

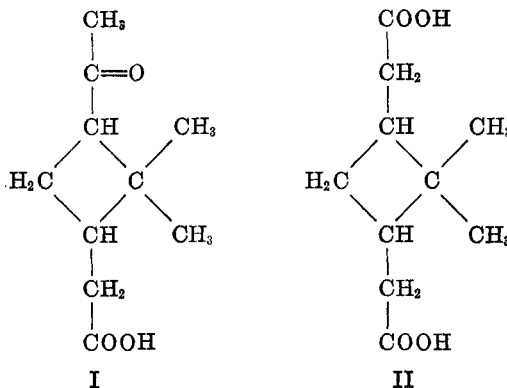
SYNTHESIS OF *SYM*-HOMOPINIC ACID

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The oxidation of *alpha*-pinene, a constituent of turpentine, to pinonic and pinic acids has recently been investigated by this laboratory. The alkyl esters of these acids were found to be suitable for use in the synthetic lubricant and plasticizer field (1). Pinonic acid (I), a methyl keto monobasic acid, is readily prepared from *alpha*-pinene by oxidation with permanganate (2) or ozone. Its structure indicates that *sym*-homopinic acid (2,2-dimethylcyclobutane-1,3-diacetic acid) (II), a C₁₀ dibasic acid, could be prepared from pinonic acid by the use of the Willgerodt reaction (3). Guha and Ganapathi (4, 5) prepared *trans-sym*-homopinic acid from *cis*-diethyl norpinate by reduction to the glycol, conversion of the glycol to the dibromide, thence to the dinitrile, followed by saponification to the acid.

Esters of *sym*-homopinic acid should be valuable as synthetic lubricants and plasticizers. Because of its higher molecular weight and symmetrical nature, this acid should have some advantage over pinic acid in the preparation of plasticizers and synthetic fibers.



Preliminary experiments indicated that the Kindler modification (6-8) using a dry amine and sulfur was preferable for this conversion over the original Willgerodt procedure. Several different amines were evaluated at 128° for 16 hours so that the yield of *sym*-homopinic acid from different types of amines could be compared. Results of these runs are given in Table I. Amines used included aniline, cyclohexylamine, di-*n*-butylamine, *n*-hexylamine, morpholine, piperidine, pyridine, and tri-*n*-butylamine. Primary and tertiary amines were studied as well as the more commonly used secondary amines. Some conversion to *sym*-homopinic acid was obtained with all the amines studied, but morpholine gave the best yields.

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TABLE I
EFFECT OF VARIOUS AMINES ON THE YIELD OF *sym*-HOMOPINIC ACID
(0.10 mole pinonic acid,^c 0.20 mole amine, and 0.20 mole sulfur)

AMINE	REACTION TEMP., ^b °C.	REACTION TIME (HRS.)	CRUDE PRODUCT, G.	NEUT. EQUIV.	TOTAL MILLI-EQUIV. ACIDS	MARVEL-RANDS ANALYSIS		YIELD, ^d %
						Mono-basic, ^c %	Homo-pinic, ^c %	
Aniline.....	128	16	10.6	220	48.2	56	24	5.8
Cyclohexylamine.....	128	16	11.2	303	36.4	23	76	13
Di- <i>n</i> -butylamine.....	128	16	18.4	176	104.2	44	36	20
Di- <i>n</i> -butylamine.....	159	6	17.3	172	100.4	46	39	21
Di- <i>n</i> -butylamine.....	159	9	18.2	168	108.0	58	41	24
<i>n</i> -Hexylamine.....	129	16	7.7	199	38.7	53	45	9.3
Morpholine.....	128	16	17.5	127	138.0	1	90	66
Piperidine.....	109	24	17.5	139	126.0	8	82	55
Pyridine.....	115	20	16.7	179	93.3	68	25	12
Tri- <i>n</i> -butylamine.....	216	5	13.3	227	58.8	90	8	2.4
Tri- <i>n</i> -butylamine.....	128	16	19.2	180	106.6	64	21	12

^a Crude acid used was 94% by weight pinonic acid.

