[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, REED COLLEGE]

The Action of Sodium Methoxide on Methyl Esters[1]

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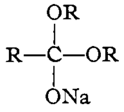
This paper presents three principal observations: (A) No precipitate forms in a scrupulously dry methanolic solution of sodium methoxide and methyl benzoate during several hours at room temperature although a white precipitate forms immediately if the ingredients have not been dried with extreme care. (B) A 74% yield of dimethyl ether has been obtained from the reaction of methanolic sodium methoxide with methyl benzoate at 100°. (C) The rate of reaction of sodium methoxide with methyl mesitoate is somewhat less than with methyl benzoate, while methyl 2,4,6-tribromobenzoate reacts much faster.

Tischtschenko[4] made an observation equivalent to (A) in 1912, but it appears to have been overlooked, and recent authoritative books[5,6,7] have contained an erroneous conclusion of Claisen[8] and von Pechmann[9] that the action of dry alcoholic alkoxides on esters gave rise to the formation of precipitates of type I,

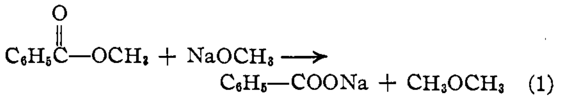


$$\mathrm{R{-}C(OR)(OR)(ONa)}$$

I

Neither Claisen nor von Pechmann had analytical proof for the structures they postulated; Tischtschenko showed by analysis that their precipitates were merely sodium benzoate contaminated with traces of sodium alkoxide, and reasoned that they resulted from ordinary saponification due to traces of water present in the starting materials. Our observation supports Tischtschenko.

Isolation of dimethyl ether from the action (equation 1) of sodium methoxide on methyl benzoate is not novel; the ether has twice[10,11] been obtained from this reaction performed under solvent-free conditions at 175–200°.[12] The significance of our observation lies in the relatively mild conditions employed, and in the substantial yield obtained.[13] Magnani and McElvain[10] reported



$$C_6H_5\overset{\overset{\displaystyle O}{\|}}{C}{-}OCH_3 + NaOCH_3 \longrightarrow C_6H_5{-}COONa + CH_3OCH_3 \quad (1)$$

1% of benzyl benzoate as a by-product from the solvent-free reaction. Careful examination of our reaction mixture revealed no trace of benzyl benzoate; this leads us to believe that only difficulties in isolating dimethyl ether from methanol solution restrained us from obtaining it in even higher yield.

The formation of dimethyl ether according to equation (1) is a case of the Williamson synthesis, a reaction well known for esters of sulfuric and sulfonic acids, but not previously recognized for esters of carboxylic acids. It probably involves nucleophilic displacement (S_N2 substitution) on the methyl carbon of the ester. To differentiate between this mechanism and a mechanism involving attack on the carbonyl carbon, we performed the experiments summarized in Table I. One would expect attack on the carbonyl carbon atoms of methyl mesitoate and methyl 2,4,6-tribromobenzoate to be slow[14] but that the rate of attack on methyl carbon would be affected by the bulky *ortho* substituents only as they exerted electronic effects. In particular, by analogy with other reactions known to involve nucleophilic displacement at the alkyl carbon of esters,[15,16] we expected that rate would be directly related to the strength of the corresponding acid. Since one hindered ester

TABLE I

CLEAVAGE OF ESTERS IN FOUR HOURS AT 100°

Ester	Cleavage by methoxide, %	Cleavage by hydroxide, %	Dissociation constant of acid
Methyl mesitoate	4 ± 2	22	3.8×10^{-5}[a]
Methyl benzoate	15 ± 1	100[b]	6.8×10^{-5}
Methyl 2,4,6-tribromobenzoate	55 ± 4[c]	105 ± 8[c]	3.9×10^{-2}[d]

[a] Beilstein, Vol. IX, p. 553. [b] Assumed. [c] Values for cleavage of methyl 2,4,6-tribromobenzoate represent difference between base consumed and bromide released (through aromatic substitution). [d] Beilstein, Vol. IX, p. 361.

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[4] Tischtschenko, Woelz and Tabcewicz-Lubkowsky, *J. prakt. Chem.*, **86**, 322 (1912).

[5] Watson, "Modern Theories of Organic Chemistry," second edition, Oxford Press, New York, N. Y., 1941, p. 128.

[6] Remick, "Electronic Interpretations of Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, p. 396.

