Isomerization and Disproportionation of *d*-Limonene on Silica Gel

G. L. K. HUNTER AND WILLIAM B. BROGDEN, JR.

U. S. Fruit and Vegetable Products Laboratory,[1] *Winter Haven, Florida*

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d-Limonene, from rectified orange essential oil, in the presence of silica gel at elevated temperatures exhibited disproportionation *via* a two-phase process. A study was made showing the disappearance of *d*-limonene with time at 100° and 150° to give initially α-terpinene, γ-terpinene, terpinolene, and isoterpinolene which, subsequently, disproportionated into 1-*p*-menthene, *trans*-2-*p*-menthene, 3-*p*-menthene, *t*-8(9)-*p*-menthene, and *p*-cymene. The isomerization products of *d*-limonene also were studied. The reactions were monitored by gas chromatography and constituent identity confirmed by infrared spectroscopy.

As part of the study of flavor changes in orange products it became necessary to elucidate the chemical composition of the whole oil. The procedure for the separation of the terpenes from the terpenoids on a silicic acid column, published by Kirchner and Miller,[2] was employed using silica gel. It had been observed that terpene hydrocarbons isomerized when passed through a silica gel column at room temperature;[3] Rudakov and Shestaeva[4] have shown that silica gel free of aluminum oxide did not promote isomerization of α-pinene at 100°; further, they showed that deposition of 0.1% aluminum oxide on silica gel raised the activation 1500-fold equivalent to the level of clays.

The disproportionation of *d*-limonene in the presence of palladium–barium sulfate catalyst[5] and palladized asbestos[6] has been reported to occur under rather vigorous conditions to give mostly *p*-cymene and *p*-menthane with some *p*-menthenes in the former. It has been shown also that *p*-menthenes undergo isomerization in the presence of sodium organo-sodium catalyst under reflux.[7] The present paper shows that these reactions can be accomplished using silica gel under mild conditions.

Limonene (I) was isomerized at 100° into terpinolene (II), α-terpinene (III), γ-terpinene (IV), and isoterpinolene. Isomerization began immediately exhibiting very little disproportionation as shown in Fig. 1. These reactions can be explained by assuming adsorbed carbonium ions on the surface of the catalyst. It is proposed that hydrogen transfer takes place in the presence of silica gel as observed by Turkevitch and Smith[8] in the interconversion of 1-butene to 2-butene. *d*-Limonene (I) must extract a proton from the surface of the catalyst to give the 8-menthenyl carbonium ion which can give up the remaining tertiary proton to form terpinolene (II). The 8-menthenyl ion experiences a proton shift to give the 4-menthenyl carbonium ion which, upon loss of a proton, gave both α-terpinene and γ-terpinene. This reversible hydrogen shift is further evidenced by the presence of trace quantities of dipentene during the silica gel isomerization of II, III, IV, and V.

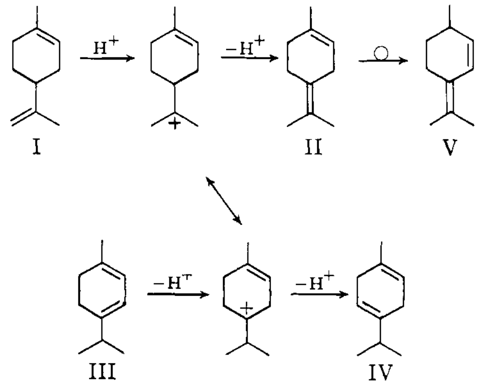

Figure 2 shows the initiation and short duration of the isomerization phase at 150° as evidenced by the rapid conversion of *d*-limonene into *p*-menthadienes requiring only two minutes. Isoterpinolene (V) appears only after terpinolene (II) had achieved very close to its maximum concentration which is attributed to isomerization of II to the more stable conjugated con-