^b Reaction temperatures other than the reflux temperature of the amine were effected by a constant temperature oil-bath.

^c Based on per cent of total titer present in this peak.

^d Millimoles *sym*-homopinic acid per 100 millimoles of pinonic acid in the charge.

TABLE II
EFFECT OF SOME VARIABLES ON THE YIELD OF *sym*-HOMOPINIC ACID

REACTION TIME (HRS.)	MOLES PER 0.10 MOLE OF PINONIC ACID ^a		CRUDE PRODUCT, G.	NEUT. EQUIV.	TOTAL MILLIEQUIV. ACIDS	MARVEL-RANDS ANALYSIS		YIELD, ^c %
	Morpholine ^e	Sulfur				Mono-basic, ^b %	Homo-pinic, ^b %	
8	0.20	0.20	18.7	135	138.6	12	84	62
16	.20	.10	18.1	139	129.7	31	64	45
16	.20	.15	18.5	128	145.4	8	83	64
16	.20	.20	17.5	127	138.0	1	90	66 ^d
16	.20	.25	18.7	139	135.0	4	88	63
16	.20	.30	18.6	169	109.2	13	75	44
16	.20	.40	12.0	184	65.2	4	85	30
63	.20	.20	17.0	122	140.0	2	95	71
16	.30	.20	17.3	119	145.4	5	87	67
16	.10	.20	18.2	154	118.6	37	47	30

^a Crude acid used was 94% by weight pinonic acid.

^b Based on per cent of total titer present in this peak.

^c Millimoles *sym*-homopinic acid formed per 100 millimoles of pinonic acid in the charge.

^d When these conditions were duplicated on a large scale using 1.88 moles of pinonic acid, a yield of 82% was obtained.

^e Reaction temperature approximately 128°, reflux temperature of morpholine.

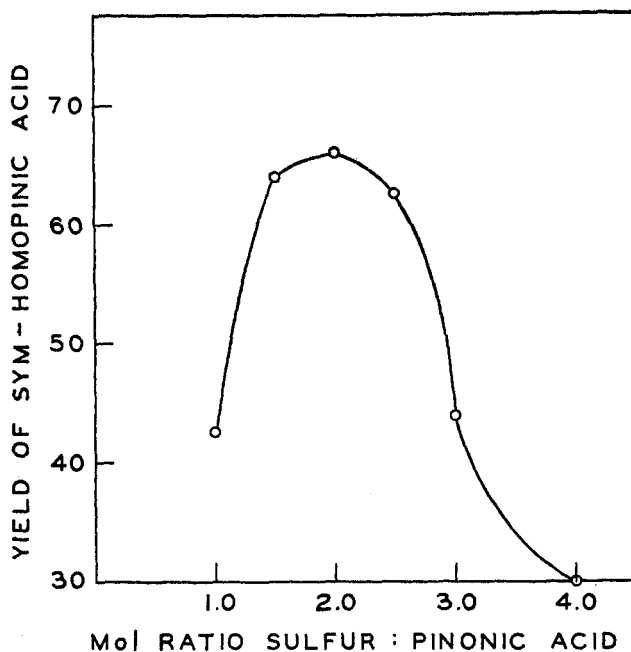


Fig. 1

Since morpholine gave the best yields, a more thorough study was made with it to determine the optimum reaction time and mole ratios of sulfur and amine to pinonic acid. Data from these experiments are given in Table II. Since one mole of morpholine per mole of pinonic acid would be required to neutralize the acid, 2 moles of morpholine would be expected to be required for best results. As shown in Table II, the yield was less with a 1:1 ratio, while 3 moles of morpholine per mole of pinonic acid gave little improvement over the 2:1 ratio. A reaction time of 16 hours gave slightly better yields than 8 hours and little improvement was obtained for longer reaction times. The effect of the molar ratio of sulfur to pinonic acid is shown in Figure 1. Molar ratios between 1.5:1 to 2.5:1 (Sulfur:pinonic acid) gave little differences in yield of *sym*-homopinic acid. However molar ratios outside these limits decreased the yield considerably.