[7] "Organic Syntheses," Coll. Vol. I, second edition, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 106.

[8] Claisen, *Ber.*, **20**, 646 (1887).

[9] von Pechmann, *ibid.*, **31**, 503 (1898).

[10] Magnani and McElvain, THIS JOURNAL, **60**, 813 (1938).

[11] Adickes, von Müllenheim and Simson, *Ber.*, **66**, 1904 (1933).

[12] Dibenzyl ether has likewise been obtained by the action of sodium benzylate on benzyl benzoate (ref. 11). This reaction is of nuisance importance in preparation of benzyl benzoate by the Tischtschenko reaction (ref. 7).

[13] Reaction of sodium methoxide with methanol cannot have generated any important fraction of the dimethyl ether formed, for de Lange, *Rec. trav. chim.*, **38**, 101 (1919), detected only 2.5% of such reaction in twenty four hours at 180°.

[14] Both esters are hindered to about the same extent. *Cf.* Shriner and Adams, in Gilman's "Organic Chemistry," second edition, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 362.

[15] Ether formation from sodium ethoxide and ethyl benzenesulfonates; *cf.* Morgan and Cretcher, THIS JOURNAL, **70**, 375 (1948).

[16] Alkylation of trimethylamine by methyl carboxylic esters; *cf.* Hammett and Pfluger, *ibid.*, **55**, 4079 (1933).

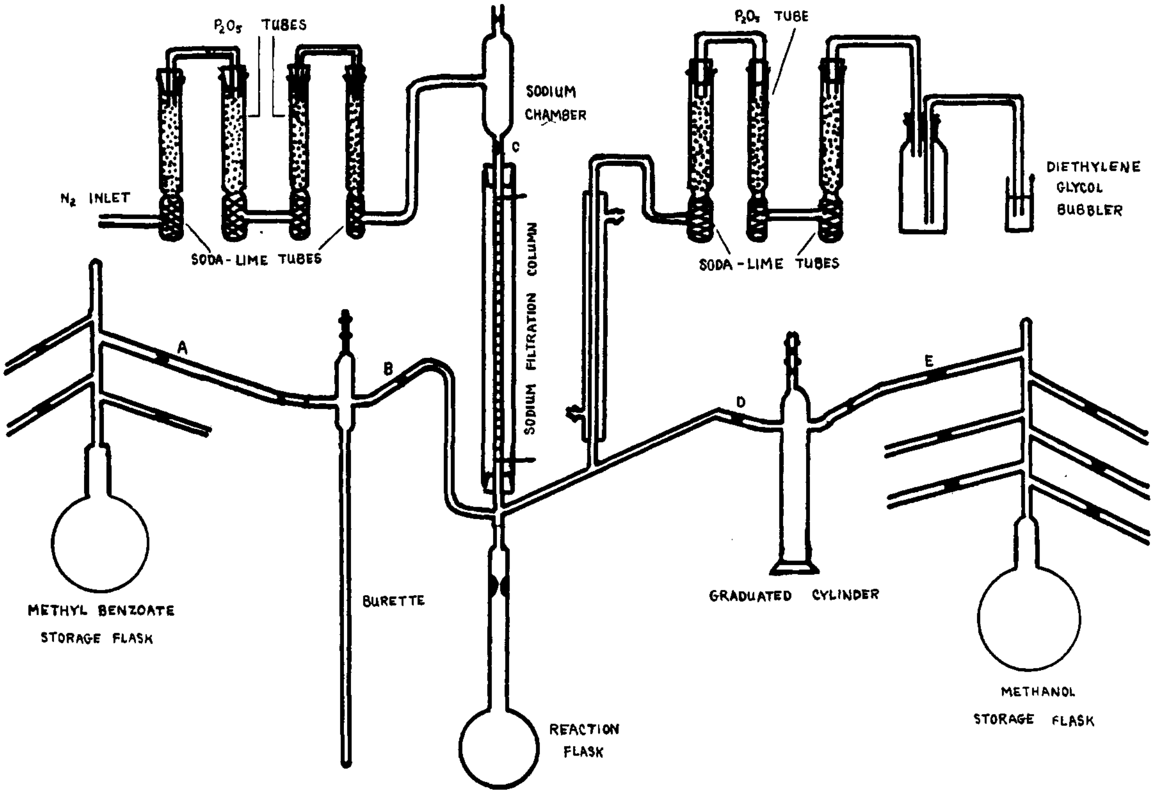

Fig. 1.—Apparatus for preparation of reaction mixture for dimethyl ether isolation experiment.

reacted with methoxide faster than methyl benzoate, and one slower, and since rate was directly related to acid strength, our expectations are confirmed.

