with $Ce(SO_4)_2$ and heat]: NMR ($CDCl_3$) δ 6.23 (m, 2 H, -CH=CH-), 6.05 (d, J = 2 Hz, 1 H, -C=CH), 5.48 (d, J = 2 Hz, 1 H, -C=CH), 4.45 (d, 1 H, γ-lactone -OCH-), 2.75-3.45 (br m, 5 H, -CH-), 1.18-1.92 (br m, 4 H, $-CH_2-$). The oil solidified on standing at room temperature; subsequent sublimation at 45 °C (1.2 mm) gave an analytical sample of **24** as a white powder: mp 55-56 °C; IR (KBr) 1740 (γ-lactone C=O), 1655 (exocyclic C=C), 1630 cm^{-1} (endocyclic C=C); UV (MeOH) λ_{max} 208 nm (ϵ_{max} 10 334); mass spectrum M^+ (EI) 202 (m/e of M^+ = 202.101 obsd, 202.099 calcd). Anal. ($C_{13}H_{14}O_2$) C, H.

Measurements of the Rate of Cysteine Addition. The rates of cysteine addition to α-methylene γ-lactones were measured following a modified version of the procedure of Kupchan et al.[1b] To 50 mL of 10^{-4} cysteine in 0.067 M phosphate buffer (pH 7.4) under a N_2 atmosphere was added 0.5 mL of a 10^{-2} M THF solution of the lactone. At intervals of approximately 3 min 3.6 mL of the reaction mixture was removed and assayed according to the procedure of Grassetti and Murray using 2,2'-dithiopyridine.[39]

The phosphate buffer was prepared using doubly distilled water. Spectral grade THF and Me_2SO were used and the THF was distilled from $LiAlH_4$ before use. The cysteine and 2,2'-dithiopyridine were obtained from Aldrich Chemical Co.

The results were analyzed using least-squares curve-fitting procedures with all rates based on the best line through at least six points. The lines through the points used all had correlation coefficients of 0.99 assuming second-order kinetics.

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Antitumor Agents. 32.[1] Synthesis and Antitumor Activity of Cyclopentenone Derivatives Related to Helenalin

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Several new cyclopentenones related to helenalin have been synthesized as potential alkylating antitumor agents. The procedure involved the transformation of 2-methyl-2-carbethoxycyclopentanone (**2**) to an ethylene ketal **3**, bromination of **3** followed by dehydrobromination to yield a ketal olefin **5**, reduction of **5** to the alcohol **6**, conversion of **6** to the corresponding hydroxycyclopentenone **7**, and esterification of **7** to afford the cyclopentenone esters **8**-**11**. Biological assays indicated that only cyclopentenones possessing a conjugated ester side chain, such as **9** and **10**, demonstrated significant in vitro cytotoxicity against the growth of tissue culture cells originating from human epidermoid carcinoma of the larynx (H.Ep.-2) as well as in vivo antitumor activity in Walker 256 carcinosarcoma in rats and P-388 lymphocytic leukemia in mice.

Previous papers of this series demonstrated that a β-unsubstituted cyclopentenone ring of helenalin (**1**) related sesquiterpene lactones, such as plenolin and tenulin, contributes significantly to in vitro cytotoxicity (H.Ep.-2)

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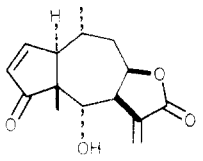

