to warm to room temperature overnight. Filtration gave a brown solid which was dissolved in aqueous NaOH, filtered, and acidified with HCl to give a yellow solid. Recrystallization from 95% EtOH gave 1.9 g (37%) of product, mp 219–221° dec. *Anal.* ($C_{11}H_9NO_3$) C, H, N.

8-Chloro-4-nitroso-1-naphthol.—The reaction of nitrous acid with N,N-diethyl-N'-(8-chloro-1-naphthyl)ethylenediamine[7] as above gave 42% of product as a pale yellow solid, mp >300°. *Anal.* ($C_{10}H_6ClNO_2$) C, H, N.

8-[(2-Diethylaminoethyl)amino]-6-methoxy-5-nitrosoquinoline (VIII).—To a solution of 7.4 g (0.027 mole) of 8-[(2-diethylaminoethyl)amino]-6-methoxyquinoline[12] in 95% EtOH containing 7 ml of concentrated HCl at 5° was added an aqueous solution of 1.87 g (0.027 mole) of $NaNO_2$. The mixture was stirred for several hours, diluted with H_2O, and made basic with NaOH. The green-brown solid which resulted was removed by filtration, dried, and recrystallized from C_6H_6 to give 4.1 g (50%) of the product as a yellow solid, mp 135.5–137°. *Anal.* ($C_{16}H_{22}N_4O_2$) C, H, N.

N-(3-Methoxypropyl)-1-naphthylamine.—A mixture of 144 g (1.0 mole) of 1-naphthol, 95 g (1.06 mole) of 3-methoxypropylamine, and 174 g (1.0 mole) of $Na_2S_2O_4$ in 600 ml of H_2O was heated in a bomb for 8 hr at 150°. The mixture was removed from the bomb, made strongly basic with NaOH, and extracted with Et_2O. The extracts were dried (Na_2SO_4), the solvent was removed *in vacuo*, and the residue distilled to give 95.4 g (44%) of the product, bp 126–128° (0.2 mm). *Anal.* ($C_{14}H_{17}NO$) C, H, N.

N-(2-Ethylbutyl)-1-naphthylamine.—A mixture of 42.9 g (0.3 mole) of 1-naphthylamine and 30.0 g (0.3 mole) of 2-ethylbutyraldehyde in 400 ml of C_6H_6 containing 1.0 g of *p*-toluenesulfonic acid was heated under reflux for 3 hr. H_2O was removed with a water take-off head. The mixture was concentrated to dryness and hydrogenated over 0.5 g of PtO_2 in 250 ml of EtOH for 16 hr at an initial temperature of 25° and a hydrogen pressure of 3.87 kg/cm². The catalyst was removed by filtration and the solvent was removed *in vacuo*. Distillation of the residue gave 23.4 g (34%) of the product, bp 106–108° (0.09 mm). *Anal.* ($C_{16}H_{21}N$) C, H, N.

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2,2-Dimethyl-3-vinylcyclobutaneacetic Acid, a Fungistatic Agent Derived from Pinene[1a]

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Pure 2,2-dimethyl-3-vinylcyclobutaneacetic acid was prepared by pyrolysis of pinolic acid and some acyl esters followed by selective epoxidation of the ethylidene homolog which was produced along with the vinyl compound. Tests indicate that 2,2-dimethyl-3-vinylcyclobutaneacetic acid is comparable to 10-hendecenoic acid in its fungistatic activity against *Aspergillus niger*, *Aspergillus oryzae*, and *Aspergillus flavus*.

10-Hendecenoic acid and its salt are reported to have unusually good fungistatic action.[2] Because both 10-hendecenoic acid and a recently described acid, 2,2-dimethyl-3-vinylcyclobutaneacetic acid,[3] contains a terminal vinyl group it was believed that the latter acid may also be an effective fungistatic agent. Tests on *Aspergillus niger*, *Aspergillus oryzae*, and *Aspergillus flavus* suggest that the test material is as fungistatic as 10-hendecenoic acid. Since di-*n*-hexyl pinate[4] and lauryl pinonate[5] are not fungistats, the fungicidal properties of the vinylcyclobutane derivative must be due to the vinyl group rather than the dimethylcyclobutaneacetic acid moiety which is present in all three compounds. In addition to the biological activity the acid has a more pleasant odor than 10-hendecenoic acid.