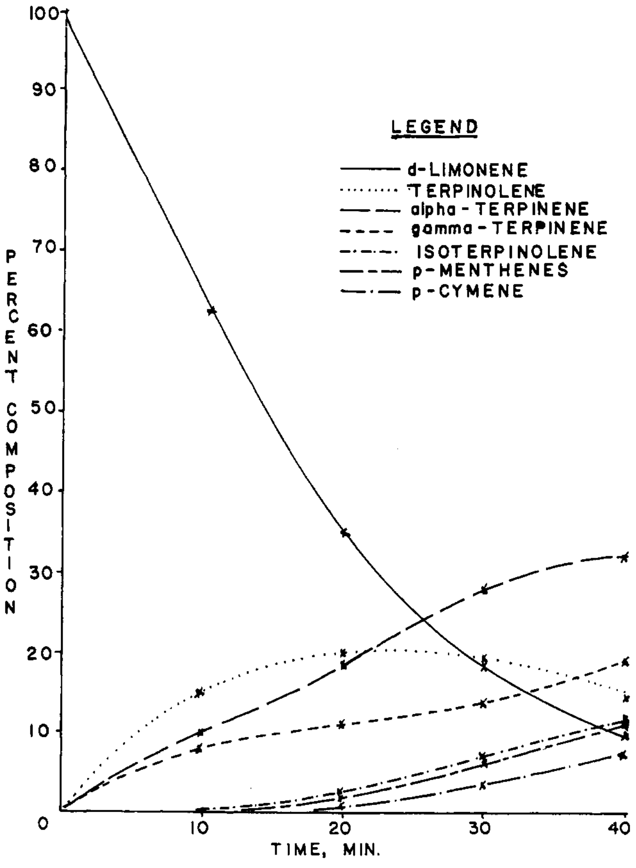

Fig. 1.—Isomerization of *d*-limonene at 100°.

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[1] One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. References to specific products of commercial manufacture are for illustration only and do not constitute endorsement by the U. S. Department of Agriculture.

[2] J. G. Kirchner and J. M. Miller, *Ind. Eng. Chem.*, **44**, 318 (1952).

[3] B. A. Arbuzov and Z. G. Isaeva, *Izv. Akad. Nauk, SSSR, Otdel. Khim. Nauk*, 843 (1953); *Chem. Abstr.*, **49**, 1654i (1955).

[4] G. A. Rudakov and M. M. Shestaeva, *Zh. Obshch. Khim.*, **29**, 2062 (1959); *Chem. Abstr.*, **54**, 8880h (1960).

[5] H. E. Eschinazi and H. Pines, *J. Am. Chem. Soc.*, **78**, 1176 (1956).

[6] H. E. Eschinazi and E. D. Bergmann, *ibid.*, **72**, 5651 (1950).

[7] H. Pines and H. E. Eschinazi, *ibid.*, **78**, 1178 (1956).

[8] J. Turkevitch and Smith, *J. Chem. Phys.*, **16**, 466 (1948).

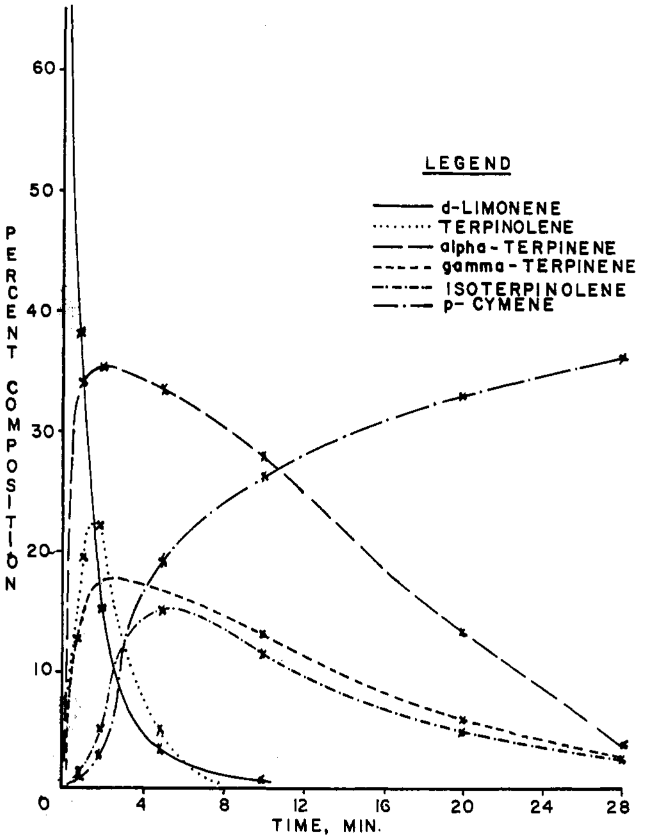
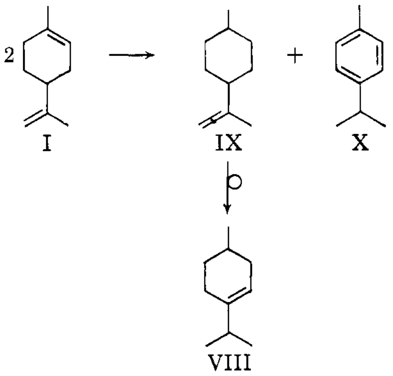
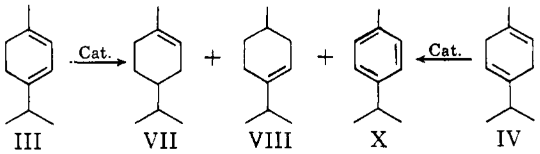


