6-Methylanthranilamide. A mixture of 5.2 grams (0.04 mole) of 2-cyano-*m*-toluidine (*3*) and 35 ml. of 50% aqueous sulfuric acid was stirred under reflux for 5 hours. The solution was cooled and made alkaline with 40% sodium hydroxide. The resulting solid was filtered to give 1 gram of recovered starting material. The filtrate was neutralized with acetic acid and extracted first with chloroform and then with 1-butanol. The extracts were washed with water, dried (sodium sulfate), and evaporated separately. The residues were combined and recrystallized from chloroform. Yield 1.5 grams (31%), m.p. 138–139° C.

Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.66. Found: C, 63.58; H, 7.04; N, 18.59.

Methyl *N*-(*p*-Aminophenylcarbamoyl) Anthranilate (Ix). A mixture of 6.3 grams (0.02 mole) of Iv, 0.5 gram of 10% palladium on carbon, and 250 ml. of acetic acid was hydrogenated on a Parr apparatus under 3 atm. of hydrogen. The catalyst was filtered, and the filtrate was added to a stirred mixture of ice water and chloroform. To this mixture was added slowly 10% sodium hydroxide until the solution was neutral. The layers were separated, and the aqueous layer was extracted three times with chloroform. The combined chloroform layers were washed with water until neutral, dried, and evaporated in vacuo at room temperature. The residue was recrystallized.

If dimethylformamide was used in place of acetic acid in the hydrogenation and the filtered reaction solution was diluted with water, the resulting solid was the cyclized 3-(*p*-aminophenyl) quinazoline-2,4-dione, m.p. 335–337° C. (uncorrected) (pyridine-ether).

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 66.14; H, 4.72; N, 16.53. Found: C, 65.98; H, 4.59; N, 16.32.

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RECEIVED for review February 6, 1968. Accepted June 11, 1968. For a more complete Table I, order NAPS Document NAPS-00086 from ASIS National Auxiliary Publications Service, c/o CCM Information Sciences, Inc., 22 West 34th Street, New York, New York 10001; remitting $1.00 for microfiche or $3.00 for photocopies.

Thermal Isomerization of Methyl Abietate

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Methyl abietate has been found to isomerize at 200° C. at about the same rate as the free acid. The same final equilibrium distribution of palustrate (14%), neoabietate (5%), and abietate (81%) was obtained as observed for the free acid. Disproportionation, however, was extensive in the case of the ester in contrast to the free acid. The addition of base to the ester very strongly inhibited isomerization and prevented disproportionation.

IN A PREVIOUS investigation concerning the isomerization of the four conjugated dienoic resin acids, the authors reported for the first time that abietic acid at 200° C. was isomerized to a final equilibrium mixture of 14% palustric, 5% neoabietic acid, and 81% abietic acid (*7*). The same final distribution of acids was also noted for the first time when levopimaric, palustric, and neoabietic acids were treated in the same fashion. Disproportionation under these conditions was found to be negligible.

The methyl esters of levopimaric (*4*), palustric (*3*), and neoabietic (*5*) acids have been found to isomerize to methyl abietate very slowly as compared with the acids. No report has been made in the literature concerning the reverse isomerization of methyl abietate to methyl palustrate, neoabietate, and levopimarate. It was, therefore, decided to investigate this problem.

Methyl abietate was sealed in borosilicate glass tubes under nitrogen and heated in a bath at 200° C. The tubes were removed at intervals and analyzed by means of GLPC (*2*), optical rotation, and ultraviolet absorption spectrum. The results are summarized in Tables I and II. Three interesting observations were made. First, methyl abietate isomerizes at 200° C. to give the same final equilibrium ratio of abietate (81%), palustrate (14%), and neoabietate (5%) as the free acid (Table I). Second, the ester isomerizes at essentially the same rate as the free acid. Third, the ester undergoes rather extensive disproportionation (Table II) as compared with the free acid which does not disproportionate under these conditions.

The isomerization of methyl abietate was repeated at 180° C. and the same ratio of abietate, palustrate, and neoabietate was obtained. Disproportionation also occurred at the lower temperature, but at a slower rate. The isomerization followed first order kinetics with respect to the loss of methyl abietate for the first 50 minutes; $k = 3.67 \times 10^{-5}$ sec.$^{-1}$ at 180° C.; $t_{1/2} = 5.3$ hours. These values are essentially the same as those reported (*7*) for the isomerization of the free acid at 180° C.

In the work on the free acid (*7*), it was shown that the addition of a small amount of base strongly inhibited the isomerization. Consequently, the addition of a 5 mole

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Table I. The Isomerization of Methyl Abietate at 200° C.[a]

Products of Isomerization, %	Time, Hours						
	0	0.5	1.0	2.0	5.0	8.0	24.0
Methyl abietate	100	81.2	79.1	78.5	78.8	79.5	80.4
Methyl palustrate	0	14.5	14.6	14.7	14.7	14.5	14.6
Methyl neoabietate	0	4.3	6.3	6.8	6.5	5.0	5.0

[a] The presence of esters other than abietate, palustrate, and neoabietate are omitted in the calculations.