This report covers new information on the synthesis and isolation of the vinylcyclobutaneacetic acid and results of fungistatic tests of the acid compared with 10-hendecenoic acid.

Pyrolysis of pinolic acid, 2,2-dimethyl-3-(1-hydroxyethyl)cyclobutaneacetic acid, or its acetate gave a mixture of 2,2-dimethyl-3-vinyl- and 2,2-dimethyl-3-ethylidenecyclobutaneacetic acids.[3] A comparison of this mixture with 10-hendecenoic acid gave somewhat discouraging results.[6]

In the present work, the ratio of vinyl to ethylidene compounds was considerably less than previously reported. To improve the yield of desired product, the pyrolyses of some esters other than the acetate were investigated (Table I). Pivalic and 3,3-dimethylhexanoic acid esters gave substantially better yields than the other esters. Separation of products was effected by selective epoxidation of the olefin mixture with *m*-chloroperbenzoic acid (MCPA) in ether. The vinyl compound was less readily attacked than the ethylidene derivative and distillation of the partially epoxidized mixture gave dimethylvinylcyclobutaneacetic acid free of the ethylidene derivative.

Thoi[7] and Trave[8] and other workers have given the name *cis-dl*-pinolic acid to the solid isomer, mp 105°

(1) (a) Presented at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967; (b) The University of Mississippi; (c) Naval Stores Laboratory; (d) Agricultural Research Service.

(2) K. S. Markley, "Fatty Acids," Part I, 2nd ed, Interscience Publishers, Inc., New York, N. Y., 1960, p 122.

(3) J. D. Park, R. L. Settine, and G. W. Hedrick, *J. Org. Chem.*, **27**, 902 (1962).

(4) S. Berk, H. Ebert, and L. Teitell, *Ind. Eng. Chem.*, **49**, 1115 (1957).

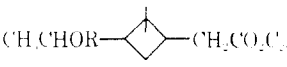
(5) H. B. Summers, G. W. Hedrick, F. C. Magne, and R. Y. Mayne, *ibid.*, **51**, 549 (1959).

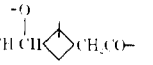
(6) R. Mayne, unpublished results, 1961.

(7) Le-van Thoi, *Ann. Chim.* (Rome), **10**, 35 (1931).

(8) R. Trave, *Chim. Ind.*, **85**, 908 (1958).

TABLE I
PYROLYSIS OF ESTERS OF ETHYL PINOLATE



R	Yield of ester, %	Ester bp, °C (mm)	$n^{25}D$	Yield, %	Pyrolysis product % vinyl	% ethylidene	Formula[b]
CH_3CO[a]	80	100–101 (9)	1.4442	77	48.0	51.4	$C_{16}H_{24}O_4$
C_6H_5CO	89	170–171 (0.01)	1.5091	92	56	44	$C_{25}H_{28}O_4$
$CH_2CH_2CH_2C(CH_3)_2CH_2CO$	86	111–112 (0.01)	1.4495		59.5	40.5	$C_{27}H_{38}O_4$
$(C_6H_5)_2CHCO$	84	195–196 (0.1)	1.5251		50.2	49.8	$C_{36}H_{32}O_4$
$(CH_3)_3CCO$	82	104–105 (0.1)	1.4440	100	64.0	36.0	$C_{21}H_{30}O_4$
				87	51	49	

[a] Composition of pyrolysate differs from ref 2 because of improved glpc techniques. [b] All compounds with a formula gave correct analyses for C, H.

(aqueous EtOH). A second material, a liquid obtained in small yield from the filtrate, has been called *trans-dl*-pinolic acid. The nomenclature of Thoi and Trave has been used in this report.

