The Reaction of N-Bromosuccinimide with Bicyclo[2.2.1]-5-heptene-*endo*-*cis*-2,3-dicarboxylic Anhydride[1]

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N-Bromosuccinimide was found to add to the double bond of bicyclo[2.2.1]-5-heptene-*endo-cis*-2,3-dicarboxylic anhydride in the presence of benzoyl peroxide to yield the *cis* adduct, *exo*-5-bromo-*exo*-6-succinimidobicyclo-[2.2.1]heptane-*endo-cis*-2,3-dicarboxylic anhydride (**12**). In addition, N-bromosuccinimide rearranges under the conditions of the reaction to give β-bromopropionyl isocyanate.

N-Bromosuccinimide (NBS) has been used extensively as an allylic brominating agent for approximately twenty years.[4] Bloomfield[5a] and Hey[5b] first suggested that this reaction proceeded by a radical chain mechanism, and further support for this postulation was provided by Schmid and Karrer.[6] More recently, Dauben and McCoy[7] reported a very thorough investigation of the reaction of NBS with cyclohexene in carbon tetrachloride. These workers, and the earlier workers, suggest that the succinimidyl radical is generated in an initiation step and then proceeds to abstract an allylic hydrogen atom in the propagation step. Although this mechanism has been widely accepted, another mechanism (Goldfinger mechanism) has been proposed in which succinimidyl radicals are not involved.[8] In the Goldfinger mechanism it is suggested that the function of NBS is simply to provide a constant low concentration of molecular bromine, the molecular bromine being responsible for the allylic bromination. Evidence supporting the Goldfinger mechanism in benzylic brominations with NBS has been recently reported.[9]

If succinimidyl radicals are actually involved in radical brominations with NBS, one might expect such radicals to add to the double bonds under the proper conditions. Walling[10] has suggested that the abstraction of hydrogen atoms by the succinimidyl radical in preference to addition to the double bond is due to the greater bond energy of the N–H bond in the succinimide produced, as compared to the N–C bond which would result from the addition of the succinimidyl radical to the alkene. However, the literature contains a number of examples in which NBS reacts with alkenes to give 1:1 adducts. For example, dihydropyran has been reported to react with NBS to give 2-succinimido-3-bromotetrahydropyran.[11] Methylenecyclobutane forms an adduct with NBS in low yield,[12] and vinylacetonitrile gave a low yield of 3-bromo-4-succinimidobutyronitrile with NBS.[13] In none of these cases, however, is it clear that succinimidyl radicals were involved.

The possible decomposition of other N-haloamides and -imides to yield similar free radicals is likewise not clear. N-Bromophthalimide also adds to dihydropyran in carbon tetrachloride solvent, but in a reverse direction to that observed with NBS.[14] With substituted dihydropyrans, the position of substituents appears to influence the type of products produced.[15] N-Bromotrifluoroacetamide and N-bromotrichloroacetamide add to cyclohexene, but under identical conditions the former gave predominantly ring bromination of toluene, whereas the latter gave side-chain bromination of toluene.[16]

When methylenecyclobutane and cyclohexene were allowed to react with NBS in benzene solution, N-phenylsuccinimide was isolated in each case among the products, but in low yield.[12,17] On the other hand, N-(cyclohepta-2,4,6-trienyl)succinimide was isolated in a high yield in the reaction of cycloheptatriene with NBS.[18] Again, in none of these cases has the existence of the intermediate succinimidyl radical been conclusively established. Succinimidyl radicals do, however, appear to be involved in the propagation step in the formation of *dl*-N-α-methoxy-*p*-nitrobenzylsuccinimide[19] and *dl*-N-α-(*p*-bromophenoxy)benzylsuccinimide[20] by the reaction of NBS with *p*-nitrobenzylmethyl ether and *p*-bromophenylbenzyl ether, respectively. Good yields of the succinimidyl derivatives were obtained by increasing the molar ratio of NBS to the ethers and by removing the molecular bromine produced in the reaction. These observations were considered consistent with the proposed free-radical mechanism.[20]

A study of the reaction of NBS with alkenes in which the only allylic hydrogen atoms are at bridgehead posi-

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[1] Taken in part from the dissertation of C. D. Kennedy presented to the Graduate School Faculty of Oklahoma State University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, May, 1963. A preliminary account of this work was presented at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., Sept., 1962.

[2] Research and Development Department, Continental Oil Company, Ponca City, Okla.

[3] National Defense Education Act Fellow, 1959–1962.

[4] K. Ziegler, A. Spath, E. Schaaf, W. Schumann, and E. Winkelmann, *Ann.*, **551**, 80 (1942); C. Djerassi, *Chem. Rev.*, **43**, 271 (1948); T. D. Waugh, "NBS, Its Reactions and Uses," Arapahoe Chemicals, Inc., Boulder, Colo., 1951; L. Horner and E. H. Winkelmann, *Angew. Chem.*, **71**, 349 (1959).

[5] (a) G. F. Bloomfield, *J. Chem. Soc.*, 114 (1944); (b) D. H. Hey, *Ann. Rept. Chem. Soc.*, **41**, 184 (1944).

[6] H. Schmid and P. Karrer, *Helv. Chim. Acta.*, **29**, 573 (1946).

[7] H. J. Dauben, Jr., and L. L. McCoy, *J. Am. Chem. Soc.*, **81**, 4863 (1959); H. J. Dauben, Jr., and L. L. McCoy, *ibid.*, **81**, 5404 (1959).

[8] J. Adam, P. A. Gosselain, and P. Goldfinger, *Nature*, **171**, 704 (1953); F. L. J. Sixma and R. H. Riem, *Proc. Koninkl. Ned. Akad. Wetenschap.*, **B61**, 183 (1958); *Chem. Abstr.*, **53**, 2123*f* (1959); B. P. McGrath and J. M. Tedder, *Proc. Chem. Soc.*, 80 (1961).

