60–80 mesh Chromosorb W (AW-DMCS) at injector, column, and flame ionization detector temperatures of 200, 170, and 210°, respectively. The helium carrier was regulated at 25 ± 1 ml/min. Hydrogen and compressed air flows were 37 and 181 ml/min, respectively. Known aliquots of the pyrolyzed and unpyrolyzed salts were then injected, and the amide yields found.

The procedure of prior purification using the copper column before quantitation utilizing the Pyrex column worked only for the short-chain amides, i.e. the methyl-, dimethyl-, and *n*-butylamides, since the long-chain amides could not be collected. However, the long-chain amides were detected upon injection onto the Pyrex U-tube column at temperatures above 230°. The dodecylamide was purified by vacuum distillation, and was then quantitated at 250° on the Pyrex U-tube column.

The pyrolysis products were identified by GC–mass spectroscopy done with a flame ionization/gas–liquid chromatograph and an MS-12 mass spectrometer. The GC column used was a 6 ft × 3.5 mm i.d. stainless steel tube, packed with 10% SE-30 impregnated 60–80 mesh Chromosorb W (AW-DMCS), injector and detector temperatures being 232 and 350°, respectively. The temperature program involved holding the column at 70° for 6 min after injection and then heating the column to 200° at 4°/min; the column was held at 200° until all short-chain amides eluted. The flow rates of compressed air, hydrogen, and helium carrier were 500, 35, and 20 ml/min, respectively. The amide, 2,4-dichlorophenol, and 2,4-D methyl ester were identified from their retention times and mass spectra with authentic standards.

The best conditions for isothermal separation of a mixture of the short-chain amides on the Pyrex U-tube column were found by varying the temperature between 165 and 200°, while monitoring the resolution of the peaks. All other conditions were as described above.

RESULTS AND DISCUSSION

Pyrolysis of the methyl-, *n*-butyl-, *n*-dodecyl-, and dimethylamine salts of 2,4-D at 160° caused formation of the corresponding amides in yields of 75 ± 3, 77 ± 4, 40 ± 2, and 46 ± 3%, respectively; 2,4-dichlorophenol was also produced in 2 ± 0.2% yield. The remainder was undecomposed salt. Pyrolysis at 190° increased the yields to 77 ± 4, 82 ± 4, 80 ± 3, and 82 ± 4%, respectively, and the yield of 2,4-dichlorophenol increased to 5.0 ± 0.6% for all salts. Only a trace of unreacted salt survived pyrolysis at 190°. The balance of the pyrolysis products at 190° were nonvolatile under the GLC conditions used.

The GC yields above were computed using acetonitrile as solvent and the Pyrex U-tube column. An additional GC peak appeared when methanol was the solvent; this was the methyl ester of 2,4-D. The yields of ester from the pyrolyzed salts were higher than those from the unpyrolyzed compounds, implying the amides solvolyzed to some extent. Only a trace of the corresponding amide was found on direct GC of the unpyrolyzed lower chain amine salts.

The major advantage of this analytical method is that the amide function retains the identity of both acid and amine, and so the original amine salt can be identified. The retention of the nitrogen in the amide group also allows use of a nitrogen detector.

A mixture of methyl-, dimethyl-, and *n*-butylamides of 2,4-D is resolved isothermally between 165 and 185°. However, the long-chain amides require temperatures above 230°. Pyrex columns must be used to quantitate the amides since the yields obtained using the copper column were lower than those obtained on the Pyrex columns.

A minor disadvantage of the present method is that conversion to the amide is not completely quantitative necessitating the use of calibration curves.

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Synthesis and Herbicidal Activity of *N,N*-Diethyl-2-(1-naphthyloxy)propionamide and Its Optical Isomers

Extensive field tests have shown *N,N*-diethyl-2-(1-naphthyloxy)propionamide or Devrinol to be a highly active preemergence herbicide. The two optically active stereoisomers were synthesized separately and their herbicidal activities were evaluated. The D(−) isomer was found to be about eightfold more active than the L(+) isomer.

Considerable interest has been generated on the relationship between the steric configuration of aryloxypropionic acids and the growth regulating effects in plants (Aberg, 1953, 1965; Matell, 1953; Sjoberg, 1960). Our interest in this area is to study the herbicidal activity of the derivatives of naphthyloxyalkanoic acids. Among those derivatives we have prepared, *N,N*-diethyl-2-(1-naphthyloxy)propionamide or Devrinol (1) was found, after extensive evaluation and field trial studies, to have high preemergence herbicidal activity. The synthesis of 1 was reported by Tseng et al. (1973). We wish to report in this paper the synthesis of the optical isomers of 1 and their comparative herbicidal activities.