The rate of a process involving carbonyl attack would also increase with increasing strength of the acid. This effect is not, however, great enough to overcome the handicap of steric hindrance in the case of esters of 2,4,6-tribromobenzoic acid. For example, Sudborough and Karve[17] found that conversion of ethyl *p*-toluate to methyl *p*-toluate occurred rapidly under the influence of methanolic methoxide, while esters of 2,4,6-tribromobenzoic acid remained unchanged under similar conditions. That methoxide cleaves methyl 2,4,6-tribromobenzoate more rapidly than methyl benzoate therefore demonstrates that carbonyl attack is not involved.[18] The cleavage of methyl esters by methoxide thus appears to be one of those rare instances of carboxylic ester cleavage through nucleophilic displacement at the alkyl carbon.[16]

Experimental[19]

Methyl benzoate, b. p. 199.3–199.6°, for the dimethyl ether isolation experiment was distilled into the methyl benzoate storage flask shown in Fig. 1. From this about 10 ml. was distilled out under reduced pressure, connection to the pump being provided through a drying system. After sealing, the remainder was used in the experiments. That for the rate experiments was stored in glass-stoppered bottles in a desiccator.

Methyl mesitoate, $n^{21}\text{D}$ 1.5087, was prepared according to Newman.[20]

2,4,6-Tribromobenzoic Acid.[21]—Concentrated sulfuric acid (890 ml.) was cooled to below 0° by addition of solid carbon dioxide, and 31.6 g. of sodium nitrite was added with rapid stirring. To this solution, 165 ml. (1.59 moles) of 50% hypophosphorous acid was added with care not to allow the temperature to rise above 0°; cooling was achieved by periodic addition of Dry Ice. Next a solution of 65 g. (0.175 mole) of crude 2,4,6-tribromo-3-aminobenzoic acid (prepared by bromination of *m*-aminobenzoic acid) in 1600 ml. of glacial acetic acid was added; the rates of addition of reagent and Dry Ice were balanced to maintain the temperature at about −10°. Mechanical stirring was continued until the initially formed precipitate had completely dissolved, and the mixture was allowed to stand in the refrigerator for forty-eight hours. After most of the acetic acid had been vaporized by a current of steam, the mixture was cooled and the precipitated product collected, suspended in water and brought into solution by addition of sodium carbonate; after filtration, the acid was reprecipitated by addition of hydrochloric acid. The resulting cream colored crystals, m. p. 187.5–190°,[22] weighed 53.2 g. (85%).

Methyl 2,4,6-Tribromobenzoate.—A solution of 53.2 g. of the acid and a slight excess of potassium hydroxide in 150 ml. of water was stirred with 37.4 g. of methyl sulfate for ninety minutes, and then heated for twenty-five minutes on the steam-bath. After cooling and addition of excess saturated sodium carbonate solution, a reddish

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[17] Sudborough and Karve, *J. Indian Inst. Sci.*, **3**, 1 (1920).

[18] We thank a Referee for observing that our experiments do not exclude the possibility of cleavage of methyl 2,4,6-tribromobenzoate via a reverse Tischtschenko reaction; *cf.* ref. 10.

[19] Melting points are uncorrected.

[20] Newman, THIS JOURNAL, **63**, 2431 (1941).

[21] This is the general method of Kornblum, "Organic Reactions," Vol. II, p. 296.

[22] Sudborough, *J. Chem. Soc.*, **67**, 596 (1895), reported m. p. 187° for 2,4,6-tribromobenzoic acid.

oil solidified as pink crystals which were collected by filtration; yield, 27.5 g. (50%); m. p. 63–66°.[23] After recrystallization from dilute isopropyl alcohol, m. p. 68–69°. Acidification of the filtrate from the crude ester caused 26 g. (49%) of unreacted tribromobenzoic acid to precipitate.

Methanol.—Two grades of anhydrous methanol were prepared, both from C. P. methanol which contained (according to label) no appreciable impurities other than one per cent. of ethanol. Methanol for preparation of sodium hydroxide solutions was dried with magnesium[24] and stored in glass-stoppered bottles. It was added to the reactions by means of a graduated cylinder; there was brief exposure to the atmosphere.