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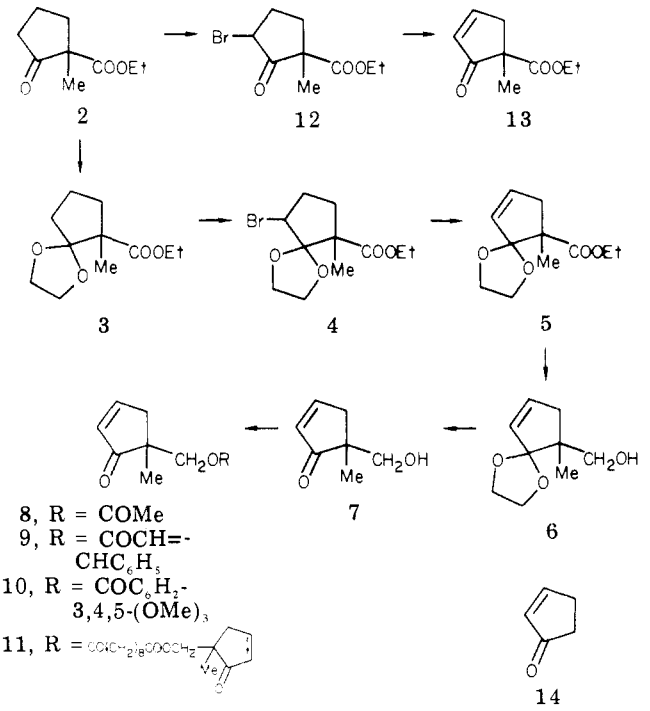
and in vivo antitumor activity (Walker 256 carcinosarcoma in rats and P-388 lymphocytic leukemia in mice).[2,3] The β-unsubstituted cyclopentenone ring appears to act as an alkylating agent via a Michael-type addition reaction with bionucleophiles.[4,5] The importance of a C-6 hydroxyl group for enhanced cytotoxic antitumor activity in either a bicyclic or a tricyclic ring system with a saturated α-methylene grouping of the γ-lactone ring of helenalin-related compounds has also been noted.[1] The C-6 hydroxyl group might be involved in direct binding of these compounds to the receptor site in tumor cells. In this report we describe the synthesis and cytotoxic antitumor activity of hydroxyl group bearing cyclopentenones related to helenalin in order to clarify the role of the C-6 hydroxyl group in a monocyclic cyclopentenone ring system. In addition, certain esters of this monocyclic cyclopentenone were also prepared to determine if modified esters (which were active in the intact helenalin series) would be just as active in a simpler cyclopentenone series.

Synthesis. Scheme I summarizes the synthesis of these cyclopentenones related to helenalin (compounds **7**–**11**). 2-Methyl-2-carbethoxycyclopentanone (**2**) which was obtained by condensation of ethyl adipate, was converted to the ethylene ketal **3** by reaction with ethylene glycol and *p*-toluenesulfonic acid in dry benzene according to Eschenmoser.[6] Bromination of **3** with pyridinium bromide perbromide gave **4**, which was then dehydrobrominated with 1,5-diazabicyclo[5.4.0]undec-5-ene in dry benzene to yield **5** in 72% yield. Reduction of **5** with $LiAlH_4$ in dry ether furnished the alcohol **6**. Subsequent removal of the protecting group of **6** with 10% HCl in acetone afforded the desired hydroxymethylcyclopentenone whose elemental analysis as well as spectral data was in accord with the assigned structure **7**. The esters **8**–**11** of compound **7**, especially the conjugated esters **9** and **10**, were prepared since previously it was shown that such conjugated system enhanced cytotoxicity and antitumor activity of helenalin and related compounds.[1,7,8] The bifunctional alkylating cyclopentenone sebacate **11** was also prepared as it was found that several *O,O'*-bis(acrylyl)-α,ω-alkanediols demonstrated significant cytotoxicity (H.Ep.-2).[9] Thus, compound **7** was esterified with pyridine-Ac_2O to yield the acetate **8** and with cinnamoyl chloride, trimethoxybenzoyl chloride, and sebacyl chloride in dry benzene and dry pyridine to give rise to the corresponding cinnamate **9**, trimethoxybenzoate **10**, and sebacate **11**, respectively. For the structure–activity correlation purposes, the carbethoxycyclopentenone **13** was also prepared by bromination of **2**, followed by dehydrobromination of **12** by a modified procedure of the one previously reported.[10]