[9] G. A. Russell, C. DeBoer, and K. M. Desmond, *J. Am. Chem. Soc.*, **85**, 365 (1963); R. E. Pearson and J. C. Martin, *ibid.*, **85**, 354 (1963).

[10] C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 383.

[11] J. R. Shelton and C. Ciadella, *J. Org. Chem.*, **23**, 1128 (1958).

[12] E. R. Buchman and D. R. Howton, *J. Am. Chem. Soc.*, **70**, 2517 (1948).

[13] W. J. Bailey and J. Bello, *J. Org. Chem.*, **20**, 525 (1955).

[14] C. D. Hurd, J. Moffat, and L. Rosnati, *J. Am. Chem. Soc.*, **77**, 2793 (1955).

[15] F. Korte, R. Heinz, and D. Schorb, *Ber.*, **94**, 825 (1961).

[16] J. D. Park, H. J. Gerjovich, W. R. Lycan, and J. R. Lacher, *J. Am. Chem. Soc.*, **74**, 2189 (1952).

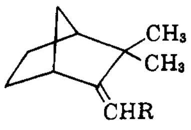
[17] D. R. Howton, *ibid.*, **69**, 2060 (1947).

[18] H. L. Dryden, Jr., and B. E. Burgert, *ibid.*, **77**, 5633 (1955).

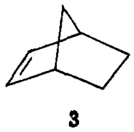
[19] D. G. Markees, *J. Org. Chem.*, **23**, 1490 (1958).

[20] L. L. Braun and J. H. Looker, *ibid.*, **26**, 574 (1961).

tions of the norbornane-type skeleton should be particularly interesting. In such systems the intermediate bridgehead radicals, if formed, could not be stabilized by resonance since this would be in violation of Bredt's rule,[21] and the reaction might be expected to take a different course from the usual allylic bromination. Roberts and co-workers[22,23] studied the reaction of NBS with two such bicyclic systems, camphene (**1**) and norborynylene (**3**), almost fifteen years ago and the reaction did take an unexpected path. 8-Bromocamphene (**2**) was produced from camphene (**1**),[22] and 3-bromonortricyclene (**4**) was formed from norbornylene (**3**).[23] Recently, bicyclo[2.2.2]octene (**5**) was found to react with NBS to give *endo*-8-bromobicyclo[3.2.1]-2-octene (**6**).[24] All of the bromo compounds **2**, **4**, and **6** were produced under conditions identical with those used in the normal allylic bromination with NBS, conditions generally assumed to be radical in nature. In each case, succinimide was formed just as in normal allylic brominations.



1, R = H
2, R = Br



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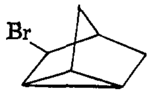

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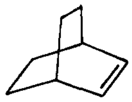

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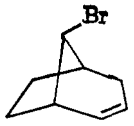

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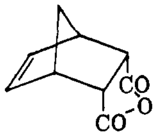
It is difficult to visualize how **2** and **6** could be formed by a radical mechanism involving the succinimidyl radical in a propagation step. Actually, in the formation of both **2** and **6**, the authors in each case suggested that a bromine atom first adds to the double bond of **1** and **5**, respectively, and in the case of **1** the intermediate then loses a hydrogen atom, and in the case of **5** the intermediate radical rearranges and then loses a hydrogen atom by abstraction. These observations are thus consistent with the Goldfinger mechanism. The formation of **4** could be rationalized by either the Bloomfield-Hey (reaction in which succinimidyl radicals react with the alkene to generate the intermediate substrate radical) or the Goldfinger mechanisms. Of course, **2**, **4**, and **6** could arise by ionic mechanisms. It should be noted that abstraction of a bridgehead hydrogen atom of **5** might have been expected, since the bridgehead hydrogen atoms of bicyclo[2.2.2]octane are abstracted by chlorine atoms eight times more readily than the secondary hydrogen atoms.[25] In norbornyl systems bridgehead radicals are known but they have not been produced by abstraction of the bridgehead hydrogen atoms.[26]

In view of the unusual results obtained in the reaction of NBS with bicyclic alkenes containing only bridgehead allylic hydrogen atoms, we decided to investigate the reaction of NBS with bicyclo[2.2.1]-5-heptene-2,3-dicarboxylic anhydride (**7**). The *endo* anhydride group in **7** would be expected to make formation of a nortricyclene-type product such as **8** difficult because of the steric strain that would be introduced in the formation of the semi-*trans* fused anhydride ring of **8**.



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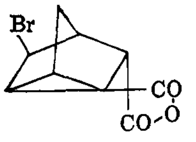

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The reaction of **7** with NBS was carried out in refluxing carbon tetrachloride in the presence of a catalytic amount of benzoyl peroxide. Identical results were obtained in the presence or absence of light, but no reaction occurred in the absence of benzoyl peroxide, and variation of the amount of benzoyl peroxide used had no effect on the yield of products. No succinimide was produced in the reaction, in contrast to that observed in the reactions of **1**, **3**, and **5** with NBS.

When water was added to the carbon tetrachloride reaction solution, after refluxing, there was a vigorous evolution of carbon dioxide arising from hydrolysis of β-bromopropionyl isocyanate (**9**), produced from NBS in the reaction. By distilling the reaction solution prior to the addition of water, the liquid β-bromopropionyl isocyanate was isolated and, when methanol, rather than water, was added to the carbon tetrachloride solution, crystalline methyl β-bromopropionylcarbamate was isolated in 51% yield (based on starting NBS). β-Bromopropionyl isocyanate has been previously reported to be formed in good yield from NBS in the presence of a free-radical initiator, an unreactive alkene, and in an inert solvent.[27] After the addition of water to the carbon tetrachloride solution, a viscous oil separated from the solution and it yielded a crystalline product **10** after extensive washing with ether. The product **10** could be isolated in two different polymorphic forms which showed different infrared spectra as potassium bromide pellets but identical spectra in dioxane solution, and each gave identical products in all chemical reactions. The infrared spectrum of **10** in dioxane showed strong absorption at ν 1746, 1738, and 1710 cm.$^{-1}$, and elemental analysis showed it to possess the empirical formula $C_{13}H_{14}BrNO_6$. Thus the elements of $C_4H_6BrNO_2$ (NBS or some rearrangement product therefrom) had added to **7** and the anhydride grouping was no longer intact. That **10** was a dicarboxylic acid was shown by preparation of the dimethyl ester **11** ($C_{15}H_{18}BrNO_6$) with diazomethane. The n.m.r. spectrum of **11** clearly showed the presence of the two ester methyl groups at δ 3.58 and 3.68. The n.m.r. spectrum also showed the absence of olefinic protons. The dimethyl ester **11** was isolated in 84% yield based on alkene **7** consumed in the reaction with NBS, but 76% of the alkene did not undergo reaction. Treatment of **10** with acetic anhydride gave an anhydride (**12**) which was reconverted