The crude acid products obtained from these runs were weighed, neutral equivalents were determined, and the total equivalents of acid were calculated. Apparently some decarboxylation occurred in all runs and was influenced by the amount of sulfur used. The crude product contained *sym*-homopinic acid, unreacted pinonic acid, probably a monobasic acid resulting from the decarboxylation of *sym*-homopinic acid, and traces of mineral acid as well as sulfur-containing impurities. The crude acids were analyzed by the Marvel and Rands method (9) of partition chromatography. By this method, pinonic acid has a peak effluent volume of 30 ml. and *sym*-homopinic acid has a peak effluent volume of 130 ml. Traces of sulfuric acid were not eluted. The monobasic acid resulting from de-

carboxylation of *sym*-homopinic acid was not separated from the unreacted pinonic acid. However, *sym*-homopinic acid could be separated from impurities by this method.

Large-scale preparations were made using 1.00 to 4.00 moles of pinonic acid with a molar ratio of 2 moles of sulfur and 2 moles of morpholine per mole of pinonic acid. Yields of 74 to 82% of *sym*-homopinic acid were obtained.

The crude "acids" were dark semi-solid products with an objectionable odor. Purification of the crude products was accomplished by either of two methods: (a) treatment with activated carbon in an aqueous solution, followed by crystallization from water, and recrystallization from benzene, (b) vacuum-distillation of the crude product and recrystallization of the best fractions from benzene and then from water. Method (a) often required two treatments with activated carbon to obtain a good product, and a substantial amount of acid was lost on the carbon. Method (b) was difficult to carry out as the sulfur impurities decomposed and gave off gases which raised the pressure during distillation. Substantially pure homopinic acid was obtained by both methods.

EXPERIMENTAL

*Preparation of pinonic acid*². Commercial-grade *alpha*-pinene, d_4^{20} 0.8691, n_D^{20} 1.4680, $[\alpha]_D^{25}$ +21.2°, was oxidized with potassium permanganate (2) in a solution buffered with ammonium sulfate at -2° to 0°. The reaction solution was filtered to remove manganese dioxide and concentrated to $\frac{1}{3}$ its original volume. The solution was filtered to remove potassium sulfate. The solution was acidified with sulfuric acid to pH 1-2; crude crystalline pinonic acid was removed by filtration and liquid pinonic acid was decanted from the filtrate. The crude crystalline pinonic acid obtained after drying had the following constants: neutral equivalent 188, m.p. 93-98°, $[\alpha]_D^{25}$ +16.2° (2% in chloroform). Pure *dl*-pinonic acid has neutral equivalent 184, m.p. 103-104° (10); pure *d*-pinonic acid (11) has m.p. 68-69°, $[\alpha]_D^{25}$ +95° (in chloroform). From analysis by the Marvel and Rands method (9) and neutral equivalent data, the weight-percent pinonic acid was calculated to be 94%. This stock sample was used in all preparations in this study.

Willgerodt procedure. A run was made at 150° for 16 hours using the original Willgerodt (3) procedure. A sample analyzed by the Marvel and Rands method (9) showed 73% of the acid present was *sym*-homopinic acid but a yield of only 13% was obtained.