Biological Results. Compounds prepared in this study were first assayed for their in vitro cytotoxicity against the growth of tissue culture cells originating from human epidermoid carcinoma of the larynx (H.Ep.-2) according to a rapid microtiter method previously described.[11] A comparison of the ED_{50} values for the cytotoxicity of the compounds listed in Table I disclosed that the introduction of a conjugated ester side chain to the cyclopentenones, such as in compounds **9** and **10**, enhanced the cytotoxicity although **9** and **10** showed only marginal activity. However, since ethyl cinnamate itself was totally inactive, this

Scheme I



would indicate that the cyclopentenone ring in **9** is the essential moiety responsible for cytotoxicity.[2] The other hydroxymethyl or nonconjugated ester-bearing cyclopentenones **7**, **8**, **11**, and **13** were inactive although their cytotoxicity was higher than the cyclopentenone per se (**14**).

The in vivo antitumor activity of these compounds against the Walker 256 carcinosarcoma in Sprague–Dawley male rats according to the standard NCI protocol[12] also illustrated a parallel result. As shown in Table II, only compounds **9** and **10** were active. Especially, compound **10** demonstrated potent activity in low dose (1.25 mg/kg). Other derivatives (**7**, **8**, **11**, and **13**) were inactive except for **14** which showed significant activity. Similar significant marginal antileukemic activity exhibited by compounds **9** and **10** was also observed in the P-388 assay (Table II). Further investigations of the structure–activity relationships of cyclopentenone-bearing sesquiterpene lactones and related compounds are in progress.

Experimental Section

Chemistry. Unless otherwise specified, melting points were determined on a Thomas-Hoover melting point apparatus and were uncorrected. IR spectra were recorded on a Perkin-Elmer 257 grating spectrophotometer. NMR spectra were measured with a Jeolco C-60 HL spectrometer (Me_4Si) and chemical shifts reported in δ (ppm) units: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and the J values in hertz. Mass spectra were determined on an AEI MS-902 instrument at 70 eV using a direct inlet system. Silica gel for column chromatography refers to Mallincrodt Silica AR cc-7 (200–325 mesh); silica gel for preparative TLC refers to Merck silica gel GF-254; and silica gel for TLC refers to Merck silica gel G developed with suitable solvent systems and visualized by spraying with 10% sulfuric acid and heating. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Ga.; Integral Microlab, Inc., Raleigh, N.C.; or M-H-W Laboratories, Garden City, Mich.

2-Methyl-2-carbethoxycyclopentanone (2) was prepared in 80% yield according to the methods of Eschenmoser[6] or Sato:[14] bp 70–74 °C (0.8 mm).

2-Methyl-2-carbethoxycyclopentanone Ethylene Ketal (3). A mixture of 2-methyl-2-carbethoxycyclopentanone (**2**, 53.2 g, 0.312 mol), ethylene glycol (24.83 g, 0.40 mol), and *p*-toluene-

Table I. Cytotoxicity and Physical Constants of Cyclopentenone Derivatives Related to Helenalin

compd	formula	analyses[a]	mp or bp (mm), °C	recrystn solvent	ED_{50},[b] μg/mL (H.Ep.-2)
1	$C_{15}H_{18}O_4$		170-172[c]	c-C_6H_{12}	0.08
7	$C_7H_{10}O_2$	C, H	oil		15.80
8	$C_9H_{12}O_3$	C, H	78-88 (0.8)		18.30
9	$C_{16}H_{16}O_3$	C, H	oil		3.50
10	$C_{17}H_{20}O_6$	C, H	83-85	Et_2O-petr Et_2O	3.60
11	$C_{24}H_{34}O_6$	*d*	oil		14.60
13	$C_9H_{12}O_3$	C, H	80-90 (3)		17.20
14	C_5H_6O	*e*			>50.0
ethyl cinnamate		*e*			>50.0

[a] Where analyses are indicated only by symbols of the elements, analytical results obtained for these elements were within ± 0.4% of the theoretical values. [b] The values of ED_{50} are used for expressing the potency of cytotoxicity which is the calculated effective dose that inhibits the net cell growth to 50% of control growth. [c] See ref 7. [d] *m/e* 418.2349 ($C_{24}H_{34}O_6$). [e] Product of Aldrich Chemical Co., Inc.

