[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

# The Reactions of Aliphatic Nitro Compounds: Alkylation by Allyl-type Halides[1]

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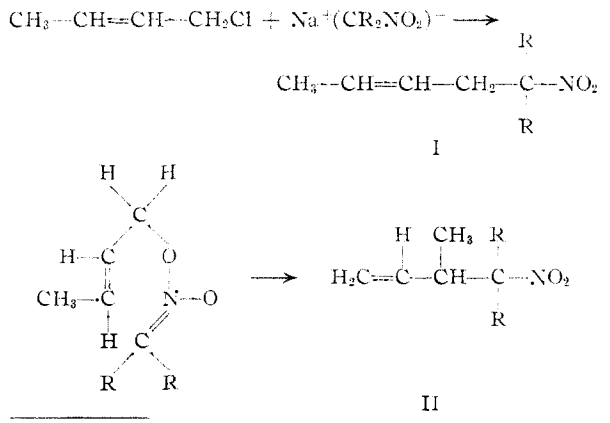
Salts of ethyl nitromalonate and ethyl nitroacetate were alkylated on carbon by allyl bromide and crotyl chloride. The product of the alkylation of ethyl nitromalonate by crotyl chloride contains an uninverted crotyl group as shown by identity of the carbon skeleton with that of ethyl *n*-butylnitromalonate produced by the nitration of ethyl *n*-butylmalonate. The failure of the crotyl group to become inverted in the alkylation indicates that direct carbon alkylation can take place without the formation of an intermediate nitronic ester.

The reaction between the salt of a nitroalkane and a substituted benzyl halide has recently been applied[3] to the preparation of substituted benzaldehydes. The production of an aldehyde was attributed to the formation by O-alkylation of a nitronic ester which then decomposed, in the characteristic manner of such compounds, into (a) an oxime related to the original nitro compound and (b) an aldehyde related to the benzyl halide or alkylating agent. It was found that where the yield of aldehyde was low, the yield of C-alkylated material was high; this was attributed to a rearrangement of an initially formed nitronic ester, by way of an inner cyclic complex, into a C-alkylated product. Since such alkylation was observed only with those halides which carried nitro groups in positions which were ortho and/or para with respect to the $-CH_2Cl$ group, it was further postulated that a successful rearrangement was dependent upon the formation of an anion stabilized by resonance in which the nitro group can accommodate the negative charge.

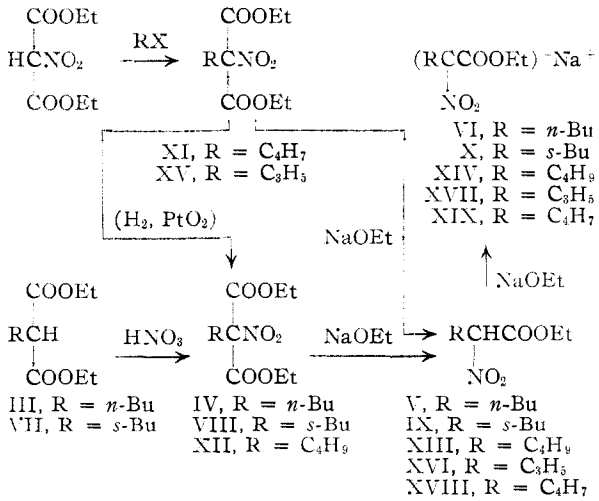
The aim of the present investigation was to attempt alkylations of nitro compounds with vinylogs of benzyl halides to see if a nitro substituent were necessary, and to determine, if possible, the validity of the proposed mechanism. It was expected that the ease of displacement of halide ion from a benzyl halide would be mirrored by similar activity in allyl-type halides. Furthermore, if a crotyl halide, in particular, were used, the determination of the presence in any C-alkylated product of a normal (I) or a rearranged (II) crotyl group would shed light on whether there had been a direct alkylation on carbon, or whether an initially formed nitronic ester had undergone rearrangement.



## Discussion

It was found that salts of ethyl nitromalonate and ethyl nitroacetate were readily alkylated by allyl bromide and crotyl chloride; and all of the available evidence, including ultimate conversion to nitro acids having the appropriate carbon skeleton, as shown in the reaction scheme, led to the conclusion that the products were not nitronic esters, but were substances in which the alkyl group was attached to carbon.