Methanol for the dimethyl ether isolation experiment and the methoxide–methyl ester rate studies was dried by aluminum amalgam (prepared from the metals).[25] The entire dehydration, including distillation, was carried out without exposure to the atmosphere. The flask in which the dehydration reaction was run had standard taper glass fittings, one of which was an inverted "V" combination reflux and distilling condenser which led through an all-glass seal into the receiver (the methanol storage flask of Fig. 1). After distillation, the receiver was sealed off from the condenser and from the outlet to the air, which was protected by a series of drying tubes.

Isolation of Dimethyl Ether from a Sodium Methoxide–Methyl Benzoate Reaction.—The reaction was run in a 500-ml. heavy-walled round-bottom flask made for us by the Scientific Glass Apparatus Co. In order to exclude all traces of moisture during preparation of the reaction mixture, the apparatus shown in Fig. 1 was designed. Before each unit of the apparatus was used, it was dried by evacuating and flaming a number of times. The buret and graduated cylinder were finally sealed under vacuum.

Initially magnetic seals A and E were broken and there were distilled into the buret methyl benzoate to the 17.6-ml. mark, and into the graduated cylinder methanol to the 99-ml. mark. Seals were made between the storage flasks and measuring chambers. Magnetic seal D was then broken, and about 50 ml. of methanol was distilled into the reaction flask. While nitrogen passed in through the drying tubes and out the charging tube, 10 g. of sodium metal, cut under xylene and quickly dried on a blotter, were placed in the sodium chamber. The charging tube was sealed, magnetic seal C broken, and nitrogen flow resumed. With the electrically heated sodium filtration column at about 110°, the sodium was melted by a flame, and forced down through constrictions in the column and into the reaction flask by the nitrogen stream. Crusts of sodium hydroxide, etc., were removed by this filtration.[26] With nitrogen still flowing, additional methanol was distilled into the reaction flask until the level in the graduated cylinder had fallen to the 1-ml. mark. This distillation served to wash down sodium metal which had solidified in the neck of the reaction flask. Next magnetic seal B was broken, and methyl benzoate was distilled into the strongly cooled reaction flask until the level in the buret had fallen to the 44.2-ml. mark. Finally the reaction flask itself was sealed at the constriction in its neck. No precipitate was visible in this solution after several hours at room temperature.

The reaction flask was heated in a thermostat at 99 ± 1° for fifty-two hours. At the end of this period a heavy white precipitate had formed. The flask was cooled to the temperature of Dry Ice, opened, and quickly sealed to a reflux condenser, the top of which was sealed to a coiled condenser leading downward to a receiver. Both this condenser and the receiver were submerged in a bath cooled by solid carbon dioxide. With the reflux condenser cooled by tap water, the reaction flask was held at 70° for four hours. A colorless liquid collected in the receiver. The reflux condenser and reaction flask were closed off by means of a stopcock and the liquid was distilled on an ice-salt-bath into another similar condenser and receiver. The second receiver was briefly removed from its cooling bath and a file scratch made at the surface of the liquid. A stopcock between the two receivers was closed, a thermometer was inserted so that the bulb penetrated the liquid surface, and the liquid was distilled into and condensed in a 250-ml. round-bottom flask. The boiling point was −23 to −22° (uncor.).[27] After closing a stopcock between the second receiver and the round bottom flask, boron trifluoride gas was bubbled through the liquid until boron trifluoride passed out the condenser with which the flask was provided. The cooling bath was removed and the liquid brought to a steady reflux; the vapor temperature was 126–126.5°. The dimethyl ether–boron trifluoride complex boils at 126°.[28]

The amount of sodium methoxide employed in this experiment was found to be 0.35 mole by gravimetric sodium determination on the residue from the first distillation. Nine and six-tenths milliliters of water was required to fill the second receiver up to the file scratch; this corresponds to 7.3 g., or 0.158 mole of dimethyl ether, using the density value 0.7565.[27] This amounts to a 74% yield based on the 26.6 ml. (28.9 g.) of methyl benzoate employed.

Reactions of Various Esters with Methoxide.—Roughly equal amounts of a sodium methoxide solution prepared as above were transferred to a number of ampoules through a manifold in such a way that there was no exposure to atmospheric moisture. The ampoules were sealed after filling; each was provided with an inlet tube and an outlet tube, both protected by magnetic seals.