Table II. Effects of Cyclopentenone Derivatives Related to Helenalin on Inhibition of Tumor Growth

		P-388 lymphocytic leukemia		Walker 256 ascites	
compd	N[d]	av days survived	T/C[a]	av days survived	T/C[a]
1	6	13.4/10.4	127 (16.8)[e]	26.33/8.33	316 (2.5)
7	6	10.6/10.1	105 (5)	6.83/6.8	100 (2.5)
8	6	10.6/10.1	105 (5)	8.4/8.0	105 (2.5)
9	6	13.0/9.9	131 (4)	21.5/15.8	136 (2.5)
10	6	12.3/8.83	140 (5)	25.2/11.3	223 (1.25)
11	6	10.8/9.9	109 (4)	18.5/17.2	108 (2.5)
13	6	10.4/10.1	103 (5)	7.0/6.8	103 (2.5)
14	6	10.6/8.83	121 (5)	15/8.0	188 (2.5)
melphalan[b]	6	16.3/9.68	168 (25)	23.0/7.25	317 (2.5)
5-fluorouracil[c]	6	19.7/10.6	186 (25)		

[a] A compound is active if it exhibits a T/C (mg/kg) ≥ 125%.[12] [b] Wellcome Research Laboratories, Research Triangle Park, N.C. [c] Calbiochem, La Jolla, Calif. [d] N is the number of animals per group. [e] See ref 13 for T/C values at different dose levels.

sulfonic acid (0.5 g) in dry benzene (300 mL) was stirred for 16 h at 110 °C (oil bath temperature) using a Dean-Stark trap to remove the water formed during the reaction. The solvent was evaporated in vacuo and the oil residue was partitioned between Et_2O (200 mL) and 5% $NaHCO_3$ (25 mL). The ether layer was washed with H_2O, dried with anhydrous Na_2SO_4, and evaporated to yield a yellowish liquid which upon vacuum distillation gave 41.8 g (73%) of **3**: bp 84–87 °C (1.5–1.6 mm) [lit.[6] bp 115–120 °C (11 mm)]; IR (neat) 1730 cm^{-1} (COOEt); NMR ($CDCl_3$) δ 1.20 (3 H, t, J = 7.0 Hz, OCH_2CH_3), 1.21 (3 H, s, CH_3-2), 3.80 (4 H, m, OCH_2CH_2O), and 4.10 (2 H, q, J = 7.0 Hz, OCH_2CH_3).

5-Methyl-5-carbethoxy-2-bromocyclopentanone Ethylene Ketal (4). Pyridinium bromide perbromide (36 g, 0.09 mol) was added portionwise to a stirring ice-cold solution of 2-methyl-2-carbethoxycyclopentanone ethylene ketal (**3**, 12.6 g, 0.06 mol) in dry THF (100 mL) and the solution stirred at room temperature for 2 h. The precipitate was filtered and the filtrate, after concentration in vacuo, was partitioned between Et_2O (100 mL) and 5% $NaHCO_3$ (40 mL). The ether layer was washed with saturated brine solution, dried over Na_2SO_4, and evaporated. Vacuum distillation of the yellowish oil yielded 4.3 g (14.6%) of **4**: bp 115 °C (1.0 mm). Anal. ($C_{11}H_{17}O_4Br$) C, H, Br.