Investigation of the details of the carbon skeleton of these C-alkylation products furnished a clue to the reaction mechanism. Ethyl *n*-butylmalonate (III) was nitrated, and the nitro compound so produced (IV) was subsequently treated with sodium ethoxide. This last caused a partial decarbethoxylation of the malonic ester to the corresponding ethyl *n*-butylnitroacetate or ethyl $\alpha$-nitrocaproate (V). The treatment of V with sodium ethoxide gave a sodium salt (VI), m.p. 212–214°. In exactly similar fashion, but starting from ethyl *s*-butylmalonate (VII), it was possible to prepare an ester (IX) which gave a positive test for a secondary nitro compound and which was presumed from its method of preparation to be ethyl *s*-butylnitroacetate or ethyl $\alpha$-nitro-$\beta$-methylvalerate; IX gave a sodium salt (X) which melted at 231–233°. On the other hand, the alkylation of ethyl nitromalonate by crotyl chloride gave an unsaturated ester, XI, which could be readily hydrogenated to a saturated compound, XII. After XII was submitted to



(1) Presented at the Meeting-in-miniature of the New York Section of the American Chemical Society, February 8, 1952.

(2) Based on a portion of the dissertation submitted by Robert J. Kelly to the Department of Chemistry, New York University, February, 1952, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) H. B. Hass and M. L. Bender, THIS JOURNAL, **71**, 1767, 3482 (1949).

partial decarbethoxylation, the resulting material (XIII) was transformed into a sodium salt (XIV) which melted at 209–211°. Mixtures of VI and XIV displayed no depression of the melting point, whereas mixtures of XIV and X, and of X and VI, melted over the range of 205–215°. Thus it must be concluded that VI and XIV, and hence V and XIII, and IV and XII, too, were identical. (It was impossible to compare IV and XII directly since IV, by its method of preparation, was contaminated by unnitrated material from which it could not be separated before decarbethoxylation.[4]) Since XII contained an *n*-butyl group the unsaturated ester, XI, must have contained a crotyl group that was not inverted during the alkylation.

It is thus clear that the alkylation of ethyl nitromalonate and ethyl nitroacetate by crotyl chloride (and probably by allyl bromide, too) may proceed by direct carbon alkylation. The failure of the crotyl group to become inverted points away from O-alkylation and indicates C-alkylation; for it would seem unlikely that a rearrangement based on a four-membered cyclic complex occurs here, especially since an acid-strengthening group such as nitro which would facilitate anion formation (as in *p*-nitrobenzyl chloride) is absent, and the weight of available evidence points to a six-membered cyclic complex for the usual allylic rearrangement as exemplified by the Claisen rearrangement.[5] Furthermore, any base-catalyzed rearrangement of an allyl-substituted nitronate ester would have to pass through the intermediate stage of a resonance-stabilized allylic anion which in turn should yield a mixture of normal and inverted products.

## Experimental

**Ethyl Allylnitromalonate (XV).**—In a 3-neck, 500-ml. round-bottom flask equipped with a dropping funnel, a reflux condenser protected by a $CaCl_2$ tube, and a stirrer, 39.0 g. (0.16 mole) of potassium ethyl nitromalonate was dissolved in 200 ml. of absolute ethyl alcohol by warming the mixture on a steam-bath. To this solution was added 21 g. (0.17 mole) of allyl bromide (Eastman Kodak Co. reagent; redistilled, 71–72°), and the reaction mixture was refluxed for a total of 20 hours. During this period, a white solid separated; this was shown to be KBr. The reaction mixture was evaporated at reduced pressure to remove the ethanol, the residue was poured into 200 ml. of water, and this mixture was extracted with three 50-ml. portions of ether. The combined ether extracts were dried over anhydrous $MgSO_4$, and then evaporated at reduced pressure. Distillation of the crude product gave 13.3 g. (34% yield) of ethyl allylnitromalonate (XV): b.p. 98–100° (2 mm.), $n^{24}D$ 1.4449, $d^{24}_4$ 1.117. *Anal.* Calcd. for $C_{10}H_{15}NO_6$: C, 48.98; H, 6.17; N, 5.71. Found: C, 49.10; H, 5.93; N, 5.90.