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[21] F. S. Fawcett, *Chem. Rev.*, **47**, 219 (1950).

[22] J. D. Roberts and E. R. Trumbull, *J. Am. Chem. Soc.*, **71**, 1630 (1949).

[23] J. D. Roberts, E. R. Trumbull, W. Bennett, and R. Armstrong, *ibid.*, **72**, 3116 (1950).

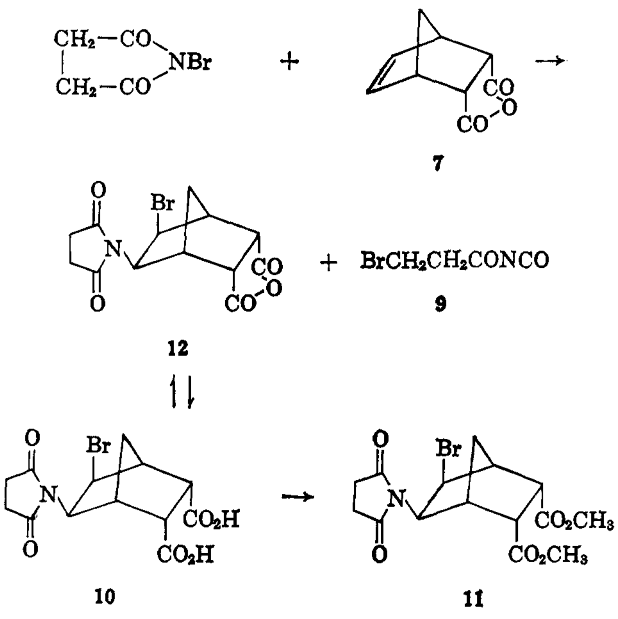
[24] N. A. LeBel, J. E. Huber, and L. H. Zalkow, *ibid.*, **84**, 2226 (1962).

[25] A. F. Bickel, J. Knotnerus, E. C. Kooyman, and G. C. Vegter, *Tetrahedron*, **9**, 230 (1960).

[26] V. Scholkopf, *Angew. Chem.*, **72**, 147 (1960), and references therein.

[27] (a) H. W. Johnson, Jr., and D. E. Bublitz, *J. Am. Chem. Soc.*, **79**, 753 (1957); (b) J. C. Martin and P. D. Bartlett, *ibid.*, **79**, 2533 (1957); (c) H. W. Johnson, Jr., and D. E. Bublitz, *ibid.*, **80**, 3150 (1958).

SCHEME I

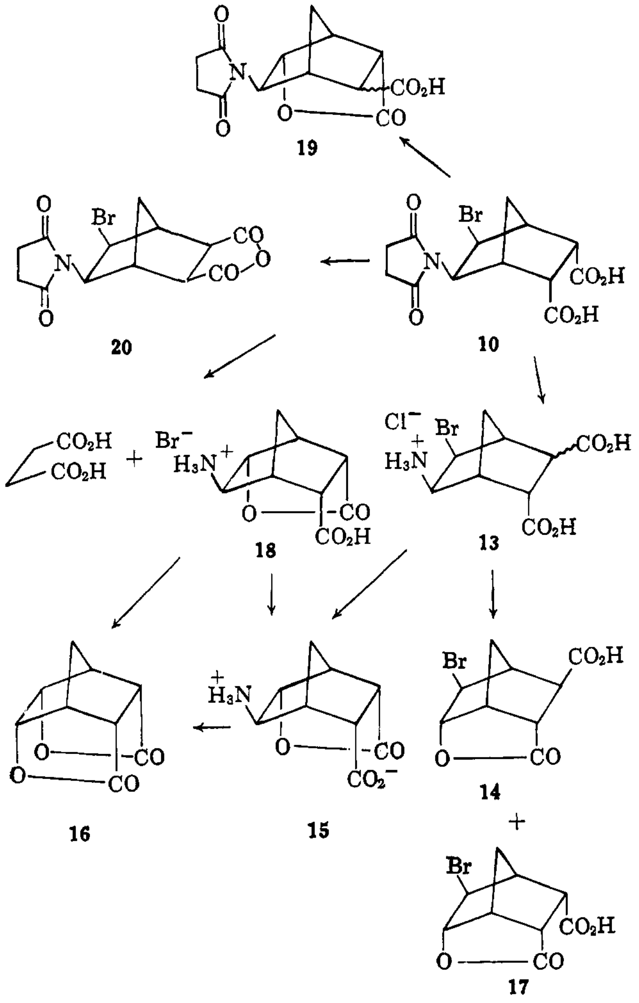


into 10 with water. The anhydride 12 is apparently the primary product in the reaction of NBS with 7, but isolation of the diacid 10 from the original reaction mixture was found easier than isolation of the anhydride 12. (See Scheme I.)