Fig. 2.—Isomerization and disproportionation of *d*-limonene at 150°.

figuration as is also the case with the predominant formation of III over IV. Figure 3 shows the disproportionation of these substances as the latter phase progressed to give 1-*p*-menthene (VII), *t*-2-*p*-menthene (VI), 3-*p*-menthene (VIII), *t*-8-(9)-*p*-menthene (IX), and *p*-cymene (X). None of the other isomeric *p*-menthenes have been found to be present in the mixtures. Further treatment of these products with silica gel failed to yield *p*-menthane, the completely disproportionated product. Treatment of VI and VIII separately with silica gel at 150° for one hour yielded only the starting materials; however, IX under these conditions, isomerized to VIII. It was observed that the concentration of IX increased in proportion to the decrease in the concentration of *d*-limonene with subsequent formation of *p*-cymene (X). Since the concentration of IX remained proportional to that of *d*-limonene during the transformations it is postulated that IX is a direct disproportionate of I. Its concentration remained small due to isomerization to 3-*p*-menthene (VIII). Eschinazi and Bergmann[6] had observed this disproportionation and, in addition, reported the presence of *p*-menthane. They propose a scheme based on the hydrogen transfer studies of Ipatieff, *et. al.*[9] This same mechanism could account for the presence of VII and VIII from III and IV, respectively. The absence of 4(8)-*p*-menthene is attributable to steric factors inhibiting the proposed concerted mechanism. Hydrogen transfer appeared to occur by 1,4-addition as a consequence of polarization of the conjugated diene. This postulation is based on the absence of 4(8)-*p*-menthene which would be expected from a 1,2-addition of II. α-Terpinene gave VI which is believed to be its principal source, and II gave VIII contributing to its abnormally high yield.

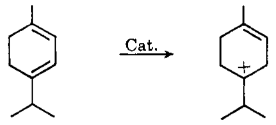




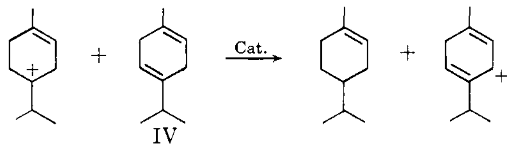
It is proposed that a catalytic hydrogenation occurred concurrently with the disproportionation reactions described above. *p*-Cymene (X) dimerized[9] to give 1,3,3,6-tetramethyl-1-*p*-tolylinden (XII) and two moles of hydrogen. Compound XII has been found to be a constituent of the polymeric residue.

It was of interest to study the behavior of the isomeric products of *d*-limonene. γ-Terpinene (IV), α-terpinene (III), terpinolene (II), and isoterpinolene (V) were individually treated with silica gel at 150° according to the method used for *d*-limonene. In each case isomerization occurred rapidly to give the product obtained from *d*-limonene including dipentene followed by the typical disproportionation compounds exhibited by *d*-limonene on silica gel. Dimers and polymers were formed at 150° as has been reported in heterogeneous catalytic systems with terpenes.[10–12] These were observed to occur primarily during disproportionation.

The major source of the endocyclic *p*-menthenes is probably through disproportionation of the isomeric *p*-menthadienes. As an example α-terpinene reacts with the catalyst to form a carbonium ion.



An exchange reaction probably occurs.



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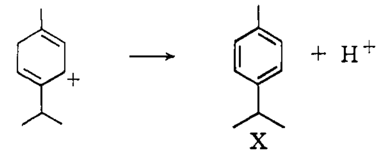
[9] V. N. Ipatieff, H. Pines, and R. C. Olberg, *J. Am. Chem. Soc.*, **70**, 2123 (1948).

[10] G. Dupont, R. Dulou, and G. Thuet, *Bull. Soc. Chim.*, **8**, 891 (1941); *Chem. Abstr.*, **37**, 4716 (1943).