The vinyl and ethylidene homolog from the pyrolysis of a mixture of *cis*- and *trans-dl*-pinolic acid or acyl derivatives of ethyl pinolate used in the present work were easily discernible in glpc. The same was true for the epoxides. In the chromatograms for the mixture of hydrocarbons there were only two components, the vinyl and ethylidene compounds. However, the chromatogram for the vinyl compound when free of the other olefin showed two major peaks which presumably were *cis* and *trans* isomers corresponding to the isomers of pinolic acid. In this paper, this mixture of *cis* and *trans* isomers is referred to as vinyl or pure vinyl to differentiate it from the other olefin. Analyses of the epoxides from the olefins by glpc indicated the presence of two components from the ethylidene oxide and three from the mixture of vinyl compounds. The stereochemistry of these products was not investigated. However, it is reasonable to expect there may be a number of diastereoisomers from the epoxides.

Experimental Section[9]

Results of Fungistatic Tests.—Pure 2,2-dimethyl-3-vinylcyclobutaneacetic acid was tested against *A. niger*, ATCC 10535, *A. oryzae*, NR11 A5246, and *A. flavus*, a toxigenic strain, using 10-hendecenoic acid as a positive control. The chemicals were dissolved and diluted in mineral oil to the desired concentrations. The oil dilution was then mixed in a sterile Waring Blendor for 30 sec with a melted nutrient agar having strong buffering capacity at pH 6.4. The agar was made by adding 100 ml of solution A to 150 ml of melted solution B. Solution A consisted of 3.0 g of $NaNO_3$, 0.5 g of KCl, 0.5 g of $MgSO_4 \cdot 7H_2O$, and 30 g of dextrose in 300 ml of 1 *M* K_2PO_4 buffer at pH 6.4, all diluted to 400 ml and sterilized by filtering through a Millipore filter. Solution B consisting of 5 g of agar plus 150 ml of 0.016% $Fe_2SO_4 \cdot 7H_2O$ (final concentration 0.01%) was autoclaved. After all ingredients and test chemicals were mixed in the blender, the medium was poured back into the flask, air bubbles were allowed to disappear slightly, and it was then poured into Petri dishes. The pH was checked with Hydrion paper in the hardened agar.

To inoculate, a drop of spore suspension of each test organism in 0.05% Tween 20 was placed in the center of an inverted plate. Three plates of each concentration of chemical were used for each fungus, unless otherwise indicated in the table. The plates were incubated 7 days at 30° and then two diameters of the colony were measured. The results are given in Table II.

TABLE II
FUNGISTATIC TESTS OF 10-HENDECENOIC ACID AND 2,2-DIMETHYL-3-VINYLCYCLOBUTANEACETIC ACID

Sample	Growth of mold[a] *A. oryzae*[b]	*A. niger*[b]	*A. flavus*[c]
Mineral oil only	56.5	34.3	60.0
10-Hendecenoic acid			
0.060 *M*, 1.105%, pH 6.2	0	0	0
0.003 *M*, 0.055%, pH 6.3	26.7	21.5	47.0
0.002 *M*, 0.036%, pH 6.4	42.2	29.5	55.0
0.001 *M*, 0.018%, pH 6.4	45.4	36.0	37.3
Pure dimethylvinylcyclobutaneacetic acid			
0.060 *M*, 1.010%, pH 6.2	0	0	0
0.030 *M*, 0.505%, pH 6.3	0	0	0[d]
0.006 *M*, 0.101%, pH 6.3	8.2	8.7	17.0[d]
0.003 *M*, 0.050%, pH 6.4	13.0	23.5	36.0[d]

[a] Diameters of the colonies in millimeters. [b] Average of six diameters. [c] Average of four diameters. [d] Average of two diameters.

Judging from the average size of the colonies given in the table, it may be said that pure 2,2-dimethylvinylcyclobutaneacetic acid at pH 6.4 was as fungistatic as the 10-hendecenoic acid at pH 6.3 against all three organisms. All concentrations of the former acid used (down to 0.003 *M* or 0.050%) either inhibited or delayed the growth of the three organisms, and 0.050% or 0.030 *M* completely stopped the growth for 1 week. The pure acid in this test gave better results than the mixed isomers had given in 1961. At that time, complete inhibition of only one organism was accomplished with 0.030 *M* although the growths of both organisms were slowed by 0.003 *M* solutions.