CHEMICAL METHOD

The NMR spectra were obtained on a Varian HA-60-IL spectrometer in deuteriochloroform solution with tetramethylsilane as an internal reference. The mass spectra

Table I. Biological Activities of Racemic, D-, and L-*N,N*-Diethyl-2-(1-naphthyloxy)propionamide

Compound	Soil incorp. rate, ppm	% control			
		Crabgrass	Foxtail	Watergrass	Av
Racemic	0.1	14	0	30	15
	0.2	67	34	50	50
	0.4	95	61	81	79
	0.8	100	92	94	95
D form	0.1	54	0	31	28
	0.2	84	73	75	77
	0.4	99	91	93	94
	0.8	100	94	99	98
L form	0.1	0	0	0	0
	0.2	6	0	18	8
	0.4	25	0	27	17
	0.8	59	5	51	38
	1.6	82	38	78	66
	3.2	99	89	94	95

were measured on a Varian MAT CH-5 spectrometer. The ir spectra were recorded on a Perkin-Elmer 457 spectrophotometer. Melting points are uncorrected. The optical rotations were determined on a Bendix Polarimeter Series 1100.

Preparation of Ethyl L(−)-Lactate (3). Ethyl L(−)-lactate was prepared from L(+)-lactic acid (**2**) (Sigma Chemical Co.) according to the method described by Listowsky et al. (1970). It had: NMR ($CDCl_3$) δ 1.30 (t, 3 H, methyl), 1.42 (d, 3 H, methyl), 3.05 (br s, 1 H, hydroxy), 4.23 (q, 3 H, methylene and methine); ir (film) 3430 (OH), 1730 (C=O) cm^{-1}; $[\alpha]^{20}D$ −9.33°.

Preparation of Ethyl *O*-(*p*-Toluenesulfonyl)-L(−)-lactate (4). Ethyl L(−)-lactate (24 g, 0.2 mol) and *p*-toluenesulfonyl chloride (39 g, 0.2 mol) were dissolved in 200 ml of anhydrous ether. While stirring the solution and maintaining the temperature at 5°, triethylamine (21 g, 0.2 mol) was added dropwise. After 4 hr, the reaction mixture was allowed to stand overnight at room temperature. To the resulting solution, 250 ml of ice water was added and the ether layer was worked up to obtain 59.8 g (97%) of solid: mp 31.5–32.5°; $[\alpha]^{20}D$ −39.7°; ir (KBr) 1755, 1740 (C=O), 1370, 1200 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 1.29 (t, 3 H, methyl), 1.50 (d, 3 H, methyl), 2.44 (s, 3 H, methyl), 4.09 (q, 2 H, methylene), 4.91 (q, 1 H, methine), 7.25–7.88 (m, 4 H, aromatic); MS (*m/e*) 272 (parent ion) (lit. Tseng et al., 1971).

Ethyl D(−)-[2-(1-Naphthyloxy)propionate] (5). Ethyl *O*-(*p*-toluenesulfonyl)-L(−)-lactate (21 g, 0.1 mol) dissolved in 100 ml of tetrahydrofuran was allowed to react with 0.1 mol of anhydrous sodium 1-naphthoxide. The reaction mixture was kept at 80° for 3 hr. Upon work-up, 10.8 g (94%) of a light brown liquid was obtained: $[\alpha]^{20}D$ −26.95°; ir (film) 1750, 1735 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.18 (t, 3 H, methyl), 1.73 (d, 3 H, methyl), 4.18 (q, 2 H, methylene), 4.91 (q, 1 H, methine), 6.60–8.50 (m, 7 H, aromatic); MS (*m/e*) 244 (parent ion) (lit. Tseng et al., 1971).

Resolution of (+)- and (−)-[2-(1-Naphthyloxy)propionic Acids] (6a and 6b). The resolution of (+)- and (−)-[2-(1-naphthyloxy)propionic acids] was carried out according to the method of Fourneau and Balaceano (1925): (+)-[2-(1-naphthyloxy)propionic acid] (**6a**), mp 121.5–123° and $[\alpha]^{20}D$ +45.15°; (−)-[2-(1-naphthyloxy)propionic acid] (**6b**), mp 121–124° and $[\alpha]^{20}D$ −44.04°.

