in the Assignment of Structure to *r*-2-Ethyl-5-methyl-*c*- and -*t*-5-(2-methylbenzyloxy)-1,3-dioxane. *Carbohydr. Res.* **1989**, *186*, 320–325.

Haines, A. H. Fluoro-substituted Benzo-crown Polyethers. *Tetrahedron Lett.* **1980**, *21*, 285–286.

Haines, A. H.; Karntiang, P. Synthesis of Some Polyethers from Carbohydrate Derivatives and Related Compounds and Their Interaction with Sodium and Potassium Cations. *Carbohydr. Res.* **1980**, *78*, 205–211.

Haines, A. H.; K. C. Symes, K. C.; Wells, A. G. The Interaction of some Carbohydrate Derivatives with Sodium Ions in Acetone Solution. *Carbohydr. Res.* **1975**, *41*, 85–92.

Hansson, C.; Wickberg, B. Selective Dealkylation of Activated Aromatic Ethers. *Synthesis* **1976**, 191–192.

Isaac, E. R.; Barker, M. D. (Shell Internationale Research, Maataschappij, N.V.). Herbicidal and Fungicidal 2-Alkylglycerol Derivatives. Ger. Offen. 2 046 476, 1971; *Chem. Abstr.* **1971**, *75*, 20383d. See also: 2-Alkylglycerol Derivatives and Their Use as Herbicides. Brit. Patent 1 293 546, 1972.

Jeffcoat, B. The Basis of Selectivity of 4-(2,6-Dichlorobenzyloxymethyl)-4-ethyl-2,2-dimethyl-1,3-dioxolane (WL-29226), a New Pre-emergence Herbicide for Use in Cereals. *Pestic. Sci.* **1977**, *8*, 43–53.

Kirby, P.; Turner, R. G. WL-29226 – A new Selective Herbicide for use in Cereals. *Proc. Br. Weed Control Conf.* **1974**, *12*, 817–824.

Konz, M. J. (FMC Corp.). Herbicidal 1,3-Dioxolanes. U.S. Patent 4 035 178, 1977; *Chem. Abstr.* **1977**, *87*, 184514w.

Konz, M. J. (FMC Corp.). Herbicidal 1,3-Dioxolanes. U.S. Patent 4 207 088, 1980.

Kutney, J. P.; Abdurahman, N.; LeQuesne, P.; Piers, E.; Vlattas, I. A New Total Synthesis of dl-Quebrachamine and dl-Aspidospermine. A General Entry into Aspidosperma Alkaloids. *J. Am. Chem. Soc.* **1966**, *88*, 3656–3657.

Nakatsuji, Y.; Nakamura, T.; Okahara, M.; Dishong, D. M.; Gokel, G. W. Enhancement of Cation Binding in Lariat Ethers Bearing a Methyl Group at a Quaternary, Pivot Carbon Atom. *J. Org. Chem.* **1983**, *48*, 1237–1242.

Nakatsuji, Y.; Mori, T.; Okahara, M. Synthesis of Bis(bromoethyl) Dimethyl Crown Ethers and Complexation Properties of Their Derivatives Having Electron-Donating Sidearms. *Tetrahedron Lett.* **1984**, *25*, 2171–2174.

Pedersen, C. J. Cyclic Polyethers and Their Complexes with Metal Salts. *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036.

Pedersen, C. J. Ionic Complexes of Macrocyclic Polyethers. *Fed. Proc.* **1968**, *27*, 1305–1309.

Sammes, P. G.; Street, L. J.; Kirby, P. Preparation and Properties of Some Phytotoxic 2-Benzyloxy-8-oxabicyclo[3.2.1]-octane Derivatives. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2729–2734.

Shotorbani, G. A.; Buchanan, J. G.; Edgar, A. R.; Shanks, C. T.; Williams, G. C. *C*-Nucleoside Studies. Part 13. A New Synthesis of 2,3,5-Tri-*O*-benzyl-α (and β)-D-ribofuranosylethyne Involving Benzyloxy Participation and a Synthesis of Showdomycin. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2267–2272.

Verheyden, J. P. H.; Richardson, A. C.; Bhatt, R. S.; Grant, B. D.; Fitch, W. L.; Moffatt, J. G. Chiral Synthesis of the Antibiotics Anisomycin and Pentenomycin. *Pure Appl. Chem.* **1978**, *50*, 1363–1383.

Young, S. T.; Hill, K. L. (FMC Corp.). Herbicidal Substituted Dioxanes. Ger. Offen. 2 243 685, 1973; *Chem. Abstr.* **1973**, *78*, 159624p. See also: Herbicidal cis-Substituted Dioxanes. Brit. Patent 1 406 849, 1975.