When 10 was refluxed in concentrated hydrochloric acid and the aqueous solution was extracted with ether, succinic acid was obtained. Evaporation of the hydrochloric acid solution gave an amine hydrochloride (13) whose infrared spectrum showed $\nu_{\max}^{\mathrm{KBr}}$ 2700–3000, 1720, 1590, 1507, and 1400 cm.$^{-1}$. When 13 was treated with nitrous acid, the known bromolactone acid 14 was obtained. When 13 was passed through a basic ion-exchange column, a lactone zwitterion (15) was obtained, which, when treated with sodium nitrite, gave the known dilactone 16. These data demonstrated that NBS reacted with 7 without skeletal rearrangement of 7 to give an adduct (12) in which the succinimidyl group and bromine atom had become attached at C-5 and C-6. In addition, the isolation of the known lactones 14 and 16 under the conditions described showed the bromine atom to be in the *exo* (β) configuration in the adduct 12. The isolation of 14 and 16 with carboxyl groups of different stereochemistry at C-3 can be explained as follows. The amine hydrochloride 13 is undoubtedly a mixture of the two isomers differing in stereochemistry at C-3. The isomerization of *cis-endo* carboxyl groups to the *trans* arrangement with concentrated hydrochloric acid in such systems is well known.[28] Thus, when the mixture 13 was treated with nitrous acid, the known lactone 14 fortunately crystallized (18% yield), the isomeric lactone 17 remaining in solution. However, when the amine hydrochloride mixture 13 was passed through a basic ion-exchange column, and the product was treated with nitrous acid, the known dilactone 16 was obtained in 50% yield. Under these conditions the isomer of 13 with an *exo* carboxyl group at C-3 would remain on the basic ion-exchange column.

When an aqueous solution of 10 was heated on the steam bath for 3 days, a quantitative yield of succinic acid was obtained from the ether extract. The remaining aqueous solution containing the lactone amine hydrobromide 18 gave the dilactone 16 on the addition of sodium nitrite, whereas passage of the aqueous solution through a weakly basic ion-exchange resin gave 15 in 86% yield. Thus hydrolysis of the succinimido group and lactonization occurred in the hydrolysis of 10 under neutral conditions. (See Scheme II.)

SCHEME II



The adduct 10 when refluxed in pyridine gave the lactone 19 in which the succinimido grouping was retained. Heating of 10 gave the anhydride 20, isomeric with the previously mentioned anhydride 12, and the same lactone 19 obtained previously as described above. The formation of lactone 19 provides additional evidence for the *exo* configuration of the bromine atom in 10. The stereochemistry of the carboxyl group at C-2 in 19 cannot be unequivocally assigned on the basis of the evidence at hand.

The evidence thus far presented strongly supports the structure depicted for 10 and the stereochemistry indicated at C-2, C-3, and C-5. However, further evidence was sought in order to assign the configuration of the succinimido group at C-6. If the amino group at C-6 in 15 were *endo*, then pyrolysis of this compound would be expected to yield the lactone–lactam 21, since pyrolysis of 22 has been shown to yield 23.[29] Since 15 was obtained by the hydrolysis of 10 with water fol-

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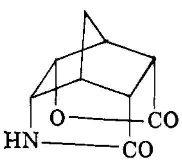
[28] K. Alder and G. Stein, *Ann.*, **504**, 216 (1933).

[29] W. S. Worral, *J. Am. Chem. Soc.*, **82**, 5707 (1960).



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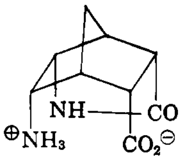

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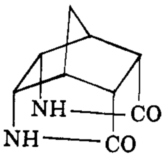

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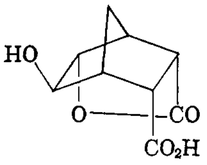
lowed by passage through a weakly basic ion-exchange column, the stereochemistry at C-6 in **15** would be expected to be the same as in **10**. Heating of **15** to >310° gave only unchanged **15**. Additional evidence to support the exo configuration at C-6 was provided by the conversion of **15** to **16** with nitrous acid. If the amino group in **15** had been *endo*, then one would expect to isolate, in addition to **16**, either of the known lactones **24** or **25**. Lactone **24** would result from displacement of the *endo* diazonium group by water, whereas **25** would be expected from the intermediate nonclassical carbonium ion **26**.[30] The nortricyclene derivative **25** has been reported by acid hydrolysis of **27**, presumably *via* intermediate **26**.[30] Failure to detect either **24** or **25**, when **15** was treated with nitrous acid suggests that the amino group in **15** is *exo* and the diazonium group formed upon treatment with nitrous acid is displaced by the *endo* carboxyl group at C-2. The strongest chemical evidence to support the *exo* configuration of the various substituents at C-6 was provided by conversion of **15** to the benzenesulfonamido derivative **28** which was found to differ from the isomeric derivative **29**.[31] Lactone **29**, on heating at reduced pressure, gave **30**, as expected of the *endo* benzenesulfonamido group at C-6.[31]



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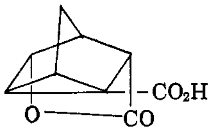

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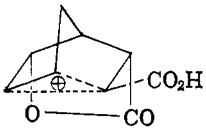

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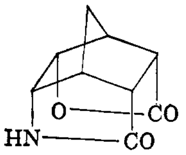

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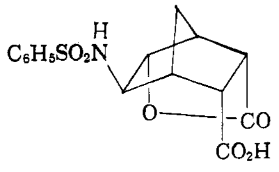
The nuclear magnetic resonance spectra of **15** and **28** also supported the assigned *exo* configuration of the C-6 substituent.[32] It has been shown that a single *exo* substituent such as is present in **15** and **28** produces nonequivalence in the C-7 protons leading to AB type spin-spin splitting with $J = 11$–13 c.p.s., whereas in the absence of *exo* substituents such as in **29** and **30**, the C-7 protons give a sharp singlet signal.[32] The observed C-7 signals were as follows: **15**, δ 2.05, 2.38 ($J = 13$ c.p.s.); **28**, δ 1.84, 2.18 ($J = 12$ c.p.s.); **29**, δ 1.80; and **30**, δ 2.00. In addition, the n.m.r. spectra of **10**, **11**, and **12** showed that the C-5 and C-6 protons were *cis* ($J_{5,6} = 7$ c.p.s.) and, therefore, *endo*, since the bromine atom at C-5 has already been shown to be *exo*.[32]