Ethyl (+)-[2-(1-Naphthyloxy)propionate] (7a). Previously resolved (+)-acid **6a** (1 g, 0.005 mol) in 10 ml of ethanol, 200 ml of benzene, and 0.02 g of *p*-toluenesulfonic acid was refluxed until no more water distilled over azeotropically. From the resulting solution, a viscous liquid of 0.76 g was obtained; $[\alpha]^{20}D$ +33.2°. The ir, MS, and NMR spectra were identical with those of **5**.

Ethyl (−)-[2-(1-Naphthyloxy)propionate] (7b). Previously resolved (−)-acid **6b** was esterified as above for the (+)-acid. The product had $[\alpha]^{20}D$ −40.4°. The ir, MS, and NMR spectra were identical with those of **5**.

***N,N*-Diethyl-L(+)-[2-(1-naphthyloxy)propionamide](1a).** This compound was prepared from (+)-[2-(1-naphthyloxy)propionic acid] according to the method described by Tseng et al. (1973). It had: $[\alpha]^{20}D$ +119.17°; ir (KBr) 1627 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.93 (t, 3 H, methyl), 1.09 (t, 3 H, methyl), 1.70 (d, 3 H, methyl), 3.35 (m, 4 H, methylene), 5.08 (q, 1 H, methine), 6.70–8.40 (m, 7 H, aromatic). Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.02; H, 7.82; N, 5.03.

***N,N*-Diethyl-D(−)-[2-(1-naphthyloxy)propionamide](1b).** This compound was prepared by the method used to prepare **1a**. It had: $[\alpha]^{20}D$ −121.35°; mp 90-92°. The ir, MS, and NMR spectra were identical with those of **1a**. Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 74.82; H, 7.78; N, 4.95.

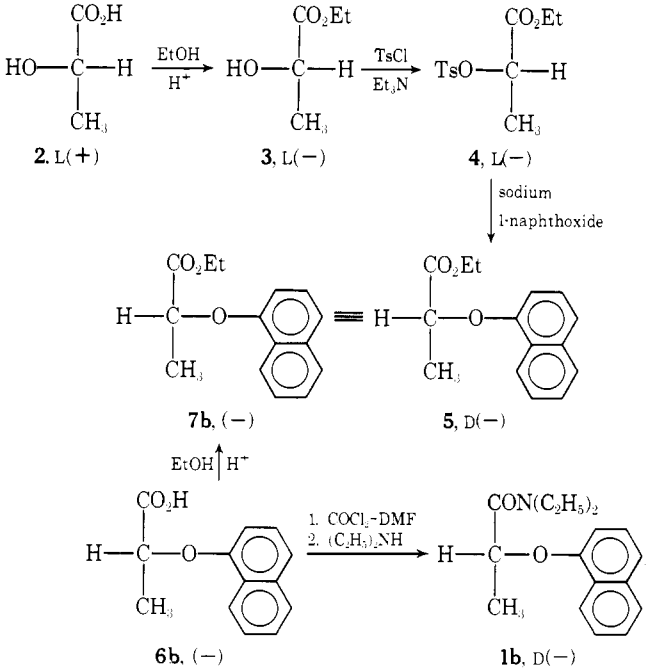
BIOLOGICAL METHOD

The herbicidal activity of the racemic, D(−)-, and L(+)-*N,N*-diethyl-2-(1-naphthyloxy)propionamide was determined in 5 in. × 7 in. × 2⅔ in. flats in a greenhouse test. An acetone stock solution of each compound and three replications of the various treatments were soil incorporated into a loamy sand soil in a 5-gal cement mixer. Seed of *Digitaria sanguinalis* (crabgrass), *Setaria glauca* (foxtail), and *Echinochloa crusgalli* (watergrass) was sown 0.5 in. deep in rows in each flat. Flats were watered by sprinkling. The shoot growth of each plant species was harvested after 3 weeks at soil level, dried, and weighed. The percent control ratings are set at 0 for no control (equivalent to untreated check) and at 100 for complete control of all shoot growth.