[11] V. E. Tishchenko and G. A. Rudakov, *Zh. Prikl. Khim.*, **6**, 691 (1933); *Chem. Abstr.*, **28**, 4052 (1934).

[12] M. Ya. Levshuk, *et al.*, *Z. Prikl. Khim.*, **13**, 1178 (1940).

A proton is lost to give *p*-cymene.



X

The presence of an abundance of hydrogen acceptors probably was responsible for the absence of *p*-menthane.

Experimental

Analytical Procedure.—Reactions were monitored from initiation to completion by gas chromatography using an F and M flame ionization detector in conjunction with a 250 ft. × 0.020 in. i.d. capillary column. The column was coated with Carbowax 20 M and maintained at a temperature of 85°. A preparatory column measuring 0.5 in. × 36 ft. containing 30% Carbowax 20 M on Chromosorb P at a temperature of 130° was used to obtain sufficient material for infrared analysis. The material represented by each peak was trapped and identified by comparison of their infrared spectra with those of authentic compounds or spectra. This system was incapable of separating *t*-8(9)-*p*-menthene from *t*-2-*p*-menthene; therefore, the former was estimated by its characteristic peaks at 1620 cm.$^{-1}$ and 883 cm.$^{-1}$ in the infrared.[5] Since the analytical procedure must accommodate very small quantities, the analysis was accomplished entirely by gas chromatography. The instrument was calibrated for 1-μl. injection of *d*-limonene. The quantities of each constituent, as shown in Fig. 1–3, were estimated as a part of the total chromatographic peak area. The nonvolatile constituents were calculated to be the difference between the area represented by one microliter of *d*-limonene and that obtained from the total peak area of the volatile constituents.

***d*-Limonene (I).**—Chromatographically pure *d*-limonene was obtained by rectification of cold pressed Valencia orange oil.[13]

Silica Gel.[14]—The silica gel used for these experiments was Fisher cat. no. S157, 28–200 mesh suitable for chromatography. This material was more active than Mallencrodt's analytical reagent grade precipitated silicic acid suitable for chromatography which gave the same products, but required more time. Least active was Baker's silica gel suitable for chromatography which required a 20-fold reaction period to give the same products. Research Specialties' silica gel-G for thin-layer chromatography was also shown to contain a very high activity. These materials vary from lot to lot and their activity should be determined before use on systems which are prone to isomerization or disproportionation.

***d*-Limonene (100°).**—A slurry of *d*-limonene and silica gel was divided into four test tubes. The composition of the slurry was not found to be critical; however, it was such that a thin layer of liquid formed at the top. The test tubes were placed in a water bath at 100°. The first tube was analyzed after remaining in the bath for 10 min. Each successive tube was removed in 10-min. intervals and analyzed so that the last tube remained in the bath a total of 40 min. The reaction was quenched by cooling in tap water upon removal from the bath. A microliter of material was withdrawn directly out of the slurry for analysis. The remainder was filtered and upon standing in the refrigerator showed no change in composition. The yield of volatile constituents was 95% or better, being within experimental error.

***d*-Limonene (150°).**—The procedure described above was repeated using a Silicone 710 bath at 150°. Samples were analyzed at intervals of 1, 2, 5, 10, 20, and 30 min. for analysis of the volatile constituents shown in Fig. 2. The ratio of volatile constituents to polymer formation were carried out for longer periods to show a leveling out of polymer formation after 1 hr. (See Table I.)