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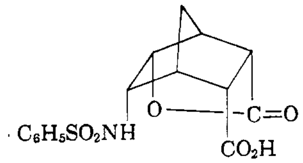

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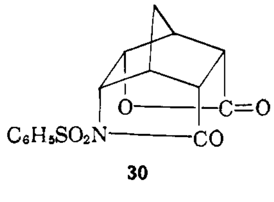

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The observation that NBS does not add to **7** in the absence of benzoyl peroxide, and the failure of variation in peroxide concentration to effect the yield of **10** suggests a radical chain mechanism involving succinimidyl radicals as chain carriers. The *cis-exo* addition of NBS is analogous to the formation of *cis-exo*-5,6-di-bromobicyclo[2.2.1]heptane-*endo-cis*-2,3-dicarboxylic anhydride in the bromination of **7**.[33] By contrast, the isomer of **7** containing the *cis-exo* anhydride grouping gives the *trans* dibromide on bromination.[34]

Since the rearrangement of NBS to β-bromopropionyl isocyanate (**9**) has been reported to require the presence of an alkene,[27] an attempt was made to determine if the adduct **12** was the precursor of the isocyanate. When **12** was subjected to the original NBS–alkene reaction conditions, no isocyanate was formed and no decomposition of the adduct occurred.

Thin layer chromatography of the crude reaction product failed to show the presence of products resulting from the addition of molecular bromine to the alkene as might have been expected if the NBS had been transformed into succinimide and molecular bromine, as proposed in the Goldfinger mechanism. The failure to isolate succinimide likewise supports this observation.

A referee has pointed out that Ziegler also found that N-bromophthalimide added to an appreciable extent to cyclohexene and he has confirmed this. One of the arguments offered by opponents of the Bloomfield–Hey mechanism has been the inability of workers to isolate bisuccinimidyl arising by coupling of succinimidyl radicals. Some supporters of the mechanism have suggested that this was due to the great instability of bisuccinimidyl.[7] Bisuccinimidyl has now been synthesized and found to be surprisingly stable.[35] Since the submission of this manuscript, additional support of the Goldfinger mechanism has appeared.[36,37]

Experimental

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-5 spectrophotometer and n.m.r. spectra were determined with the Varian A-60 spectrometer using tetramethylsilane as an internal standard ($\delta = 0$). Elemental analyses were performed by Midwest Microlabs, Indianapolis, Ind.

The Reaction of N-Bromosuccinimide (NBS) with Bicyclo[2.2.1]-5-heptene-*endo-cis*-2,3-dicarboxylic Anhydride (7).—In a typical experiment N-bromosuccinimide (8.90 g. of Eastman

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[30] L. H. Zalkow and C. D. Kennedy, *J. Org. Chem.*, **28**, 852 (1963).

[31] L. H. Zalkow and C. D. Kennedy, *ibid.*, **28**, 3309 (1963).

[32] L. H. Zalkow and C. D. Kennedy, unpublished results.

[33] J. A. Berson and R. Swidler, *J. Am. Chem. Soc.*, **76**, 4060 (1954).

[34] D. Craig, *ibid.*, **73**, 4889 (1951).

[35] E. Hedaya, R. L. Hinman, and S. Theodoropulos, *ibid.*, **85**, 3052 (1963).

[36] P. S. Skell, D. L. Tuleen, and P. D. Readio, *ibid.*, **85**, 2850 (1963).

[37] C. Walling, A. L. Rieger, and D. D. Tanner, *ibid.*, **85**, 3129 (1963).

reagent grade), **7** (8.20 g.), benzoyl peroxide (0.1 g.), and carbon tetrachloride (35 ml.) were refluxed for 2.5 hr. The initially heterogeneous mixture became homogeneous after 0.5 hr. and became turbid after about 1.0 hr. of refluxing. The light brown reaction solution was cooled after the reflux period and worked up either by the addition of water, by the addition of methanol, or by distillation as described below.

Procedure 1.—Water (20 ml.) was added dropwise with stirring to the cooled reaction solution whereupon there was a vigorous evolution of carbon dioxide, identified by the formation of a precipitate on bubbling the gas through a saturated solution of barium hydroxide. After no further evolution of gas could be detected, the mixture was separated into three layers, an aqueous layer (top), a carbon tetrachloride layer (bottom), and a viscous oily layer (middle) in which, on standing 24 hr., crystalline solid formed. After 48 hr. the aqueous and carbon tetrachloride layers were removed. The remaining viscous oil was extensively extracted (ten portions, 20-ml. each) with ether. The ether-insoluble solid was leached twice with 10-ml. portions of acetone. The adduct diacid **10** (0.58 g.) gave m.p. 225–227°, $\nu_{\max}^{\text{KBr}}$ 1772, 1728, and 1688 cm.$^{-1}$ (adduct "A") (Two polymorphic forms of the adduct **10**, "A" and "B," were obtained either as a mixture or one was obtained separately from the other, unpredictably, under presumably identical conditions as described above. Both "A" and "B" gave the same melting point, and the melting point was not depressed on admixture. They differed only in their infrared spectra as KBr pellets.) or 1750, 1700, and 1662 cm.$^{-1}$ (adduct "B").

The ether and acetone solutions from the above extractions were combined and evaporated on a steam bath to give an oily solid and the above extraction procedures were repeated to yield an additional 0.70 g. of **10**, m.p. 224–227° in a second crop, and 0.33 g., m.p. 223–225° in a third crop. The combined yield of **7** was 1.61 g. Both adducts "A" and "B" gave $\nu_{\max}^{\text{dioxane}}$ 1746, 1738, and 1710 cm.$^{-1}$. Evaporation of the dioxane solutions of adducts "A" and "B" both yielded adduct "B." An analytical sample of adduct "B," m.p. 227–228°, was prepared by recrystallization from a 1:1 ethanol–water solution. The infrared spectrum of adduct "B" did not change on recrystallization.