Small-scale Kindler procedure runs. The reactions listed in Tables I and II were all carried out in the following manner: 18.4 g. (0.10 mole) of pinonic acid was placed in a 200-ml. round-bottom flask and the required amount of amine and sulfur was added and mixed by slight shaking. The contents were refluxed using an electrically heated mantle. In those runs where the reaction temperature was lower than the boiling point of the amine in the charge, a constant temperature oil-bath was used. After the reaction was completed 100 ml. of 20% sodium hydroxide solution was added and the mixture was refluxed 16 hours. After cooling, two extractions with ether were made to remove neutral material. The aqueous solution was slowly acidified to pH 2 with 1:1 sulfuric acid. The exhaust fumes were bubbled through a sodium hydroxide solution to absorb the gases evolved. After cooling, the crude acids were extracted with 3 portions of ether. The combined ether extract was washed with saturated sodium sulfate solution, dried over sodium sulfate, and filtered. The ether was evaporated and the crude acids were dried at 60-70° *in vacuo*. The crude product was weighed and the neutral equivalent was determined electrometrically in an aqueous solution. A Marvel and

² Prepared by H. B. Summers, Jr., Naval Stores Research Division.

Rands analysis (9) was made on each sample and the yield of *sym*-homopinic acid present (based on pinonic acid charged) was determined.

Large-scale preparation of sym-homopinic acid. In a 2-liter round-bottom flask, 368 g. (1.88 moles) of pinonic acid (94%), 128 g. (4.00 moles) of sulfur, and 348 ml. (4.00 moles) of technical-grade morpholine were mixed and were reacted by refluxing for 16 hours. An exothermic reaction occurred shortly after heating and the pot temperature rose as high as 150° in some cases. During this reaction a crystalline mixture of morpholine carbonate and morpholine hydrosulfide collected in the condenser. Later, the temperature dropped and was held at reflux temperature (128°).

After cooling, 285 g. of technical grade sodium hydroxide in 1 liter of water was added and the solution was refluxed overnight. After working up the solution in the manner described for small-scale runs, 384 g. of crude homopinic acid, having a neutral equivalent of 116, was obtained. A Marvel and Rands analysis (9) showed that 93% of the total equivalents of acid was *sym*-homopinic acid and an over-all yield of 82%.

Purification with activated carbon. The crude product described above (384 g.) was dissolved in 3 liters of boiling water and was refluxed with activated carbon for 30 minutes. The hot solution was filtered and allowed to crystallize. Some material separated as an oil and then crystallized (crop I). When crop I was recrystallized from benzene, 157 g. (0.79 mole) of acid, m.p. 114.5–118.5°, neutral equivalent 100.4, was obtained. The original aqueous solution on evaporation gave crop II, 29 g. (0.15 mole), m.p. 115–119°, neutral equivalent 100.4. After two recrystallizations of crop II from benzene, 22 g. (0.11 mole) of *sym*-homopinic acid was obtained. Further recrystallization gave no improvement. The following constants were obtained on this material: m.p. 119.5–121.0;³ Neutral equivalent, 100.2 (theory 100.1); $[\alpha]_D^{25}$ -2.4° (2% in ethanol), -5.0° (2% in chloroform), -4.0° (2% in acetone).

*Anal.*⁴ Calc'd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06.

Found: C, 60.07; H, 8.05.

The benzene mother liquor from recrystallization of crop I when concentrated gave 72 g. of dark material, neutral equivalent 135 (Calc'd as *sym*-homopinic acid, 53 g., 0.27 mole).

By refluxing the activated carbon used in the initial purification step, an additional 40 g. of crude acid, neutral equivalent 123, was recovered (Calc'd as *sym*-homopinic acid, 32 g., 0.16 mole).

Purification by distillation and recrystallization. A sample of crude product (187 g.), neutral equivalent 128, prepared by the usual procedure (74% yield), was distilled bulb to bulb at reduced pressure and the following fractions were collected:

FRAC.	WT., G.	B.P., °C.	P (MM. Hg)	NEUT. EQUIV.
1	26	200	3.2	138
2	29	203	2.8	104
3	48	207	2.6	102
4	26	206	2.5	102
5	21	213	2.1	118
Residue	31	—	—	—

When a portion (70 g.) of a composite of cuts 2 and 3 was recrystallized from benzene, 47 g., m.p. 114–119°, Neutral equivalent 100.2 was obtained. Recrystallization of 5.00 g. from benzene followed by recrystallization from water gave 4.10 g. of *sym*-homopinic acid, m.p. 119.5–121.0°, Neutral equivalent 100.2. Further recrystallization gave no purification.