**Potassium Ethyl 2-Nitro-4-pentenoate (XVII).**—In order to remove one carbethoxy group from XV, 0.084 mole of potassium ethoxide (in absolute ethyl alcohol) was added to a solution of 20.51 g. (0.084 mole) of XV in absolute ethyl alcohol. The alcohol-insoluble XVII, which precipitated within one-half hour at room temperature, was filtered off and recrystallized from absolute ethyl alcohol; yield 10.0 g. (56%), m.p. 185° dec. *Anal.* Calcd. for $C_7H_{10}NO_4K$: C, 39.79; H, 4.77; N, 6.63; K, 18.51. Found: C, 39.58; H, 4.95; N, 6.89; K, 18.38.

**Ethyl 2-Nitro-4-pentenoate (XVI).**—An excess of carbon dioxide was bubbled through an aqueous solution of 10.0 g. (0.047 mole) of XVII in order to form the free ester, XVI. An ether extract of this aqueous mixture was dried over anhydrous $MgSO_4$, the ether was evaporated and the residue was distilled to give 6.5 g. (80% yield) of XVI, a colorless liquid; b.p. 72.5° (2 mm.), $n^{25}D$ 1.4381. *Anal.* Calcd. for $C_7H_{11}NO_4$: C, 48.55; H, 6.40; N, 8.09. Found: C, 48.28; H, 6.10; N, 8.16.

**Ethyl 2-Nitro-4-pentenoate (XVI) (from Ethyl Nitroacetate).**—In apparatus similar to that used for the preparation of ethyl allylnitromalonate, an absolute ethanol solution of 0.11 mole of sodium ethoxide was added slowly to an absolute ethanol solution of 15.0 g. (0.11 mole) of ethyl nitroacetate. After warming this mixture on a steam-bath for 10–15 minutes, 14.5 g. (0.12 mole) of allyl bromide was added. This reaction mixture was refluxed for a total of 24 hours. The isolation and purification of the product was carried out just as described for ethyl allylnitromalonate. This gave 2.0 g. (10% yield) of a colorless liquid; b.p. 67–69° (2 mm.), $n^{25}D$ 1.4390.

To a solution of 1.0 g. (0.0058 mole) of this product in absolute ethyl alcohol was added 0.0058 mole of potassium ethoxide (in absolute ethyl alcohol) at room temperature. The solid which slowly precipitated had a melting point of 184–185°; it was shown by the method of mixed melting point to be identical with XVII, the product of the decarbethoxylation of XV.

**Ethyl Crotylnitromalonate (XI) and Ethyl 2-Nitro-4-hexenoate (XVIII).**—In similar fashion, the alkylation of potassium ethyl nitromalonate by allyl bromide gave a 25% yield of XI; b.p. 113–6° (2 mm.), $n^{25}D$ 1.4480, $d^{25}_4$ 1.103. *Anal.* Calcd. for $C_{11}H_{17}NO_6$: N, 5.40. Found: N, 5.45.

When XI was treated with potassium ethoxide in the manner previously described, a 50% yield was obtained of nearly white potassium ethyl 2-nitro-4-hexenoate (XIX); m.p. 192–194° dec. *Anal.* Calcd. for $C_8H_{12}NO_4K$: N, 6.22; K, 17.35. Found: N, 6.36; K, 17.35. Acidification of XIX by carbon dioxide, as described earlier, gave a 50% yield of XVIII; b.p. 71–72° (2 mm.), $n^{24}D$ 1.4442. *Anal.* Calcd. for $C_8H_{13}NO_4$: N, 7.48. Found: N, 7.56.

The alkylation of ethyl nitroacetate as described above by crotyl chloride instead of allyl bromide gave an 11.5% yield of XVIII; b.p. 70–72° (2 mm.), $n^{24}D$ 1.4445. Identification was achieved through the potassium salt (m.p. 192–194° dec.), which gave no depression of the melting point when mixed which a sample of XIX obtained from the decarbethoxylation of XI.