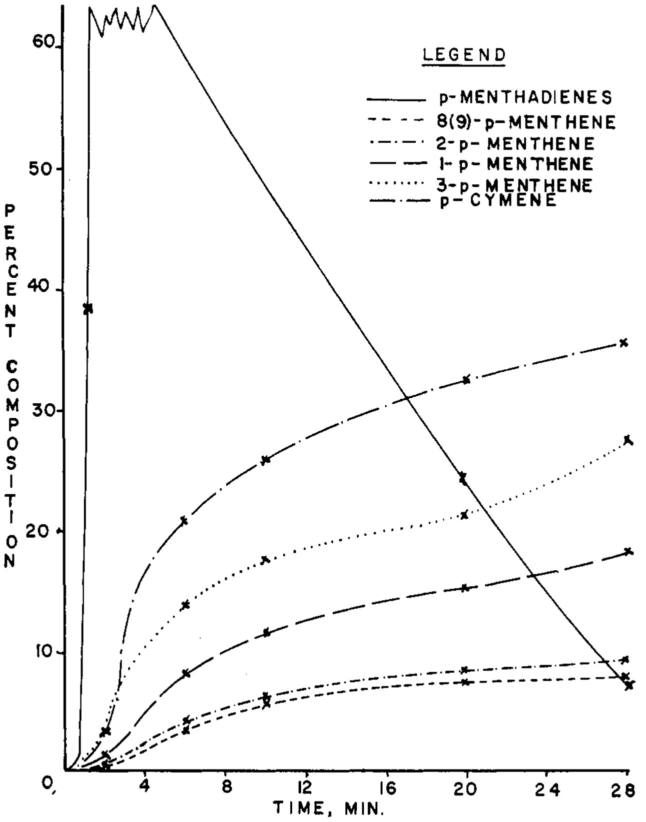


Fig. 3.—Disproportionation of the *p*-methadienes from limonene at 150°.

TABLE I

Time, min.	Yield of volatiles, %
0	100
10	62
30	46
60	33
120	30

γ-Terpinene (IV).—Fifty milliliters of *d*-limonene was slurried with silica gel and heated at 100° for 30 min. and cooled. The silica gel was removed by filtration and 20 ml. of the filtrate was placed on the preparative scale gas chromatograph.[15] The various constituents were trapped in liquid nitrogen cooled traps and thus made available the products of bond migration for further study. γ-Terpinene was slurried with silica gel and heated at 150° for 10 to 40 min. The composition of the products was essentially that shown in Fig. 3 for *d*-limonene under similar conditions including dipentene.

α-Terpinene (III).—α-Terpinene was obtained as a trapped product from the preparative scale gas chromatographic separation as described previously. It was slurried in silica gel and heated at 150° for 20 min. to give essentially the composition of products obtained for γ-terpinene.

Isoterpinolene (V).—Isoterpinolene appeared as the last peak on the chromatograph and was collected as described previously. It was slurried with silica gel for 20 min. at 150° to give essentially the same composition of products obtained from γ-terpinene with the exception of a noticeable increase in α-terpinene and γ-terpinene.

Terpinolene (II).—Terpinolene was obtained from a preparative scale gas chromatographic separation of commercial terpinolene. It was slurried with silica gel and heated for 20 min. at 150° to give essentially the same composition of products obtained from γ-terpinene.

1,3,3,6-Tetramethyl-1-*p*-tolylinden (XII).—The mixture obtained in the disproportionation of *d*-limonene was vacuum distilled and a fraction boiling at 155–160° (5.5 mm.) was subjected to infrared analysis. The spectra and boiling point were the same as that reported by Ipatieff, *et al.*[9]

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(13) Obtained from Birds Eye Division of General Foods, Florence Villa, Fla.

(14) K. G. Miesserov, *Dokl. Akad. Nauk, USSR*, **87**, 627 (1952); *Chem. Abstr.*, **47**, 3675 (1953).

[15] Column—1.5 in. × 80 ft., containing 30% Carbowax 20 M on Chromosorb P at a temperature of 150°.

8(9)-*p*-Menthene (IX) Isomerization.—A sample of IX obtained from The Glidden Co.[15] was treated with silica gel at 150° as described, for 20 min. The gas chromatographic and infrared analysis showed complete isomerization to 3-*p*-menthene (VII).

3-*p*-Menthene (VII) Isomerization.—3-*p*-Menthene, obtained by a preparative scale gas chromatographic separation of *d*-limonene disproportionation products, was treated for 1 hr. at 150° on silica gel. Analysis by gas chromatography and infrared spectroscopy showed no isomerization.

2-*p*-Menthene (VI) Isomerization.—2-*p*-Menthene, obtained by chromatography as described, when treated for 1 hr. at 150° on silica gel, showed no isomerization.

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(16) Contributed by The Glidden Co., Jacksonville, Fla.