RESULTS AND DISCUSSION

The synthesis of optically active 2-(1-naphthyloxy)propionic acid (**6**) was carried out by Fredga and Matell (1951). Since their method of synthesis gave partial racemization, we have used a different approach to establish the absolute configuration of **1**. Scheme I illustrates the se-

Scheme I



quences we have used to establish the absolute configuration of **1b**. L(+)-Lactic acid (**2**) was purchased from Sigma Chemical Co. The esterification of **2** and the tosylation of **3** did not affect the bonds linked to the asymmetric center; therefore, **3** and **4** should have the L configurations. The reaction of **4** with sodium 1-naphthoxide involves inversion of configuration, or SN2 displacement and thus **5** would have the D configuration. Resolution of racemic 2-(1-naphthyloxy)propionic acids (Tseng et al., 1973) was carried out according to the method of Fourneau and Balaceano (1925). The esterification of **6b** gave **7b**. The rotational property of **7b** suggests that **7b** has the same configuration as **5**. Therefore, **7b** should have the D configuration.

The subsequent reactions of **6b** with phosgene and then with diethylamine involved retention of configurations, and thus the product **1b** had the D configuration. The product made from **6a** would be the L configuration.

Comparative herbicidal activities of the racemic, D, and L forms of **1** are listed in Table I. The average L C_{90} for racemic, D, and L forms are 0.62, 0.33, and 2.86 ppm, respectively. This indicated that the D form is approximately eightfold more active than the L form, whereas the racemic mixture gave an intermediate response.

Matell (1953) suggested that the biologically most active forms of 2-aryloxypropionic acids could be attributed to the same steric configuration, the D configurations. Our results seem to confirm his postulation, and the postulation may even be extended to the derivatives of 2-aryloxypropionic acids.

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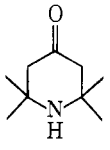
Triacetonamine Formation in Fungal Extracts

Triacetonamine is found to be an artifact formed during the acetone extraction of fungal material.

The selection of an appropriate extraction solvent is a problem which is often encountered when general screening programs are initiated for biological activity of complex mixtures. In most cases the best solvents for extraction of biological material are relatively volatile with both hydrophilic and lipophilic characteristics. Use of such solvents will result in the extraction of a broad spectrum of mainly nonpolymeric compounds. Our survey of fungi for production of certain types of mycotoxins requires such a solvent for extraction of fungal material. Acetone was selected for extraction because of its excellent solvent characteristics and relatively high volatility. Extraction of *Aspergillus oryzae* with acetone has led to the production of 2,2,6,6-tetramethyl-4-piperidone (triacetonamine) (**1**) as the major component of the extract. This compound is an artifact and its production may be avoided by use of other solvents for extraction purposes.



1

EXPERIMENTAL SECTION

Aspergillus oryzae was grown by shaking it for 10 days at 26° in 1 l. of potato dextrose broth (pH 6.4) (Lodder and Kreger-Van Rij, 1952). The mycelium and growth medium were lyophilized to dryness and the residue was extracted with acetone for 18 hr under a nitrogen atmosphere with the Soxhlet cup draining with a frequency of once every 15 min. The extract was evaporated to dryness in vacuo and the dark oily residue (2.3 g) was fractionated on a 2.5 × 30 cm column of silica gel G (<0.063 mm, EM reagent). The column was eluted with chloroform–methanol (3:1) and 20-ml fractions were collected. Fractions were monitored by thin-layer chromatography (TLC) on silica gel pre-coated 60 F-254 chromatoplates (5 × 10 cm, 0.25 mm thick, EM Laboratories Inc.). The TLC plates were developed with chloroform and substances were visualized by their reaction with iodine. Fractions 16–26 were combined and evaporated in vacuo leaving a yellow oil which was crystallized from chloroform–hexane yielding a salt of triacetonamine (225 mg, mp 134–136°) as indicated by its spectral and solubility properties. The free amine was obtained by dissolution of the crystalline material in cold 10% $NaHCO_3$ and extraction of the basic solution with chloroform. Evaporation of the solvent produced a colorless oil which was purified by sublimation at 35° (20 mmHg). The resulting colorless, crystalline material has melting point (34–36°) (Heintz, 1875), ir, NMR, and mass spectra identical with those of an authentic sample prepared from commercially available triacetonamine hydrochloride. Triacetonamine was not present in acetone extracts of sterile potato dextrose broth.

The production of triacetonamine can be avoided by not using acetone for the extraction of fungal material. Methanol was the solvent of choice in most cases in our study. Extraction of fungal material with methanol, which readily extracts triacetonamine salt from spiked samples, did not result in the isolation of this artifact from unspiked samples.

RESULTS AND DISCUSSION

Triacetonamine has been identified as an artifact of plant extractions which utilized ammonium hydroxide or ammonium iodide solutions and acetone in various steps of