Anal. Calcd. for $C_{13}H_{14}BrNO_6$: C, 43.31; H, 3.89; Br, 22.23; N, 3.89. Found: C, 43.49; H, 3.97; Br, 22.00; N, 4.10.

The same dimethyl ester **11** was obtained from adducts "A" and "B" by treatment with an excess of ethereal diazomethane. The analytical sample, m.p. 140°, was prepared by recrystallization of the diester from 95% ethanol and drying at 100° and 1 mm. pressure for 5 hr. and had $\nu_{\max}^{\text{KBr}}$ 1775 (weak), 1734, and 1707 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{18}BrNO_6$: C, 46.39; H, 4.68. Found: C, 46.57; H, 4.67.

Procedure 2.—Methanol (20 ml.) was added slowly, with stirring, to the cooled carbon tetrachloride reaction solution. Methyl β-bromopropionylcarbamate (4.75 g., m.p. 133–135°) crystallized on cooling in an ice bath. On partial evaporation of the filtrate, additional carbamate crystallized (0.77 g., m.p. 134–136°). Recrystallization of the carbamate from methanol gave m.p. 138–138.5° (lit.[27] 138–139°); $\nu_{\max}^{\text{KBr}}$ 3250, 3130, 1795, 1755, and 1693 cm.$^{-1}$. An authentic sample prepared as previously described[27a] gave m.p. 136–137° and an identical infrared spectrum.

The filtrate from above was evaporated to give an oil which was hydrolyzed by stirring with a water–acetone solution. Evaporation gave a viscous oil which was treated with 6 g. of diazomethane in ether solution (approx. 100 ml.). One-eighth of this dried (magnesium sulfate) ether solution was allowed to stand at 0° for 2 months. During this time a fraction of dimethyl ester **11** crystallized (0.140 g.), m.p. 140°; $\nu_{\max}^{\text{KBr}}$ 1775 (weak), 1734, and 1707 cm.$^{-1}$. The mother liquor was concentrated *in vacuo* at room temperature to a small volume (approx. 2 ml.) and chromatographed on Merck acid-washed alumina (174 g.) using chloroform as the eluent. The dimethyl ester of bicyclo[2.2.1]-5-heptene-*endo*-*cis*-2,3-dicarboxylic acid (0.995 g.; $\nu_{\max}^{\text{film}}$ 1737, 1438, 1367, and 1345 cm.$^{-1}$, identical with the infrared spectrum of an authentic sample prepared by a previously described[38] procedure) was eluted with 400 ml. of chloroform. This diester showed the same single spot as authentic material on thin layer chromatography using ether (R_f 0.8) or ethanol (R_f 0.6) as a solvent. All thin layer chromatograms were run on silica gel, and iodine vapor was used to develop the compounds.

A second fraction (0.378 g.) eluted from the above column chromatograph by an additional 125 ml. of chloroform showed on thin layer chromatography with ether as eluent, one major spot (R_f 0.35) and two minor spots (R_f 0.45). These two spots could be resolved only by allowing the solvent front to move 20 cm. rather than the usual 10 cm. Quantitative thin layer chromatography showed that 92% of this fraction, based on recovered material from the preparative thin layer chromatograph, was the adduct diester **11** (0.348 g.). The infrared spectrum and R_f of the adduct diester **11** from thin layer chromatography agreed identically with those of adduct diester **11** prepared as described above. Further elution of the above column chromatograph with chloroform yielded no additional material.

The quantities of materials obtained from the column chromatograph (multiplied by a factor of eight) represent a total of 7.92 g. (38.0 mmoles) of the diester of **7** and 3.9 g. (10.1 mmoles) of the adduct diester **11** recovered by the above sequences from 50 mmoles each of NBS and alkene **7**.

Procedure 3.—The carbon tetrachloride was removed from the cooled reaction solution *in vacuo* (38 mm.) at room temperature. The residue was filtered to remove the precipitated solid and the filtrate was distilled at 25 mm. to yield β-bromopropionyl isocyanate (**9**, 1.25 g., b.p. approx. 69°), identical in infrared spectrum with an authentic sample of the isocyanate prepared as previously described.[27c] The residue remaining after distillation of the isocyanate was extracted with four portions (50-ml. each) of ether, then dissolved in acetone (100 ml.) containing a small amount of concentrated sulfuric acid (2 ml.), and left open to the atmosphere for 6 days during which time the adduct diacid **10** crystallized (0.83 g.), m.p. 226–227°.

Reaction of NBS with Bicyclo[2.2.1]-5-heptene-*endo-cis*-2,3-dicarboxylic Anhydride (7) in the Absence of Radical Initiators. A.—N-Bromosuccinimide (17.8 g., 100 mmoles), bicyclic alkene **7** (16.4 g., 100 mmoles, Fisher reagent grade), and carbon tetrachloride (65 ml.) were refluxed for 3 hr. The undissolved solid was allowed to settle and the clear liquid was decanted from the hot solution. The solid which was insoluble in hot carbon tetrachloride was identified as NBS, 13.2 g. (74.5 mmoles), m.p. 170–173° (melting point of starting NBS 171–173°, mixture melting point undepressed; infrared spectra were identical). The combined hot carbon tetrachloride extracts on evaporation to dryness gave the starting alkene **7**, 14.4 g. (88 mmoles), m.p. 165–167° (melting point of starting alkene 170°, admixture with starting alkene gave m.p. 165–169°).