For each run a small sealed ampoule of dry ester was placed in the reaction flask to the neck of which the outlet tube of a methoxide ampoule was then sealed. The inlet tube was connected through glass seals to the apparatus for dispensing aluminum-dried methanol (Fig. 1). Breaking the outlet magnetic seal allowed the contents of the ampoule to flow down into the reaction flask. The inlet magnetic seal was then broken and a measured amount of methanol was distilled into the reaction flask through the ampoule; this served to wash all traces of methoxide into the flask. The flask was strongly cooled, sealed, violently shaken to break the ester ampoule within it; the period of heating at 100° was four hours.

The cooled reaction flask was opened and the contents titrated to the phenolphthalein end-point with standard sulfuric acid (about 1 *N*) to determine unreacted methoxide. Sodium methoxide present at the start of the reaction was found by gravimetric sodium analysis; the difference was taken as the extent of reaction.

From 2.72 g. (0.02 mole) of methyl benzoate and 0.1279 mole of sodium methoxide in 98 ml. of solution there was 15 ± 1% reaction. From 3.52 g. (0.0198 mole) of methyl mesitoate and 0.1308 mole of methoxide in 101 ml. of solution there was 4 ± 2% reaction. From 7.46 g. (0.02 mole) of methyl 2,4,6-tribromobenzoate and 0.128 mole of methoxide in 98 ml. of solution there was 102 ± 4% consumption of methoxide; gravimetric analysis of the products from an identical run showed 0.00936 mole (47%) of bromide ion to have been released.

Reactions of Esters with Methanolic Sodium Hydroxide.—To a reaction flask containing a sealed ampoule of dry ester there was added a measured quantity of standard methanolic sodium hydroxide. The flask was sealed, the ampoule broken, and the reaction run for four hours at 100°. The contents of the flask were titrated with standard acid to determine unreacted base. From 3.52 g. of methyl mesitoate (0.0198 mole) and 0.1308 mole of hydroxide in 100 ml. of solution there was 22% reaction (by titration); 19% of mesitoic acid was isolated from the titration mixture. From 3.21 g. of methyl 2,4,6-tribromobenzoate (0.00860 mole) and 0.0556 mole of hydroxide in 42 ml. of solution there was 133% of the expected hydrox-

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[23] Werner and Seybold, *Ber.*, **37**, 3659 (1904), reported m. p. 68°.

[24] Bjerrum and Zeichmeister, *ibid.*, **56**, 894 (1923).

[25] *Cf.* Hartley and Raikes, *J. Chem. Soc.*, **127**, 524 (1925).

[26] *Cf.* Bent and Forziati, THIS JOURNAL, **58**, 2220 (1936).

[27] Maass and Boomer, *ibid.*, **44**, 1709 (1922), reported b. p −24.9° for dimethyl ether.

[28] Gasselin, *Ann. chim. phys.*, [7] **3**, 5 (1894); *Ber.*, **28**, (Ref. 779 (1895).

ide consumption; another run with the same proportions showed 117% of the expected consumption; a third produced 20% of bromide ion.

Summary

Dimethyl ether has been isolated in 74% yield from the reaction of methyl benzoate with methanolic sodium methoxide at 100°. The reaction appears to involve nucleophilic substitution on the methyl carbon atom.

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[A CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY AND THE NEW YORK QUININE AND CHEMICAL WORKS, INC.]

The Action of *t*-Butyl Hypochlorite on α-Pinene[1,2]

BY JOHN J. RITTER AND DAVID GINSBURG

Although *t*-butyl hypochlorite has been used successfully as a chlorinating agent, its mode of action is not entirely clear. In some cases it appears to substitute a chlorine atom for a hydrogen atom, while in others it adds to an olefinic double bond with subsequent loss of *t*-butanol.[3,4,5,6]

It seemed of interest to investigate the chlorination of α-pinene (I) with *t*-butyl hypochlorite in order to discover whether the products would correspond to addition at the double bond or to direct replacement of hydrogen on C-2 or on the methyl group attached to C-4 (see numbering on structure I of the flow sheet). The formation of verbenone, verbenols, myrtenal and myrtenol on autoxidation of α-pinene[7] suggests the likelihood of a substituting attack.