Ethyl Pinolate.—Pinolic acid[10] (186 g, 1 mole) was dissolved in 500 ml of C_6H_6 containing 150 ml of EtOH and 1–2 g of *p*-toluenesulfonic acid. After refluxing overnight, under a Dean–Stark separator, the product was cooled and washed (H_2O, aqueous $NaHCO_3$), the solvent was removed, and the residue was distilled (lit.[11] 53%). By glpc analysis (168°; He 15.27 kg/cm², 50 ml/min) the ester was approximately a 5:1 *cis–trans* mixture.

Ethyl Pinolate Pivalate (Ethyl 2,2-Dimethyl-3-[1-(2,2-dimethylpropionoxy)ethyl]cyclobutaneacetate).—Pivaloyl chloride (2,2-dimethylpropionyl chloride) (50 g, 0.4 mole), freshly distilled, was added rapidly to ethyl pinolate (64.8 g, 0.3 mole), in 300 ml of C_6H_6 containing 100 ml of pyridine. The mixture was heated to 60°. After stirring about 1 hr, precipitated pyridine hydrochloride was removed by filtration. The filtrate was washed (H_2O, dilute AcOH, aqueous $NaHCO_3$, H_2O) and dried, and the solvent was removed *in vacuo*. Distillation of the residual yellow oil gave 72.4 g. The physical data for this ester with the data for four other esters similarly prepared are listed in Table I.

(9) Elemental analyses were within ±0.4% unless otherwise indicated. All boiling points are uncorrected. Glpc analyses were made with a 3.66 m × 17 mm column packed with 20% Craig polyester in Chromosorb W.

(10) J. D. Park, R. L. Settine, B. A. Parkin, Jr., and G. W. Hedrick, *J. Org. Chem.*, **27**, 868 (1962); pinolic acid used in this work had little purification and was a mixture of *cis* and *trans* isomers.[5,8]

(11) B. A. Parkin, Jr., and G. W. Hedrick, *ibid.*, **25**, 1117 (1960).

TABLE III

PHYSICAL DATA FOR ETHYL PINOLATE, OLEFINIC COMPOUNDS, AND THEIR EPOXIDES

Compd	Yield, g	Yield, %	Bp, °C (mm)	n_D (t, °C)	Formula	Analyses
Ethyl pinolate	193	90[a]	116–118 (1.0)	1.4539 (20)		
Ethyl 2,2-dimethyl-3-vinylcyclobutaneacetate	72	73.5[b]	88 (4.0)	1.4511 (25)	$C_{12}H_{20}O_2$	C, H
2,2-Dimethyl-3-vinylcyclobutaneacetic acid		100	101–102 (0.5)	1.4640 (20)	$C_{10}H_{16}O_2$	C, H, neut equiv
Ethyl 2,2-dimethyl-3-ethylidenecyclobutaneacetate epoxide	118	111[c]	105 (4.0)	1.4506 (20)	$C_{12}H_{20}O_3$	C, H
Ethyl 2,2-dimethyl-3-vinylcyclobutaneacetate epoxide	14.5	72	82–83 (0.6)	1.4536 (20)	$C_{12}H_{20}O_3$	C, H

[a] Lit.[9] 53%. [b] Based upon 50% vinyl in pyrolysate and disregarding product in forecut and intermediate fractions. Pyrolysate from pinolic acid used for convenience. [c] By glpc contained approximately 10% of the epoxide from the vinyl compound.

Pyrolysis of the Pivalate Esters.—Ethyl pinolate pivalate (60 g) was placed in a distilling flask with a 45-cm Vigreux column, thermometer well, and distilling head. The ester was heated to 325° at atmospheric pressure to crack and distil the pyrolysate. The crude product was dissolved in ether, washed (aqueous $NaHCO_3$, H_2O), and dried (Na_2SO_4). The ether was removed and the product distilled using 20-cm column packed with stainless steel helices. The distillate was analyzed for vinyl and ethylidene components by glpc (123°; He (3.5 kg/cm²), 30 ml/min). Only two peaks were observed with emergence times of 26 and 27.4 min for the ethylidene and vinyl compounds, respectively. The yield and compositions of olefinic esters from pyrolyses of the acyl esters are given in Table I.