Table II. The Disproportionation of Methyl Abietate at 200° C.

Products of Disproportionation	Time, Hours					
	0	24	32	53	78	168
Methyl dehydroabietate	0.7	14.8	18.0	21.6	24.4	34.3
Total esters other than abietate, palustrate, and neoabietate	0.7	19.1	23.4	26.4	30.8	47.6

% of potassium hydroxide to the methyl ester was examined. It was observed that isomerization was strongly inhibited at 200° C., and disproportionation essentially was prevented. This would suggest that isomerization and disproportionation are acid catalyzed reactions.

The rapid isomerization of methyl abietate and the inhibition by base led us to inquire as to the method used previously in the preparation of the methyl esters (*3-5*) of levopimaric, palustric, and neoabietic acids. A modification of the commonly employed decantation method (*1*) was used in the earlier work to prepare the diazomethane which in turn was used to esterify the acids. Methyl abietate was thus prepared using this method. The isomerization at 200° C. of this sample of methyl abietate was strongly inhibited, failing to reach equilibrium in 21 days. Disproportionation was negligible. Therefore, the esters prepared by the decantation method were contaminated by traces of base.

The effect of boiling the borosilicate glass reaction tubes with sodium bicarbonate followed by washing with distilled water was investigated. Essentially no difference was detected in the extent of isomerization and disproportionation between the alkali washed tubes and those that were not boiled in bicarbonate.

Versamid 900, the GLPC substrate used in the analytical work, was found to inhibit the isomerization, thus preventing further changes in composition during analysis. Antioxidants and free radical initiators did not affect the rate of isomerization.

A 1-to-1 molar mixture of methyl abietate and abietic acid was heated at 200° C. The rates of isomerization and of disproportionation of the ester were the same as in the absence of the added abietic acid.

The addition of a strong acid such as *p*-toluenesulfonic acid to methyl abietate catalyzes isomerization to an equilibrium mixture at room temperature. This equilibrium is not changed on heating at 180° C.

Dissolution of methyl abietate in 0.5*N* ethanolic hydrochloric acid at room temperature resulted in a final equilibrium distribution of 93% methyl abietate, 4% methyl palustrate, and 3% neoabietate. This is the same equilibrium distribution observed for abietic, levopimaric, neoabietic, and palustric acids in 0.5*N* ethanolic hydrochloric acid (*7*).

EXPERIMENTAL

The gas liquid partition chromatography (GLPC) was carried out on an F & M Model 500 employing the method of Brooks *et al.* (*2*).

Methyl Abietate. Abietic acid (*6*) was treated with an excess of an ether solution of diazomethane prepared by distillation from a mixture of base and *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (Diazald). After one hour at room temperature, the excess reagent was blown off under a nitrogen stream, and the ether solution was washed once with a 1% aqueous solution of sodium carbonate and then 5 times with water. The solution was dried over sodium sulfate, the ether removed under reduced pressure, and the ester dried over Drierite in vacuo.

Thermal Reactions (*7*). The GLPC data were found to be accurate to about ±1.0%.

Isomerization and Disproportionation of Methyl Abietate at 200° C. A GLPC analysis was measured on each sample. Seven peaks were observed in the GLPC analysis and four of these were identified as methyl abietate, palustrate, neoabietate, and dehydroabietate by means of relative retention times. The remaining three peaks are probably di- or tetrahydroabietates arising from disproportionation (Tables I and II).

Isomerization of Methyl Abietate in the Presence of Potassium Hydroxide at 200° C. Methyl abietate was dissolved in methanol containing potassium hydroxide (1-to-0.05 mole ratio). Aliquots of the clear solution were charged to the reaction tubes and the solvent removed under vacuum. After heating at 200° C. for 674 hours, 95% of methyl abietate remained unchanged and 3.2% of methyl palustrate and 1.0% of methyl neoabietate were formed. No measurable amount of disproportionation was observed.

Isomerization of Methyl Abietate at 200° C.; Prepared via Diazomethane Decantation Method. Diazomethane was generated by adding solid *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine to a mixture of ether and 40% aqueous potassium hydroxide. The ether layer was decanted directly into an ether solution of abietic acid. After heating for 21 days at 200° C., the distribution was 91.3% methyl abietate, 6.6% methyl palustrate, and 2.1% methyl neoabietate. No disproportionation was observed.

Alkali Washed Reaction Tubes. The Carius tubes were boiled with 5% sodium bicarbonate solution for 2 hours and then washed thoroughly with distilled water. The isomerization and the disproportionation of the methyl abietate proceeded at the rate and to the same extent, as in tubes that were washed with distilled water only.