Pyrazines. III. The Action of Phosphoroyl Chloride on Pyrazine N-Oxides[1,2]

B. KLEIN, N. E. HETMAN, AND M. E. O'DONNELL

Laboratory Service, Veterans Administration Hospital, and Department of Biochemistry,
Albert Einstein College of Medicine, Yeshiva University, Bronx, New York

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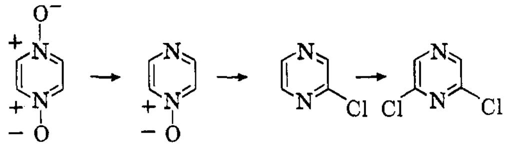
The action of phosphoroyl chloride on pyrazine N-oxides is described. Thus, pyrazine 1-oxide is converted to 2-chloropyrazine, while pyrazine 1,4-dioxide yields 2,6-dichloropyrazine. By contrast, 2-methylpyrazine 1,4-dioxide gives a mixture of dichloromethylpyrazine and a monochloromethylpyrazine N-oxide which is isomeric with the N-oxide produced by direct oxidation of 2-chloro-3-methylpyrazine or 2-chloro-6-methylpyrazine. The mechanisms of halogenation of these pyrazine N-oxides are discussed and the role of possible intermediates is examined.

Since its demonstration by Meisenheimer[3] and later by Bobranski and associates,[4a] the conversion of heterocyclic N-oxides by chlorinating agents to nuclear substituted chlorine derivatives has served as a useful syntheses.[4b,c] Among pyrazines, this procedure was used by Newbold and Spring[5] and Klein and Spoerri[6] to prepare 2-chloro-3,6-dimethylpyrazine from 2,5-dimethylpyrazine 1-oxide. When the di-N-oxide was used, the 2,5-dichloro-3,6-dimethylpyrazine was obtained. In this report, additional experiments are presented, describing the action of phosphoryl chloride on pyrazine mono- and di-N-oxide and by contrast, on 2-methylpyrazine 1,4-dioxide.

After the work presented here was completed and this manuscript was in preparation, the present authors learned of a paper by Bernardi and associates[7] also describing the action of phosphoroyl chloride on pyrazine 1,4-dioxide, 3-chloropyrazine 1-oxide, and 3-carboxamidopyrazine 1-oxide. Their observations were in essential agreement with portions of the work reported in this paper.

Pyrazine 1-oxide on treatment with phosphoryl chloride gave 2-chloropyrazine, which on further treatment with hydrogen peroxide in acetic acid formed 3-chloropyrazine 1-oxide. This agreed with an earlier observation that N-oxidation of a pyrazine bearing a halogen or an electron-donating substituent in the nucleus will take place on the nitrogen furthest from that substituent.[8] Oxidation of either 2-chloro- or 2-ethoxy-3,6-dimethylpyrazine produced the 4-oxide only. These compounds resisted further oxidation. The present investigators have prepared 2-ethoxypyrazine 1,4-dioxide by direct oxidation of 2-ethoxypyrazine.[9]

When pyrazine 1,4-dioxide was heated with excess phosphoryl chloride, 2,6-dichloropyrazine was obtained. Initially, the course of the reaction was thought to be: pyrazine 1,4-dioxide → pyrazine 1-oxide → 2-chloropyrazine → 2,6-dichloropyrazine:



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Support for this reaction sequence was derived from: (a) phosphorus halides are recognized deoxygenating agents[10]; (b) the formation of 2,6-dichloropyrazine from 2-chloropyrazine and chlorine[11]; (c) treatment of 2-hydroxypyrazine with phosphoryl bromide produced a mixture of 2-bromopyrazine and 2,6-dibromopyrazine.[12,13]

This assumption was quickly shown to be incorrect, since treatment of 2-chloropyrazine with excess phosphoroyl chloride failed to produce 2,6-dichloropyrazine. Further, the smaller yield of 2-chloropyrazine from pyrazine 1-oxide obtained under similar conditions (without the formation of the 2,6-dichloro compound) would indicate that they could not arise in sequence from the same precursor. A simultaneous or sequential ionic chlorination of both N-oxide functions would

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(1) Portions of this work were reported at the 140th National Meeting of the American Chemical Society, Chicago, Ill., September, 1961.

(2) The work reported here was supported in part by a grant (CY-5343) from the National Institutes of Health.

(3) J. Meisenheimer, *Ber.*, **59**, 1848 (1926).

(4) (a) B. Bobranski, L. Kochanska, and A. Kowaleska, *ibid.*, **71B**, 2385 (1938); (b) G. B. Bachman and D. E. Cooper, *J. Org. Chem.*, **9**, 302 (1944); (c) R. W. Goulay, G. W. Moersch, and H. S. Mosher, *J. Am. Chem. Soc.*, **69**, 303 (1947).

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(7) L. Bernardi, G. Palamidessi, A. Leone, and G. Larini, *Gazz. chim. ital.*, **91**, 1431 (1961); *Chem. Abstr.*, **57**, 2223e (1962).

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(9) Unpublished observations.

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