

POLAR EFFECTS IN BROMINATIONS WITH N-BROMOSUCCINIMIDE¹

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It has been known for some time that *N*-bromosuccinimide can react by addition to a double bond as well as by allylic substitution. Howton (1) and Farmer and Shipley (2) found that the bromination of cyclohexene (I) produced a 50% yield of 3-bromocyclohexene (II) and 6% of 1,2-dibromocyclohexane (III). It was of interest, therefore, to determine the effect of polar groups and experimental conditions on the course of this reaction.

Vinylacetonitrile (IV) was chosen as a starting point since the hydrogens are deactivated by the cyano group while the double bond is still fairly reactive. Bromination of IV in carbon tetrachloride with *N*-bromosuccinimide plus peroxide produced a 13% yield of γ -bromocrotonitrile (V), a 21% yield of 3,4-dibromobutyronitrile (VI), plus 2% of VII, a 1:1 adduct of the *N*-bromosuccinimide and IV. The fact that in V the bromine was *gamma* and not *alpha* to the cyano group was indicated by the fact that the ultraviolet absorption spectrum did not show a maximum but increased to an ϵ of 8,700 at 222 m μ . The structure of the adduct VII was indicated by analysis, molecular weight determination and by the fact that on hydrogenation it absorbed 3 moles of hydrogen and produced 1 mole of bromide ion plus *N*-(4-aminobutyl)succinimide (VIII). The structure of VIII was indicated by the fact that hydrolysis produced succinic acid and treatment of the aqueous solution with picric acid produced 1,4-diaminobutane dipicrate (IX). The addition of *N*-bromosuccinimide to the double bond of cyclohexene in small amounts had been previously reported (3).

Couvreur and Bruylants recently reported (4) that bromination of IV produced 12.5% of V and 37.5% of VI but they did not find the adduct VII. Apparently the succinimido free radical can either abstract an *alpha* hydrogen from IV or add to the double bond. The electron-withdrawing cyano group decreases the electron density on the α -carbon so that the normal removal of the hydrogen by the electron-seeking succinimido radical is retarded. The addition of the *N*-bromosuccinimide to the double bond, which is probably very similar in mechanism to that proposed by Kharasch, Jensen, and Urry (5) for the free radical addition of carbon tetrachloride to olefins, can then proceed. The high-boiling, viscous residue from the reaction very likely results from dimeric and trimeric products of a related reaction. The formation of the dibromo derivative VI must proceed by a different mechanism.

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Corey (6) recently found that *N*-bromosuccinimide with methyl vinylacetate produced only methyl 3,4-dibromobutyrate.

In an effort to suppress the first two radical reactions and allow the formation of VI to proceed, a bromination of IV was carried out in the presence of *p*-*tert*-butylcatechol but no peroxide. As was expected the yield of the dibromo VI increased to 52 % but, surprisingly enough, the yield of the substitution product V also increased to 17 %. The amount of viscous oil was decreased and no adduct VII was found. It appears that allylic substitution can proceed by an ionic as well as by a free radical mechanism. The main effect of the *p*-*tert*-butylcatechol was to inhibit the formation of the high-boiling residue.

Whether an ionic mechanism could give rise to the *gamma* bromo derivative was determined by brominating vinylacetonitrile (IV) with elemental bromine. Under these conditions an 18 % yield of γ -bromocrotonitrile (V) plus a 43 % yield of the dibromo VI were obtained. That the V was indeed the *gamma* bromo derivative was indicated by the fact that it absorbed very strongly at 220 m μ in the ultraviolet. Lespieau (7) had previously reported that bromination of IV produced an *alpha* bromo derivative. One can write a mechanism for the allylic bromination of IV that is very similar to the bromination of isobutylene, where the driving force of the reaction is the shifting of the double bond in conjugation with the cyano group.

In order to evaluate further the conditions for the addition of bromine to double bonds by *N*-bromosuccinimide, a series of unsaturated compounds were studied, first in the presence of peroxide and then in the presence of *p*-*tert*-butylcatechol or other dihydroxybenzene derivative. The results of these reactions are summarized in Table I.