B.—N-Bromosuccinimide (17.8 g., 100 mmoles), bicyclic alkene **7** (16.4 g., 100 mmoles), and carbon tetrachloride (65 ml.) were refluxed for 3 hr. The reaction mixture was allowed to cool and the unchanged starting material was removed by filtration. Water (50 ml.) was added to the filtrate with no sign of reaction, and no reaction products could be isolated. The above carbon tetrachloride remained clear, except for undissolved starting material, for the duration of the reaction period as contrasted to the marked brown color attained when radical initiator was present. A duplicate experiment of the above (no radical initiator present) was refluxed for 12 hr. with no color change

Attempted Elimination of the Bromo and Succinimido Groups from 12 as β-Bromopropionyl Isocyanate.—A mixture of the NBS adduct **12** (2.0 g., m.p. 197–197.5°), benzoyl peroxide (0.05 g.), and 3.7 ml. of carbon tetrachloride was refluxed for 24 hr. The reaction mixture remained heterogeneous during the reflux period, after which the hot mixture was filtered. The starting unchanged anhydride was recovered in quantitative yield. When water was added to the hot filtrate there was no visible evolution of gas.

Attempted Reaction of Bicyclo[2.2.1]-5-heptene-*endo-cis*-2,3-dicarboxylic Anhydride 7 with Carbon Tetrachloride under Free-Radical Conditions.—A mixture of the bicyclic alkene **7** (4.1 g.), benzoyl peroxide (0.262 g.), and carbon tetrachloride (30.8 ml.) was heated at reflux for 18 hr. The mixture became homogeneous after only a few minutes of refluxing, and at the end of the 18-hr. reflux period a viscous brown oil precipitated. The mixture was cooled, 15 ml. of water was added along with enough acetone to keep the mixture homogeneous, and the solution was stirred, open to the atmosphere, for 6 days during which time all of the solvent evaporated. The resulting product was treated with an excess of ethereal diazomethane and the ether solution was dried over anhydrous sodium sulfate, then evap-

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[38] K. Alder and W. Roth, *Ber.*, **87**, 161 (1954).

orated on a steam bath to yield an oil. A sample of this oil on thin layer chromatography, using ether as the eluent, showed only the spot (R_f 0.8) for dimethyl bicyclo[2.2.1]-5-heptene-*endo-cis*-2,3-dicarboxylate.

A mixture of the alkene **7** (4.1 g.), benzoyl peroxide (0.050 g.), and 17 ml. of carbon tetrachloride was heated at reflux for 3 hr. This solution was cooled, hydrolyzed, and treated with ethereal diazomethane as above. The ether solution was dried over anhydrous sodium sulfate and evaporated to yield an oil which gave only one spot (R_f 0.8) when chromatographed as above.

***exo*-5-Bromo-*exo*-6-succinimidobicyclo[2.2.1]heptane-*endo-cis*-2,3-dicarboxylic Anhydride (12).**—The same anhydride **12** was obtained from both polymorphic forms "A" and "B" by the following procedure. The diacid **10** (4.00 g., m.p. 225–226°) and acetic anhydride (40 ml.) were heated to reflux, then the mixture was distilled at 45 mm. (approximately 10 ml. remained undistilled). The undistilled residue was cooled and 100 ml. of carbon tetrachloride was added. The solution was decanted and cooled in an ice bath. White needle-like crystals of the anhydride **12** formed in the decanted solution. After air drying, the anhydride (2.23 g.) gave m.p. 197–197.5°; $\nu_{\max}^{\text{KBr}}$ 1850, 1785, and 1707 cm.$^{-1}$. Additional recrystallization from acetic anhydride and carbon tetrachloride did not raise the melting point.

The anhydride **12** (0.25 g.) was hydrolyzed back to the diacid **10** by heating on a steam bath in a mixture of carbon tetrachloride (30 ml.), water (30 ml.), and acetone (5 ml.) until a volume of approximately 30 ml. remained. On cooling, white crystals of the diacid **10** formed which, after air drying, gave m.p. 224–226°. The infrared spectrum of this product indicated that it was a mixture of the two polymorphic forms "A" and "B." Admixture of the diacid obtained by hydrolysis of the anhydride with either pure polymorph "A" or "B" did not depress its melting point.

Concentrated Hydrochloric Acid Hydrolysis of *exo*-5-Bromo-*exo*-6-succinimidobicyclo[2.2.1]heptane-*endo-cis*-2,3-dicarboxylic Acid (10).—A mixture of the adduct diacid **10** (5.000 g., m.p. 225–227°) and concentrated hydrochloric acid (150 ml.) was refluxed for 17.5 hr.; this solution was then continuously extracted with ether for 24 hr. Evaporation of the ether solution yielded succinic acid (1.0 g., m.p. 188.5°, identical in melting point and infrared spectrum with an authentic sample).

Evaporation of the aqueous solution on a rotary evaporator gave **13** (3.91 g.); $\nu_{\max}^{\text{KBr}}$ 2700–3000, 1720, 1590, 1507, and 1400 cm.$^{-1}$. The salt **13** (1.00 g.) dissolved in water (100 ml.) was passed through Amberlite IR-4B (45-g. wet wt. in a column 3 cm. in diameter) in a manner analogous to that described by Meyers and Miller.[39] The column was eluted with 1.0 l. of doubly distilled water. Evaporation of the effluent on a rotary evaporator gave the lactone zwitterion **15** (0.305 g.) which decomposed above 310° but sublimed unchanged at 300° and 38-mm. pressure; $\nu_{\max}^{\text{KBr}}$ 3550, 2700–3000, 1775, 1590, and 1407 cm.$^{-1}$. The further transformation of **15** to the known dilactone **16** is described in the next section.

When sodium nitrite (0.5 g.) was slowly added to **13** (0.500 g.) dissolved in 20% hydrochloric acid (10 ml.) and the solution was heated on a steam bath for 20 min. and then allowed to stand at room temperature, the known bromolactone acid **14** crystallized (0.072 g., m.p. 183.5–184.5°, lit.[40] m.p. 186°) from solution. Admixture with an authentic sample prepared as previously reported[28] did not depress the melting point; $\nu_{\max}^{\text{KBr}}$ 1750 and 1735 cm.$^{-1}$ after drying 8 hr. at 144° and 1-mm. pressure.