Ethyl 2,2-Dimethyl-3-vinylcyclobutaneacetate.—One mole (196 g) of an approximately 1:1 vinyl–ethylidene mixture, prepared from cracking pinolic acid and esterifying by the procedure used for pinolic acid above, was dissolved in 500 ml of Et_2O and treated with 108 g of 85% *m*-chloroperbenzoic (MCPA) acid (0.53 mole) dissolved in Et_2O (50 ml). The peracid solution was added dropwise at room temperature and the mixture was stirred for 4 hr after addition. *m*-Chlorobenzoic and excess *m*-chloroperbenzoic acids were extracted with aqueous Na_2CO_3. When starch–KI paper gave a negative test for peracid in the Et_2O solution, the product was dried (Na_2SO_4). Removal of solvent and a bulb-to-bulb distillation gave 197 g (97%), bp 107–135° (7.0 mm). The product was distilled using a 45-cm column packed with stainless steel helices. After removal of 4 g of forecut (mostly product), 72 g was obtained, vinyl olefin ir absorbance at 3.30, 6.04, and 11.00 μ.

An intermediate fraction was taken, then the ethylidene epoxide derivative distilled. See Table III for data.

The reaction and distillation was monitored by glpc. The relative emergence times (minutes) for the hydrocarbon mixture and the epoxides using the 20% Craig column (168°; He (5.27 kg/cm²), 50 ml/min) were ethylidene 1.42; vinyl 1.54; ethylidene epoxides 4.85 and 5.54 in a 4:1 ratio; vinyl epoxides 8.4, 8.7, and 9.3 in ratios of about 1.8:2.6:1.

Glpc chromatogram of the vinyl homolog when free of the other olefin (the above column at 123°) had two peaks with retention times of 27.6 and 29.8 min and peak areas about 5:1. It was hoped the ethylidene epoxide could be converted to ethyl pinolate for recycling by hydrogenation. Raney Ni catalyst (5%) in absolute EtOH, H_2 (84 kg/cm²) at 150° for 3 hr gave no ethyl pinolate. Starting material and a number of other substances including alcohols were present as evidenced by glpc and ir. No further work was done on this phase.

Ethyl 2,2-Dimethyl-3-vinylcyclobutaneacetate Epoxide.—The vinyl ester was epoxidized to have material for glpc analyses. For this 19.6 g (0.1 mole) of the ester in 200 ml of C_6H_6 was treated with 20.5 g of 85% *m*-chloroperbenzoic acid (0.1 mole per acid) dissolved in 100 ml of C_6H_6. After an initial slightly exothermic reaction, the mixture was agitated overnight at room temperature. Glpc analyses of an aliquot indicated only a small amount of unreacted product. The batch was washed (aqueus Na_2CO_3, H_2O) and tested for peracid with KI paper. The solvent was removed from the peracid-free solution and the product distilled through a 15-cm column packed with stainless steel helices. See data in Table III.

Additional evidence of epoxidation was obtained by conversion of the epoxide to diethyl pinate.

The epoxide (2 g, 0.1 mole) was hydrolyzed with 50 ml of 1% H_2SO_4. After stirring overnight at room temperature, all the epoxide was in solution. Sodium metaperiodate, 2 g (0.0095 mole), in 10 ml of H_2O was added and, after about 1 hr, an oil separated. The oil (an aldehyde) was extracted with ether and the solvent was removed. Excess Ag_2O prepared fresh from NaOH and $AgNO_3$ was added to oxidize the aldehyde. Extraction of insolubles with ether, filtering and acidifying the filtrate, and extracting with ether again gave monoethyl pinate (ethyl 2,2-dimethyl-3-carboxycyclobutaneacetate). The half-ester was esterified with EtOH[12] to give diethyl pinate (2 g), which was characterized by comparing the ir spectrum and refractive index with that of an authentic sample.

2,2-Dimethyl-3-vinylcyclobutaneacetic Acid.—Saponification of ethyl 2,2-dimethyl-3-vinylcyclobutaneacetic acid in 0.5 *N* alcoholic KOH gave the acid as expected. See data in Table III.

(12) J. B. Lewis and G. W. Hedrick, *J. Org. Chem.*, **24**, 1870 (1959).