**Nitration of Ethyl Alkylmalonates.**—Ethyl *n*-butylmalonate III and ethyl *s*-butylmalonate VII were nitrated by the method described by Weisblat and Lyttle.[6] It was not possible to secure the nitration products, IV and VIII, in pure form,[4] but the unreacted starting materials were readily removed when the nitro compounds were subjected to decarbethoxylation, as described below. The nitration of 67.0 g. (0.31 mole) of III gave 25.0 g. of a light yellow liquid, b.p. 95–115° (2 mm.); 67.0 g. (0.31 mole) of VII gave 12.0 g. of a liquid, b.p. 90–101° (2 mm.).

**Conversion of Nitromalonates to Nitroacetates.**—The impure products from the nitration of III and VII were converted to the corresponding nitroacetates by the action of potassium ethoxide. In order to remove one carbethoxy group from ethyl *n*-butylnitromalonate IV, 0.05 mole of potassium ethoxide (in absolute ethyl alcohol) was added to a solution of 10.0 g. of impure IV in a mixture of absolute ether and absolute ethyl alcohol at room temperature, and the mixture was allowed to stand overnight. Evaporation of the solvent left a tacky brown residue. This was mixed with water to dissolve the salt of the decarboxylated compound, ethyl α-nitrocaproate (V); the unnitrated ester III, which had been present as an impurity in IV, was removed by extraction with ether. The aqueous solution of the salt was treated with an excess of carbon dioxide to set free V which was taken up in ether. After the ether solution was dried over anhydrous $MgSO_4$, the solvent was evaporated under reduced pressure. A residue of 1.2 g. of V was obtained; $d^{23}_4$ 1.067, $n^{22}D$ 1.4321. The liquid gave a positive test for a secondary nitro compound in the Victor Meyer test.

The preparation and isolation of ethyl α-nitro-β-methylvalerate (IX) from impure VIII was carried out in exactly the same way. From 12.0 g. of impure VIII, 0.40 g. of IX was obtained; $n^{22}D$ 1.4319. The liquid also gave a positive test for a secondary nitro compound.

(4) C. Ulpiani, *Atti acad. Lincei Rom.*, [5] **13**, II, 346 (1904).

(5) D. S. Tarbell in "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, pp. 16–17.

(6) D. I. Weisblat and D. A. Lyttle, THIS JOURNAL, **71**, 3079 (1949).

The method of preparation, the occurrence of a secondary nitro grouping, and the successful execution of exactly the same reactions with the similar allyl (XV, XVI, XVII) and crotyl (XI, XVIII, XIX) compounds leave no doubt as to the structures of the *n*-butyl and *s*-butyl compounds (V and IX).

**Preparation of the Sodium Salts (VI and X) of the Nitroacetates (V and IX).**—By dissolving 0.50 g. (0.0026 mole) of V in absolute ethyl alcohol and adding 0.0026 mole of sodium ethoxide (in absolute ethyl alcohol) at room temperature, the alcohol-insoluble sodium ethyl α-nitrocaproate (VI) was precipitated. The salt was separated by centrifugation and washed several times with dry ether to give 0.38 g. (70% yield) of VI; m.p. 212–214° dec.

In exactly the same manner, 0.28 g. (0.0015 mole) of IX gave 0.21 g. (66% yield) of sodium α-nitro-β-methylvalerate (X); m.p. 231–233° dec.

**Hydrogenation of XI.**—The hydrogenation of 7.5 g. (0.029 mole) of XI dissolved in 100 ml. of acetic anhydride was conducted for three hours at room temperature and three atmospheres pressure in the presence of platinum oxide as a catalyst. Only one molar equivalent of hydrogen was absorbed under these conditions, and this was complete in less than one-half hour. The catalyst was removed by filtration, and the acetic anhydride was removed under reduced pressure. Distillation of the residue gave 5.0 g. (64% yield) of ethyl *n*-butylnitromalonate (XII); b.p. 100–104° (1 mm.), $n^{17}D$ 1.4429.

**The decarbethoxylation of XII** to ethyl α-nitrocaproate XIII was conducted in the manner previously described for the conversion of IV to V. The yield of XIII was 22%; $n^{23}D$ 1.432, $d^{23}_4$ 1.062.