Solubility of sym-homopinic acid. *sym*-Homopinic acid was soluble to the extent of at least 10% in acetone, alcohol, chloroform, and ether at room temperature. In benzene and water it was only slightly soluble at room temperature, but was quite soluble at their boiling point.

³ Guha and Ganapathi (4) reported m.p. 120–121° for *trans-sym*-homopinic acid.

⁴ Analysis by L. E. Brown, Southern Regional Research Laboratory.

Preparation of derivatives. The following derivatives were prepared:

DERIVATIVE	M.P., °C.	ELEMENTAL ANALYSIS ⁴					
		Calc'd			Found		
		C	H	N	C	H	N
Benzylamine salt (mono).....	163-165	66.42	8.20	4.56	66.42	8.21	4.62
Cyclohexylamine salt (bis).....	200-202	66.29	10.62	7.03	66.35	10.62	7.17
Dianilide.....	221-223 ⁵	75.39	7.48	8.00	74.66	7.35	8.06
<i>p</i> -Phenylphenacyl ester (bis)....	136-138	77.53	6.16	—	77.83	6.35	—

The amine salts were prepared by adding 0.022 mole of the amine dissolved in 5 ml. of acetone to 0.01 mole of the acid dissolved in hot acetone. The benzylamine salt was recrystallized twice from acetone and the cyclohexylamine salt was recrystallized twice from an acetone-alcohol mixture. The dianilide was prepared from the acid chloride in the usual manner and was recrystallized twice from 80% ethyl alcohol. The *p*-phenyl-phenacyl ester was prepared in the usual manner and was recrystallized from ethyl acetate and again from ethyl alcohol. The melting points reported were obtained by inserting capillaries in the bath at approximately 20° below the melting point. If heated from room temperature melting points 1-4° lower were obtained.

Preparation of di-n-hexyl ester of sym-homopinic acid. *sym*-Homopinic acid (303 g.), m.p. 117-120°, Neutral equivalent 100.4, was dissolved in 450 ml. of toluene and an 86% excess of redistilled *n*-hexyl alcohol, b.p. 157°, was added. Sulfuric acid (6 ml. of 18 *N*) was used as a catalyst. The mixture was refluxed and water was removed by a trap. Esterification was substantially complete after 3 hours. The solution of ester was washed successively with water, 2% sodium carbonate solution, 2% sodium hydroxide solution, and then washed to neutrality with several portions of water. Excess *n*-hexyl alcohol and toluene were removed by distillation and 559 g. of crude ester, n_D^{20} 1.4529, was obtained. Vacuum-distillation of this material through an 18-inch Vigreux column gave 522 g. of ester (94% yield), b.p. 172° at 0.5 mm., n_D^{20} 1.4535, d_4^{20} 0.9446, $[\alpha]_D^{20}$ -1.25° (homogeneous).

Anal. Calc'd for C₂₂H₄₀O₄: C, 71.69; H, 10.94.

Found: C, 71.79; H, 10.91.

SUMMARY

1. *sym*-Homopinic acid, a C₁₀ dibasic acid, was prepared from pinonic acid, a C₁₀ keto-monobasic acid, by means of the Willgerodt reaction.
2. The Kindler modification using a dry amine and sulfur gave better yields than the original Willgerodt procedure.
3. Appreciable yields were obtained with primary and tertiary amines as well as secondary amines.
4. The effect of reaction time and concentrations of sulfur and morpholine on the yield was determined. The maximum yield obtained with this amine was 82%.
5. Derivatives of *sym*-homopinic acid were prepared.

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⁵ Guha and Ganapathi (4) reported m.p. 219-220° for the dianilide of *trans-sym*-homopinic acid.

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