Southwick, Pursglove, and Numerof (8) found that benzalacetone did not react with *N*-bromosuccinimide in the absence of peroxide but gave a 47 % yield of the dibromide when peroxide was added. They had no suggestion as to the source of the hydrogen atom of the succinimide formed in the reaction. When 1 mole of benzalacetone was brominated in the presence of 0.37 mole of *p*-*tert*-butylcatechol, a 37 % yield of the dibromide was obtained. (A similar correspondence was noted in the bromination of ethyl acrylate.) The exact correspondence of the catechol and the dibromide suggests that the *p*-*tert*-butylcatechol furnishes the hydrogen to form the succinimide. In other cases, however, the amount of the dibromide greatly exceeds the amount of the dihydricphenol. In a separate experiment it was shown that catechol reacts slowly with *N*-bromosuccinimide to yield 87 % of bromine.

In an effort to determine the exact function of the dihydric phenol, catechol was substituted for *p*-*tert*-butylcatechol in several brominations. The effect of the two dihydric phenols was very similar. Resorcinol, however, strongly inhibited both the substitution and the addition reaction. Hydroquinone, probably because of its low solubility in carbon tetrachloride, has the same effect as catechol but to a much smaller extent. It is significant that Buckles (9) found no effect of *p*-*tert*-butylcatechol on the bromination of stilbene with *N*-bromoacetamide.

TABLE I
 POLAR EFFECTS IN BROMINATIONS WITH *N*-BROMOSUCCINIMIDE

| Compound ^a | <i>N</i> -Bromosuccinimide, Mole | Benzoyl Peroxide, Mole | <i>p</i> - <i>tert</i> -Butylcatechol, Mole | Product | Yield, % | Boiling Point | | | | | n_D^{25} | | |
|------------------------|----------------------------------|------------------------|---|--|-----------------|------------------------|-----|----------------------|-----|------|------------|---------------------|------|
| | | | | | | Found, °C. | mm. | Reported °C. | mm. | Ref. | Found | Reported | Ref. |
| Vinylacetonitrile (IV) | 0.67 | 0.013 | 0 | γ -Bromocrotonitrile (V) | 13 | 88-92 | 10 | 73-90 | 10 | (4) | 1.5001 | 1.4963 ^c | (14) |
| | | | | 3,4-Dibromobutyronitrile (VI) | 21 | 120-124 | 10 | 138.5-139 | 20 | (15) | 1.5165 | | |
| | | | | 3-Bromo-4-succinimidobutyronitrile (VII) | 2 | 117-117.5 ^d | | | | | | | |
| Crotonitrile | .66 | .04 | 0 | V | 17 | | | | | | | | |
| | | | | VI | 52 | | | | | | | | |
| Methyl crotonate (X) | .60 | .04 | 0 | γ -Bromocrotonitrile (V) | 40 | 58-63 | 4 | | | | 1.4979 | | |
| | | | | Methyl γ -bromocrotonate (XI) | 83 | 84-86 | 12 | 83-85 | 13 | (3) | 1.4959 | 1.498 ^e | (11) |
| Ethyl acrylate | .68 | 0 | .048 | XI | 46 | 82-86 | 12 | | | | 1.4956 | | |
| | | | | Methyl α , β -dibromobutyrate | 0 | | | | | | | | |
| Styrene | .67 | 0 | 0 | Ethyl 3,4-dibromopropionate | 25 | 72-73 | 5 | 112 | 23 | (12) | 1.4959 | 1.5015 ^o | (12) |
| | | | | Styrene dibromide (XII) ^h | 6 ⁱ | 73-74 ^d | | 72-73 ^d | | (13) | | | |
| Benzalacetone (I) | .57 | 0 | .016 | XII | 45 ^j | 73-74 ^d | | | | | | | |
| | | | | XII | 48 | 73-74 ^d | | | | | | | |
| | | | | Benzalacetone dibromide | 37 | 118-121 ^d | | 121-124 ^d | | (8) | | | |
| Cyclohexene (I) | .95 | 0 | .37 ^f | 3-Bromocyclohexene (II) | 50 ^k | 80-82 | 15 | 45-47 | 10 | (1) | | | |
| | | | | 1,2-Dibromocyclohexane (III) | 6 | 95-107 | 15 | 51-57 | 1 | (1) | | | |
| | .70 | 0 | .045 | II | 18 ^l | 78-84 | 15 | | | | | | |
| | | | | III | 40 | 95-104 | 15 | | | | | | |
| | .70 | 0 | .049 ^m | II | 41 | 80-82 | 15 | | | | | | |
| | | | | III | 12 | 95-106 | 15 | | | | | | |
| | .70 | 0 | .050 ⁿ | II | 27 ^p | 80-82 | 15 | | | | | | |
| | | | | III | 4 ^p | 95-107 | 15 | | | | | | |
| | .70 | 0 | .049 ^f | II | 7 | 78-82 | 15 | | | | | | |
| | | | | III | 58 | 95-105 | 15 | | | | | | |