Anal. Calcd. for $C_9H_9BrO_4$: C, 41.40; H, 3.47; Br, 30.61. Found: C, 41.22; H, 3.49; Br, 31.50.

Water Hydrolysis of *exo*-5-Bromo-*exo*-6-succinimidobicyclo[2.2.1]heptane-*endo-cis*-2,3-dicarboxylic Acid (10).—Diacid **10** (1.00 g., m.p. 225–227°) in 50 ml. of distilled water was heated over a steam bath for 3 days. The aqueous solution was then concentrated to a volume of 10 ml. and continuously extracted with ether for 48 hr. Evaporation of the ether extract yielded succinic acid (0.330 g., m.p. 186°). The extracted aqueous hydrolysis solution, which gave a positive silver nitrate test for bromide ion, was passed through Amberlite IR-4B(OH) as previously described[39] (25-g. wet wt. in a column 1.5 cm. in diameter). The column was eluted with 1.0 l. of water, and the effluent was evaporated on a rotary evaporator to yield the lactone zwitterion **15** (0.455 g.). The lactone zwitterion was recrystallized by dissolving it in a minimum amount of hot water and adding four times that volume of an equal mixture of ethanol and ether; the decomposition was ~310°.

When sodium nitrite (0.670 g.) was added to the ether-extracted aqueous hydrolysis solution or to the lactone zwitterion **15** (0.455 g.) dissolved in 10 ml. of 5% hydrochloric acid, the dilactone **16** was formed and crystallized from solution (0.25 g.), m.p. 268°, $\nu_{\max}^{\text{KBr}}$ 1795 and 1770 cm.$^{-1}$. An authentic sample prepared as previously described[41] gave an identical infrared spectrum.

Pyrolysis of *exo*-5-Bromo-*exo*-6-succinimidobicyclo[2.2.1]heptane-*endo-cis*-2,3-dicarboxylic Acid (10).—The diacid **10** (1.0 g., m.p. 225–227°) was heated at 230° for 2 hr. in an open beaker. The melt resolidified after 5 to 10 min. at 230°. The anhydride **20** sublimed on heating this solid at 235° and 35 mm. After 5 hr. 0.095 g. of the anhydride **20** (m.p. 110–111°; $\nu_{\max}^{\text{KBr}}$ 1862, 1780, and 1705 cm.$^{-1}$) was obtained. Resublimation did not raise the melting point.

Anal. Calcd. for $C_{13}H_{12}BrNO_5$: C, 45.63; H, 3.54. Found: C, 45.13; H, 3.93.

The anhydride **20** gave a positive Beilstein test, a neutralization equivalent of 176 when titrated with sodium hydroxide (phenolphthalein end point), and a neutralization equivalent of 334 when titrated with sodium ethoxide in absolute ethanol (phenolphthalein end point); the calculated molecular weight was 342.17.

After sublimation of the anhydride **20** appeared complete, the bath temperature was raised to 280° (35 mm.) and the lactone **19** sublimed (0.070 g.); approx. m.p. 338° with decomposition; $\nu_{\max}^{\text{KBr}}$ 1775, 1728, and 1670 cm.$^{-1}$; this lactone gave a negative Beilstein test.

Anal. Calcd. for $C_{13}H_{13}NO_6$: C, 55.91; H, 4.69. Found C, 56.34; H, 4.96.

Preparation of Lactone 19 from 10 under Basic Conditions.—A solution of diacid **10** (1.00 g., m.p. 225–227°) and dry pyridine (10 ml.) was refluxed for 2 hr. The pyridine was then evaporated on a rotary evaporator and the residual oil was dissolved in 5 ml. of water. The aqueous solution was filtered and acidified with 5 ml. of concentrated hydrochloric acid. On standing at room temperature for 6 hr., light amber-colored crystals of the hydrate of lactone **19** formed (0.475 g.); m.p. 265–270° (by raising the temp. 15°/min.); $\nu_{\max}^{\text{KBr}}$ 1767, 1712, and 1697 cm.$^{-1}$. Recrystallization from acetone–water (1:1) did not raise the melting point nor change the color of the crystals. When the lactone hydrate was heated slowly, water of hydration was given off starting at about 252° and, after melting at about 252–257°, resolidification occurred at about 275°. Further heating resulted in sublimation, and the sublimate was identical with **19** obtained as described above.

The same lactone hydrate was obtained but in lower yield by refluxing a solution of diacid **10** (1.55 g.) in aqueous 5% sodium carbonate (30 ml.) for 3 hr. The product was isolated after acidification with excess concentrated hydrochloric acid, continuous extraction of the aqueous solution with ether for 10 days, and evaporation of the ether.

Benzenesulfonation of *endo*-5-Hydroxy-*exo*-6-aminobicyclo[2.2.1]heptane-*endo-cis*-2,3-dicarboxylic Acid γ-Lactone (15).—The lactone zwitterion **15** (0.204 g. prepared as described above) and benzenesulfonyl chloride (0.183 g.) were stirred in 5% aqueous sodium hydroxide (20 ml.) for 12 hr. at room temperature. The solution was then acidified with concentrated hydrochloric acid and extracted with ether. After drying the ether solution over anhydrous sodium sulfate and evaporation to approximately 5 ml., the benzenesulfonamide **28** crystallized (0.050 g.), m.p. 188–190°. Recrystallization of an analytical sample from ether gave m.p. 194.5–195.5°; $\nu_{\max}^{\text{KBr}}$ 3240, 1780, and 1703 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{15}NO_6S$: C, 53.40; H, 4.48; N, 4.15. Found: C, 53.52; H, 4.49; N, 3.95.

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(39) C. Y. Meyers and L. E. Miller, *Org. Syn.*, **32**, 13 (1952).

(40) K. Alder and G. Stein, *Ann.*, **514**, 1 (1934).

(41) A. Winston and P. Wilder, Jr., *J. Am. Chem. Soc.*, **76**, 3045 (1954).