Chlorination of α-pinene with undistilled t-butyl hypochlorite leads to carvyl chloride (IV) and 2,6-dichlorocamphane (V). Substantial amounts of other chlorides are formed also; one of them is characterized by its hydrolysis to an alcohol, believed to be perillyl alcohol (VIIb).[8]

Carvyl chloride (IV) was identified by hydrolysis to carveol (VIII) and oxidation of the latter to carvone (IX). The physical constants of these compounds (excepting optical activity) are in very good agreement with the recorded values.[9,10] Finally, the carvone obtained was isomerized to carvacrol (X) by heating with 40% sulfuric acid, in a modification of the procedure of Rupe and Schlochoff.[11]

It was noted previously[12] that the chlorination of α-pinene with undistilled *t*-butyl hypochlorite (containing free chlorine) yielded some **2,6-dichlorocamphane** (V) which, however, failed to appear when the hypochlorite was distilled before use. Its formation may be traced to (a) rearrangement of pinene dichloride, formed by chlorine addition to α-pinene[13]; (b) chlorination of bornyl chloride which in turn might arise through addition of hydrogen chloride to α-pinene,[13] the hydrogen chloride resulting from some substitution by chlorine; (c) by addition of hydrogen chloride to pinocarvyl chloride (III) followed by Wagner–Meerwein rearrangement. The last assumption, (c), appears most likely as (a) and (b) are known to give poor yields of 2,6-dichlorocamphane,[13,14] which is formed in the present case in not inconsiderable amounts.[15]

In addition to carvyl chloride (IV), another monochloride was obtained, from which by alkaline hydrolysis and subsequent reactions of the classical type, an alcohol, an aldehyde and an acid could be obtained. The physical constants of the alcohol and the aldehyde (again excepting optical activity) are in good agreement with those reported in the literature for the corresponding *perillyl* compounds derived from natural sources.[16] In addition, the 2,4-dinitrophenylhydrazone of the aldehyde shows its principal absorption maximum at $\lambda_{max} = 3825Å$. ($\epsilon_{max} = 21,800$), which establishes the presence of an α,β-unsaturated carbonyl group, but immediately rules out the possibility of a diene system conjugated with the aldehyde group. The following three possibilities of an $\alpha,$-β-unsaturated aldehyde remain: perillaldehyde (VIIc), $\Delta^{1:8(9)}$-*p*-menthadiene-10-al (XIII) and $\Delta^{1:4(8)}$-*p*-menthadiene-10-al (XIV).

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[1] This paper is based upon a portion of the dissertation presented by David Ginsburg in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of Arts and Science of New York University, June, 1947. Present address: Daniel Sieff Research Institute, Weizmann Institute of Science, Rebovot, Israel.

[2] Presented at the meeting of the New York section of the American Chemical Society, April 25, 1947.

[3] Clark, *Chem. News*, **143**, 265 (1931).

[4] Jackson and Pasiut, THIS JOURNAL, **49**, 2071 (1927).

[5] Irwin and Hennion, *ibid.*, **63**, 858 (1941).

[6] Emling, Vogt and Hennion, *ibid.*, **63**, 1624 (1941).

[7] Blumann and Zeitschel, *Ber.*, **46**, 1178 (1913).

[8] Work published by several authors indicates that the action of N-bromosuccinimide on α-pinene, similarly leads to a complex mixture of brominated products. *Cf.* Ziegler, *et al.*, *Ann.*, **551**, 80 (1942); Buu-Hoi, *et al.*, *Bull. soc. chim. France*, 148 (1946); Roberts and Trumbull, THIS JOURNAL, **71**, 1630 (1949); du Pont, *et al.*, *Bull. soc. chim. France*, 310 (1949).

[9] Blumann and Zeitschel, *Ber.*, **47**, 2623 (1914).

[10] Simonsen, "The Terpenes," Vol. I, Second Edition, Cambridge University Press, 1947, p. 396.

[11] Rupe and Scblocboff, *Ber.*, **38**, 1719 (1905).

[12] Benson, M.S. Thesis, New York University, 1938.

[13] Aschan, *Ber.*, **61**, 38 (1928).

[14] Meerwein and Wortmann, *Ann.*, **435**, 190 (1923).

[15] It may be recalled that no decision is yet possible on the question whether dichlorocamphane is the 2,6- or the 2,10-compound: *cf.* ref. 14; Lipp, *J. prakt. Chem.*, **105**, 50 (1922); Lipp and Lausberg, *Ann.*, **436**, 274 (1924).

[16] Semmler and Zaar, *Ber.*, **44**, 52, 815 (1911).