5-Methyl-5-carbethoxy-2-cyclopentenone Ethylene Ketal (5). A mixture of 5-methyl-5-carbethoxy-2-bromocyclopentanone ethylene ketal (**4**, 2.9 g, 0.01 mol) and 1,5-diazabicyclo[5.4.0]-undec-5-ene (2.3 g, 0.015 mol) in dry benzene (50 mL) was stirred at 90 °C (oil bath temperature) for 48 h. The precipitate was filtered and the filtrate was washed with 5% cold HCl and saturated brine solution, dried over Na_2SO_4, and evaporated. Vacuum distillation of the brownish oil afforded 1.54 g (72%) of **5**: bp 90–96 °C (0.5 mm); IR (neat) 1632 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.32 (3 H, s, CH_3-5), 1.26 (3 H, t, J = 7.0 Hz, CH_2CH_3), 4.16 (2 H, q, J = 7.0 Hz, CH_2CH_3), 3.95 (4 H, m, OCH_2CH_2O), 2.14 and 3.31 (2 H, AB q, J = 17 Hz, each peak is split into J = 2.5 Hz, CH_2-4), 5.50 (1 H, dt, J = 6, 2 Hz, H-2), and 6.10 (1 H, dt, J = 6, 2.5 Hz, H-3).

5-Methyl-5-hydroxymethyl-2-cyclopentenone Ethylene Ketal (6). A solution of 5-methyl-5-carbethoxy-2-cyclopentenone ethylene ketal (**5**, 3.0 g, 0.014 mol) in Et_2O (20 mL) was added dropwise to an ice-cold stirring suspension of $LiAlH_4$ (1.5 g, 0.039 mol) in anhydrous Et_2O (50 mL) and the mixture was stirred at 40 °C (water bath temperature) for 2 h. Enough aqueous ether was used to decompose the excess hydride and the mixture filtered. The filtrate was washed with saturated brine solution, dried over Na_2SO_4, and evaporated. Vacuum distillation furnished compound **6** as an oil (1.0 g, 35%): bp 75–78 °C (1.0 mm); IR (neat) 3380 cm^{-1} (OH).

5-Methyl-5-hydroxymethyl-2-cyclopentenone (7). A solution of 5-methyl-5-hydroxymethyl-2-cyclopentenone ethylene ketal (**6**, 1.0 g, 5.3 mmol) in acetone (10 mL) and 10% HCl (2 mL) was heated at 60 °C (oil bath temperature) for 1 h. After evaporation of the solvent in vacuo, the yellowish liquid was partitioned between Et_2O (30 mL) and 5% $NaHCO_3$ (5 mL). The Et_2O layer was washed with saturated brine solution, dried, and evaporated. Chromatography of the oil on silica gel (50 g) with elution with hexane–Et_2O (1:2) gave **7** as a colorless oil (0.33 g, 50%): IR (neat) 3400 (OH), 1690 (cyclopentenone CO), and 1590 cm^{-1} (C=C); NMR ($CDCL_3$) δ 1.11 (3 H, s, CH_3-5), 2.65 (1 H, overlapped s, OH), 2.37 and 2.89 (2 H, AB q, J = 19 Hz, each peak is split into J = 2.5 Hz, CH_2-4), 3.60 (2 H, AB q, J = 10.5 Hz, CH_2OH), 6.15 (1 H, dt, J = 6, 2 Hz, H-2), and 7.80 (1 H, dt, J = 6, 2.5 Hz, H-3); MS *m/e* 127 (M + 1) and 109 [(M + 1) – 18 (H_2O)].