When XIII was treated with sodium ethoxide as described for the conversion of V to VI, a 59% yield was obtained of sodium salt, XIV, m.p. 209–211° dec. Mixtures of XIV and VI displayed no depression of the melting point, 212–214° dec. Mixtures of XIV and X, and of VI and X, melted over the same range of 205–215°.

**Acknowledgments.**—Ethyl *n*-butylmalonate was obtained through the courtesy of Professor R. T. Morrison. The analyses were done in the Microchemical Laboratory of New York University by Dr. W. C. Woodland and Dr. T. S. Ma, who supervised the laboratory, and by their assistants, Dr. E. V. Piel, Dr. H. J. Stolten, Mr. J. D. McKinley, Jr., Mr. R. H. Hansen and Mr. Paul Pemsler.

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[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT LABORATORIES, UNIVERSAL OIL PRODUCTS COMPANY]

# The Butylation of Guaiacol

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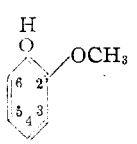
This paper establishes the course of the reaction in the butylation of guaiacol with *t*-butyl alcohol in the presence of 85% phosphoric acid as to the positions occupied by the entering *t*-butyl group. From the *t*-butylguaiacols thus obtained, three of the possible four position isomers were isolated and identified. The reaction product consists of equal amounts of 4- and 5-*t*-butylguaiacol with about 10 mole per cent. of 6-*t*-butylguaiacol. In this case, the directive influences of the hydroxy and methoxy functions are of equal strength in regard to substitution in the para positions.

In the course of preparation of alkylphenols to be evaluated as antioxidants, a procedure often employed is the butylation of a selected phenol to give a derivative with the butyl group in a position ortho or para to the hydroxyl group. The ease of alkylation and the orientation of the entering substituent can be considered as due to the activating effects of the hydroxyl group. The inability to place a *t*-butyl group in a position meta to the hydroxyl by direct alkylation[1] can be considered as evidence of this strong directive effect.

It is of interest to examine the alkylation product in the case of guaiacol, for in this compound the strong directive effect of the methoxy group competes with the directive effect of the hydroxyl group.[2-4] Regardless which one of the four available positions is occupied by the entering butyl group, the alkylation reaction must involve substitution meta to either the hydroxy or methoxy group.




This paper establishes the course of reaction in the butylation of guaiacol as to the positions occupied by the entering groups. As shown in the first two runs of Table I, guaiacol was alkylated with *t*-butyl alcohol in the presence of 85% phosphoric acid to give, in good yield, a mixture of *t*-butylguaiacols. From the mixture thus obtained, three individual compounds of the possible four were identified in amounts as indicated in Table I. The alkylation product consists of approximately equal quantities of 4- and 5-*t*-butylguaiacol with about 10 mole per cent. of 6-*t*-butylguaiacol. These results indicate that the directive influences of the hydroxy and methoxy functions are of equal strength in regard to substitution in the para position. The lack of substitution in the 3-position, ortho to the methoxy group, can be attributed to the more pronounced steric effect of this group in comparison to the steric effect of the hydroxyl group. The bulk of the methoxy group is sufficient to hinder the attack on the adjacent position by a large *t*-butyl cation.

This observation as to the comparable directive effects of the hydroxy and methoxy functions was not entirely expected. It is generally considered that the hydroxy group possesses a more powerful directive effect than methoxy.[5] This fact is evident in the nitration[6] and in the bromination of guaiacol[7] in which cases substitution in the 4- and 6-positions is realized. However, in the sulfonation of guaiacol, a mixture containing about equal amounts of the 4- and 5-sulfonic acids is obtained.[8] On the basis of strong directive effect of the hydroxy

(1) R. S. Bowman and D. Stevens, *J. Org. Chem.*, **15**, 1172 (1950).
(2) R. Q. Brewster and H. Choguill, THIS JOURNAL, **61**, 2702 (1939).
(3) T. Lea and R. Robinson, *J. Chem. Soc.*, 411 (1926).
(4) P. B. D. de la Mare and C. A. Vernon, *ibid.*, 1764 (1951).
(5) R. C. Fuson, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 282.
(6) A. Klemenc, *Monatsh.*, **33**, 701 (1912).
(7) P. Robertson, *J. Chem. Soc.*, **93**, 788 (1908).
(8) A. Rising, *Ber.*, **39**, 3685 (1906).