^a Figures adjusted to 1 mole of compound. ^b Based on *N*-bromosuccinimide; olefin always in excess. ^c n_D^{20} , for lower-boiling isomer; for high-boiling isomer, n_D^{20} 1.5168. ^d M.p. ^e At 19°. ^f Catechol used in place of *p*-*tert*-butylcatechol. ^g At 16°. ^h Plus 3.6 g. of an unidentified solid, m.p. 148-149.5°, which was shown by mixture melting point determination not to be *N*-phenylsuccinimide or β -succinimidoethylbenzene. ⁱ 90% of styrene recovered and a 22% yield of succinimide obtained. ^j 17% of styrene recovered and a 54% yield of succinimide obtained. ^k 28% of cyclohexene recovered and a 85% yield of succinimide obtained. ^l 17% of cyclohexene recovered and a 75% yield of succinimide obtained. ^m Hydroquinone used in place of *p*-*tert*-butylcatechol. ⁿ Resorcinol used in place of *p*-*tert*-butylcatechol. ^p 40% of *N*-bromosuccinimide recovered unchanged.

Kharasch and Priestley (10) reported that styrene does not react with *N*-bromosuccinimide. It was found, however, that in the present investigation a 6% yield of styrene dibromide (XII) was formed in the absence of *p*-*tert*-butylcatechol and a 45% yield was realized in its presence.

One can conclude that *N*-bromosuccinimide can react by at least two different mechanisms to produce different products. Experimental conditions and the presence of polar groups will determine the course of the reaction.

EXPERIMENTAL⁴

Materials. Carbon tetrachloride was purified by extraction with concentrated sodium hydroxide, concentrated sulfuric acid, dilute sodium bicarbonate solution, and then water. It was dried over phosphorus pentoxide and carefully fractionated.

Benzene and cyclohexene were refluxed over sodium for 24 hours and then fractionated.

N-Bromosuccinimide was carefully purified by recrystallization from ten times its weight of boiling water to produce material that assayed above 99.3% when reacted with potassium iodide in acetic acid, followed by titration with standard sodium thiosulfate.

Crotonitrile was prepared by isomerization of vinylacetonitrile with phenol and sodium according to the method of Bruylants (16).

The remaining materials were the highest purity commercial grade available. The organic reagents were purified before use by distillation or recrystallization.

Brominations with N-bromosuccinimide. All brominations were carried out in the usual manner. The results are indicated in Table I. All of the dibromides were compared with the product obtained by bromination of the corresponding olefin with elemental bromine. The dibromides of styrene, cyclohexene, and benzalacetone were identified by mixture melting point determinations. Typical brominations are listed below.

Bromination of vinylacetonitrile (IV) with N-bromosuccinimide. A mixture of 100.5 g. (1.5 moles) of vinylacetonitrile (IV), 178 g. (1 mole) of *N*-bromosuccinimide, 4.8 g. (0.002 mole) of dibenzoyl peroxide, and 750 ml. of carbon tetrachloride was heated under reflux for 2 hours; at the end of this time the *N*-bromosuccinimide layer had been replaced by a layer of brown oil. After the reaction mixture had been stored overnight at Dry Ice temperature, a third yellow oil formed on top. From this top layer was obtained 8.2 g. of a crude solid. Recrystallization of this solid from chloroform produced 4.1 g. (2%) of 3-bromo-4-succinimidobutyronitrile (VII), a 1:1 adduct of IV and *N*-bromosuccinimide, m.p. 117–117.5°.

Anal. Calc'd for $C_8H_8BrN_2O_2$: C, 39.18; H, 3.69; Mol. wt., 265.

Found: C, 39.43; H, 3.85; Mol. wt. (Rast), 245.

The proof of structure of VII is given below. Only a small amount of succinimide was isolated from the reaction mixture, indicating that a large number of succinimide groups were chemically bound in the high-boiling residue.