5-Methyl-5-acetoxymethyl-2-cyclopentenone (8). A solution of 5-methyl-5-hydroxymethyl-2-cyclopentenone (**7**, 200 mg, 1.58 mmol) in Ac_2O (2 mL) and pyridine (4 mL) was allowed to stand at room temperature overnight. Workup in the usual way afforded the acetate **8** (195 mg, 73%): bp 78–88 °C (0.8 mm); IR (neat) 1745 (OAcCO), 1710 (cyclopentenone CO), and 1595 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.12 (3 H, s, CH_3-5), 1.98 (3 H, s, $OCOCH_3$), 2.35 and 2.83 (2 H, AB q, J = 19 Hz, each peak is split into J = 2.5 Hz, CH_2-4), 4.04 (2 H, s, CH_2O), 6.18 (1 H, dt, J = 6, 2 Hz, H-2), and 7.72 (1 H, dt, J = 6, 2.5 Hz, H-3). The IR and NMR spectra are similar to those reported in the literature.[15]

5-Methyl-5-cinnamoyloxymethyl-2-cyclopentenone (9). To an ice-cold solution of 5-methyl-5-hydroxymethyl-2-cyclopentenone (**7**, 252 mg, 2 mmol) in anhydrous pyridine (0.5 mL) and dry benzene (4 mL) was added cinnamoyl chloride (500 mg, 3.02 mmol). The mixture was stirred at ambient temperature overnight and then washed with 5% HCl, H_2O, 5% $NaHCO_3$, and H_2O, dried, and evaporated. Chromatography of the viscous residue on silica gel (20 g) using $CHCl_3$ as eluent gave 255 mg

(50%) of **9** as an oil: IR (neat) 1705 (cyclopentenone CO), 1638 and 1590 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.15 (3 H, s, CH_3-5), 2.40 and 2.90 (2 H, AB q, J = 19 Hz, each peak is split into J = 2.5 Hz, CH_2-4), 4.23 (2 H, s, CH_2O), 6.25 (1 H, m, H-2), 6.36 (1 H, d, J = 17.0 Hz, COC*H*=CHPh), 7.70 (1 H, d, J = 17.0 Hz, COCH=C*H*PH), 7.40 (5 H, m, aromatic protons), and 7.75 (1 H, overlapped m, H-3).

5-Methyl-5-(3,4,5-trimethoxybenzoyl)oxymethyl-2-cyclopentenone (10). A mixture of 5-methyl-5-hydroxymethyl-2-cyclopentenone (**7**, 0.4 g, 3.2 mmol) and 3,4,5-trimethoxybenzoyl chloride (1.1 g, 4.3 mmol) in dry $CHCl_3$ (30 mL) and pyridine (3 mL) was allowed to stand at room temperature overnight. The reaction mixture was worked up in an analogous manner as described for the preparation of **9**. The viscous material was purified by preparative TLC [silica gel, benzene–EtOAc (4:1)] to furnish 0.5 g (49%) of **10**: mp 83–85 °C (Et_2O–petroleum ether); IR ($CHCl_3$) 1715 (cyclopentenone CO) and 1600 cm^{-1} (aromatic ring); NMR ($CDCl_3$) δ 1.23 (3 H, s, CH_3-5), 2.52 and 2.96 (2 H, AB q, J = 19 Hz, each peak is split into J = 2.5 Hz, CH_2-4), 3.90, 3.91, and 3.92 (9 H, 3 s, $3OCH_3$), 4.32 (2 H, s, CH_2O), 6.30 (1 H, m, H-2), 7.21 (2 H, s, aromatic protons), and 7.78 (1 H, m, H-3).

Bis(5-methyl-5-methylenyl-2-cyclopentenone)sebacate (11). A mixture of 5-methyl-5-hydroxymethyl-2-cyclopentenone (**7**, 0.517 g, 4.1 mmol) and sebacyl chloride (0.47 g, 2 mmol) in dry benzene (10 mL) and dry pyridine (1 mL) was allowed to stand at room temperature for 24 h. The mixture was worked up as in the preparation of **9**. The product was purified by preparative TLC [silica gel, Et_2O–hexane (4:1)] to yield 210 mg (25%) of **11**: oil; IR (CCl_4) 1740 (ester CO), 1715 (cyclopentenone CO), and 1595 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.13 (6 H, s, $2CH_3$), 4.06 (4 H, s, $2OCH_2$), 6.23 (2 H, m, COC*H*=CH), and 7.80 (2 H, m, COCH=C*H*).