Isomerization of Methyl Abietate in the Presence of Versamid 900 Polyamide on Chromosorb W at 200° C. To an ether solution of methyl abietate (4.2 grams) was added 42 grams of 5% Versamid 900 polyamide on Chromosorb W. Tubes were charged and heated at 200° C. The mixture was extracted with ether and analyzed (GLPC). The isomerization approached equilibrium values in 2 days (81% methyl abietate, 13.5% methyl palustrate, 5.4% methyl neoabietate). Methyl dehydroabietate formed to the extent of 3.4% in 2 days.

Isomerization of Methyl Abietate in the Presence of an Antioxidant at 200° C. Two mole % of 2,6-di-*tert*-butyl-4-methylphenol (Ionol) was added to an ether solution of methyl abietate. Isomerization and disproportionation proceeded at the same rate at 200° C. as that of methyl abietate without added inhibitor.

Isomerization of Methyl Abietate in the Presence of Free Radical Initiators. (A) Ten mole % of 2,5-dimethyl-2,5-di(*tert*-

butylperoxy)hexyne-3 (Lupersol 130) was dissolved in an ether solution of methyl abietate. Isomerization proceeded at the same rate at 200° C. as that of methyl abietate without added inhibitor. After 1 hour at 200° C., 2.3% of methyl dehydroabietate was detected, and after 24 hours at 200° C., the dehydroabietate content was 12%. (B) Cumene hydroperoxide was substituted for Lupersol 130, and essentially the same results were obtained. (C) To a solution prepared as in (A) above was added a methanol solution containing 5 mole % (based on methyl abietate) of potassium hydroxide. No isomerization or disproportionation occurred after heating at 200° C. for 4 days.

Isomerization of Methyl Abietate in the Presence of Abietic Acid at 200° C. A 1-to-1 molar mixture of methyl abietate and abietic acid was heated at 200° C. The isomerization and disproportionation proceeded at the same rate and to the same extent as that of methyl abietate alone.

Isomerization of Methyl Abietate in the Presence of *p*-Toluenesulfonic Acid. Methyl abietate and 5 mole % of *p*-toluenesulfonic acid were mixed thoroughly in a methanol-ether solution and the solvent removed under reduced pressure. The next morning, the system had reached an equilibrium mixture (at room temperature) of 94.5% abietate, 3.5% palustrate, and 1.9% neoabietate. Heating the mixture in sealed tubes at 180° C. for two hours and opening tubes at intervals showed no change in the equilibrium ratios.

Isomerization of Methyl Abietate in Ethanolic Hydrochloric Acid. The isomerization of a 1% solution of methyl abietate in 0.5*N* ethanolic hydrochloric acid was carried out as described previously (*7*). The isomerization reached equilibrium in about seven days (93.0% methyl abietate, 4.2% methyl palustrate, and 2.8% methyl neoabietate). At the end of 24 days, 5.8% of methyl dehydroabietate was observed to be present.

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Convenient O-Alkylation of Phenols

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The preparation of several aryl-methyl ethers by refluxing excess methyl iodide with the corresponding phenols is described. Dimethylformamide was the solvent used, and anhydrous potassium carbonate was the base. Yields for several phenols are given.

THE PREPARATION of aryl-alkyl ethers from phenols is frequently carried out by reaction of an alkali metal phenolate with alkyl halides or sulfates (*5*). In the presence of strong bases, oxidation of the phenol is often a complication. In a search for preparatively useful methods utilizing dipolar aprotic solvents (*1, 4*), the authors have found a particularly convenient system for the synthesis of aryl-methyl ethers.

Simple refluxing of phenols with excess methyl iodide, using anhydrous potassium carbonate as base (*2*) and dimethylformamide as solvent, gives good to excellent results with a variety of phenols as indicated in Table I. Preliminary rate studies indicate that most of the reactions are complete in less than six hours. The purity of the products was determined by gas chromatography and infrared spectroscopy.

Table I

Phenol	Halide	Products	Yield[a] %
Phenol	Methyl iodide	Anisole	80.0
Phenol	Ethyl bromide	Phenetole	77.0
Thymol	Methyl iodide	Thymol methyl ether	74.0
2-Isopropylphenol	Methyl iodide	2-Isopropylanisole	69.5
2,6-Dimethylphenol	Methyl iodide	2,6-Dimethylanisole	76.5
5-Indanol	Methyl iodide	5-Methoxyindane	84.5
1-Naphthol	Methyl iodide	1-Methoxynaphthalene	96.0
2-Naphthol	Methyl iodide	2-Methoxynaphthalene	94.5
p,p'-Biphenol	Methyl iodide	4,4'-Dimethoxybiphenyl	95.5
Catechol	Methyl iodide	Veratrole	91.5
Resorcinol	Methyl iodide	1,3-Dimethoxybenzene	69.5
Hydroquinone	Methyl iodide	1,4-Dimethoxybenzene	85.5
Pyrogallol	Methyl iodide	1,2,3-Trimethoxybenzene	55.0

[a] Based on gas chromatography.