The remaining portion of the top yellow layer was combined with the lower brown layer and the carbon tetrachloride layer and the resulting liquid was distilled through a 12-inch, helix-packed column to yield 18.9 g. (13%) of γ -bromocrotonitrile (V), b.p. 88–92° (10 mm.), n_D^{25} 1.5001, and 47.4 g. (21%) of 3,4-dibromobutyronitrile (VI), b.p. 120–124° (10 mm.), n_D^{25} 1.5165. A large amount of high-boiling residue remained in the distillation flask.

Proof of structure of 3-bromo-4-succinimidobutyronitrile (VII). Qualitative analysis by sodium fusion indicated the presence of bromine and nitrogen.

A mixture of 1 g. (0.0041 mole) of the adduct VII, 4 g. of sodium hydroxide, and 12 ml. of water was heated under reflux until evolution of ammonia ceased. The mixture then was acidified with concentrated hydrochloric acid and was heated for an additional hour. This acid solution was exhaustively extracted with ether for 3 days to obtain 0.3 g. (75%) of succinic acid, m.p. 187–189°. The mixture melting point with an authentic sample of succinic acid was 187–189°.

A mixture of 0.914 g. (0.0037 mole) of the adduct VII, 0.11 g. of platinum oxide, 0.16 g. of anhydrous sodium acetate, and 40 ml. of glacial acetic acid absorbed 256 ml. (102%) (assuming blank of 22 ml.) of hydrogen. The reaction mixture was distilled to remove about three-fourths of the acetic acid, made basic with 20% sodium hydroxide, and heated under reflux for 5 hours. Exhaustive extraction of this mixture for 3 days, followed by treatment of

⁴ All melting points are corrected. The analysis was carried out by Arthur Tomaszewski.

the extracts with picric acid, produced 0.5 g. of 1,4-diaminobutane dipicrate (IX), m.p. 249–251° (dec.) [reported (17) m.p. 250–260° (dec.)]. The isomeric 1,3-diaminobutane dipicrate melts at 240–245° (dec.) (18).

Acidification of the above ether-extracted reaction mixture with sulfuric acid, followed by exhaustive extraction with ether, produced 0.4 g. (91%) of succinic acid, m.p. 187–189°. Titration of the aqueous layer indicated the presence of 95% of one molar equivalent of bromide ion.

Bromination of vinylacetonitrile (IV) with elemental bromine. Bromine was added dropwise to an ice-cold solution of 12 g. of vinylacetonitrile (IV) in 20 ml. of carbon tetrachloride until a permanent orange color formed. The unreacted IV and carbon tetrachloride were removed by distillation and the residue was fractionated through a 6-inch Vigreux column to yield 4.6 g. (18%) of bromocrotonitrile (V), b.p. 73–90° (10 mm.), n_D^{25} 1.4979 [reported (14) b.p. 74–88° (10 mm.), *cis*-isomer, n_D^{20} 1.4963 and *trans*-isomer, n_D^{20} 1.5168] and 16.7 g. (43%) of 3,4-dibromobutyronitrile (VI), b.p. 100–100.5° (2.5 mm.), n_D^{25} 1.5165 [reported (15) b.p. 138.5–139° (20 mm.)].

Reaction of catechol and N-bromosuccinimide. A mixture of 2 g. (0.01 mole) of *N*-bromosuccinimide, 0.2 g. (0.0018 mole) of catechol and 100 ml. of dry carbon tetrachloride was heated under reflux for 2 hours. The red solution of carbon tetrachloride was removed by distillation and the red distillate was extracted with three 50-ml. portions of 2% potassium iodide solution. The liberated iodine was titrated with standard sodium thiosulfate solution. The liberated iodine corresponded to 0.0031 mole (86%) of *N*-bromosuccinimide.

SUMMARY

A series of polar effects were found to favor addition rather than allylic substitution in brominations with *N*-bromosuccinimide. An electron-withdrawing group attached directly to the *alpha* carbon greatly inhibits allylic substitution. Thus crotonitrile produces a 40% yield of the γ -bromocrotonitrile while vinylacetonitrile gives only 13% of the γ -bromo derivative but 21% of a dibromo derivative plus a small amount of a 1:1 addition product of *N*-bromosuccinimide and the nitrile. The addition of a dihydric phenol, such as catechol, that inhibits the free radical substitution reaction and yet is easily oxidized by *N*-bromosuccinimide markedly increases the addition reaction with a large number of olefins.

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