5-Methyl-5-carbethoxy-2-bromocyclopentenone (12). A solution of Br_2 (1.92 g, 0.012 mol) in AcOH (2 mL) was added dropwise to a stirring ice-cold solution of 2-methyl-2-carbethoxycyclopentanone (**2**, 1.70 g, 0.01 mol) in HOAc (1 mL) and the mixture then stirred at room temperature overnight. The product was diluted with H_2O and extracted with Et_2O. The Et_2O extract was washed with 5% $NaHCO_3$ and H_2O, dried, and evaporated. Vacuum distillation of the oily residue gave 1.7 g (70%) of **12**: bp 110–124 °C (1.2 mm) [lit.[10] bp 128–131 °C (8 mm)].

5-Methyl-5-carbethoxy-2-cyclopentenone (13). 1,5-Diazabicyclo[5.4.0]undec-5-ene (0.9 g, 7.2 mmol) was added to a solution of 5-methyl-5-carbethoxy-2-bromocyclopentanone (**12**, 1.1 g, 4.8 mmol) in dry benzene (20 mL). The mixture was stirred at 90 °C (oil bath temperature) for 2 h. Upon cooling, 10% HCl (10 mL) was added and the product extracted with Et_2O. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated. Chromatography of the residual oil on silica gel [10 g; Et_2O–hexane (1:3)] followed by distillation of the eluent gave 235 mg (29%) of **13**: bp 80–90 °C (3 mm) [lit.[10] bp 99–102 °C (10 mm)]; IR (neat) 1740 (ester CO), 1710 (cyclopentenone CO), and 1595 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.24 (3 H, t, J = 7.0 Hz, OCH_2CH_3), 1.44 (3 H, s, CH_3-5), 2.52 and 3.34 (2 H, AB q, J = 19 Hz, each peak is split into J = 2.5 Hz, CH_2-4), 4.20 (2 H, q, J = 7.0 Hz, OCH_2CH_3), 6.30 (1 H, m, H-2), and 7.92 (1 H, m, H-3).

Biological Methods. In vitro cytotoxicity was determined with H.Ep.-2 cells using the rapid microtiter technique of Huang.[11] A compound is considered active if it shows an $ED_{50} \leq 4$ μg/mL. In the in vivo Walker 256 ascites carcinosarcoma screen, 10^6 tumor cells were implanted ip into Sprague–Dawley male rats (~80 g). Test compounds were administered ip (2.5 mg/kg/day). T/C values were calculated. Melphalan was used as a positive standard.

In the P-388 lymphocytic leukemia screen, 10^6 cells (hemocytomete) were implanted ip into male DBA/2 mice (~20 g) on day 0. Test compounds were administered ip at 25 mg/kg/day for 2 weeks. T/C values were calculated from average survival times. 5-Fluorouracil was used as a positive standard.

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Serotonin Receptor Binding Affinities of Several Hallucinogenic Phenylalkylamine and *N,N*-Dimethyltryptamine Analogues

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Hallucinogenic phenylalkylamine and *N,N*-dimethyltryptamine analogues are known to affect serotonergic systems both in vivo and in vitro. Using a rat stomach fundus model, the 5-HT receptor binding affinities of several of these analogues were determined and compared. The most behaviorally potent analogues examined, DOB, DOM, and 5-methoxy-*N,N*-dimethyltryptamine, were found to possess rather high affinities (pA_2 = 7.35, 7.12, and 7.08, respectively) for the 5-HT receptors of the model system.

Though the mechanism by which hallucinogenic tryptamine analogues produce their profound mental effects has yet to be elucidated, there is evidence that serotonin (5-hydroxytryptamine, 5-HT) receptors may play a pri-

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