and showed no residual amide in the infrared. It was crystallized from ether–Skellysolve B to give 0.82 g. of XXII isomer B, m.p. 101–102.5°, unchanged on further recrystallization. Ultraviolet spectrum showed λ_{max} 227 mμ (ϵ 35,400); 274 (6950); 279 (7050); f 289 (5000). Infrared spectrum showed 3160, 3100, 3050 (NH); 1623, 1603, 1585, 1510 (C=C/NH def.) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{18}N_2$: C, 78.46; H, 8.47; N, 13.07. Found: C, 78.52; H, 8.69; N, 12.87.

Copper-Catalyzed Reactions of Benzoyl Peroxide with Norbornadiene Derivatives[1,2]

HIROSHI TANIDA AND TERUJI TSUJI

Shionogi Research Laboratory, Shionogi and Company, Ltd., Fukushima-ku, Osaka, Japan

Received October 28, 1963

The copper-catalyzed reactions of benzoyl peroxide with norbornadiene or benzonorbornadiene derivatives have been shown to give the stereospecific 7-benzoyloxy derivatives. It has proved to be a much improved method for use in syntheses than others reported hitherto. A rational mechanism involves addition of PhCOO· to the olefinic double bond, oxidation of the adduct radical into the carbonium ion intermediate, the Wagner–Meerwein rearrangement, and proton loss to form a double bond. In addition, bis(*p*-chlorobenzoyl) peroxide has proved to give the best yield of the desired esters.

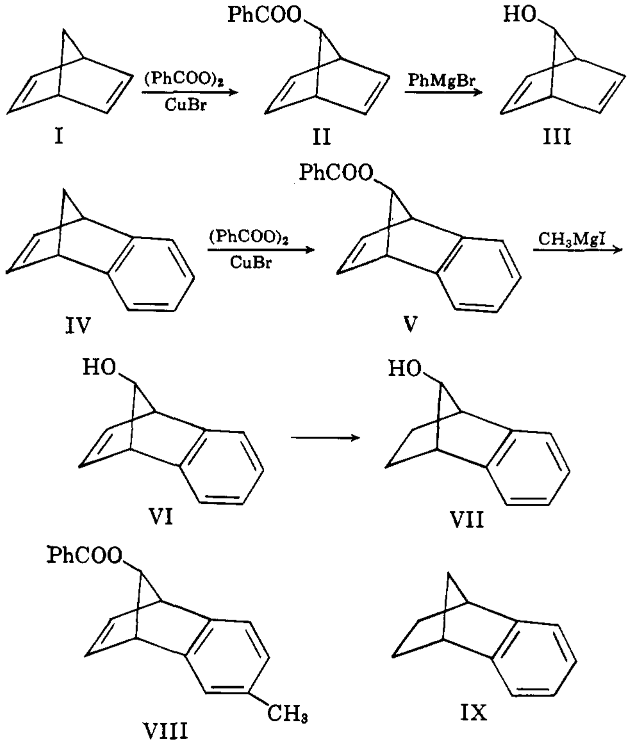
The chemistry of 7-substituted bicyclo[2.2.1]heptanes has been of considerable interest in recent years, particularly in connection with the behavior in solvolytic displacement reactions. Aside from the saturated parent compounds many unsaturated and aromatic variants have been investigated.[3] Until very recently, however, the preparations of these compounds required a long and arduous route. The formation of 7-*t*-butoxynorbornadiene by the reaction of *t*-butyl perbenzoate and norbornadiene found by Story[4] has provided a facile path to this series of compounds. However, a weak point in this reaction may be that one can not control the stereochemistry of the 7-alcohol or other derivatives which are obtained from the replacement of *t*-butyloxy group *via* 7-norbornadienyl cation.[4]

In connection with another investigation,[5] it became necessary to prepare these kinds of alcohols which had a desired stereochemistry. In a previous communication,[6] we reported that the copper-catalyzed reaction of benzoyl peroxide with norbornadiene derivatives had proved to be a much improved method for use in syntheses and also satisfactory for the above requirement. This paper deals with further improvements of our method and with detailed investigations of the reaction mechanism.

Results and Discussion

The reaction of norbornadiene (I) with benzoyl peroxide in the presence of cuprous bromide gave a 35% yield of 7-benzoyloxynorbornadiene (II) from the peroxide as the sole substitution product. The hydrolysis of II with phenylmagnesium bromide[7] yielded 7-norbornadienol (III) almost quantitatively, whose structure was identified by independent synthesis.[4] In order to elucidate the stereochemistry of this reaction, the same procedure was applied for benzonorbornadiene (IV), which is readily obtainable by the cycloaddition of benzyne with cyclopentadiene.[8] *anti*-7-Benzoyloxybenzonorbornadiene (V) was obtained in about 40% yield. The structure of V was established by hydrolysis with methylmagnesium iodide to *anti*-7-benzonorbornadienol (VI), then catalytic reduction to *anti*-7-benzonorborneol (VII), which was confirmed by independent synthesis.[3b] The *syn*-benzoyloxy-substituted product has not been obtained under a variety of reaction conditions. Applications of the above reaction to some benzonorbornadienes having substituents on the benzene ring were also successful,

CHART I



---

[1] Part IV of a series on bicyclic systems; Part III, *Bull. Chem Soc Japan*, **37**, 40 (1964).

[2] Presented, in part, at the 16th Annual Meeting of the Chemical Society of Japan, Tokyo, March, 1963.

[3] (a) S. Winstein and C. Ordronneau, *J. Am. Chem. Soc.*, **82**, 2084 (1960), and references therein; (b) P. D. Bartlett and W. P. Giddings, *ibid.*, **82**, 1240 (1960); (c) E. E. van Tamelen and C. I. Judd, *ibid.*, **80**, 6305 (1958).

[4] P. R. Story, *ibid.*, **82**, 2085 (1960); P. R. Story, *J. Org. Chem.*, **26**, 287 (1961).

[5] H. Tanida, *J. Am. Chem. Soc.*, **85**, 1703 (1963).

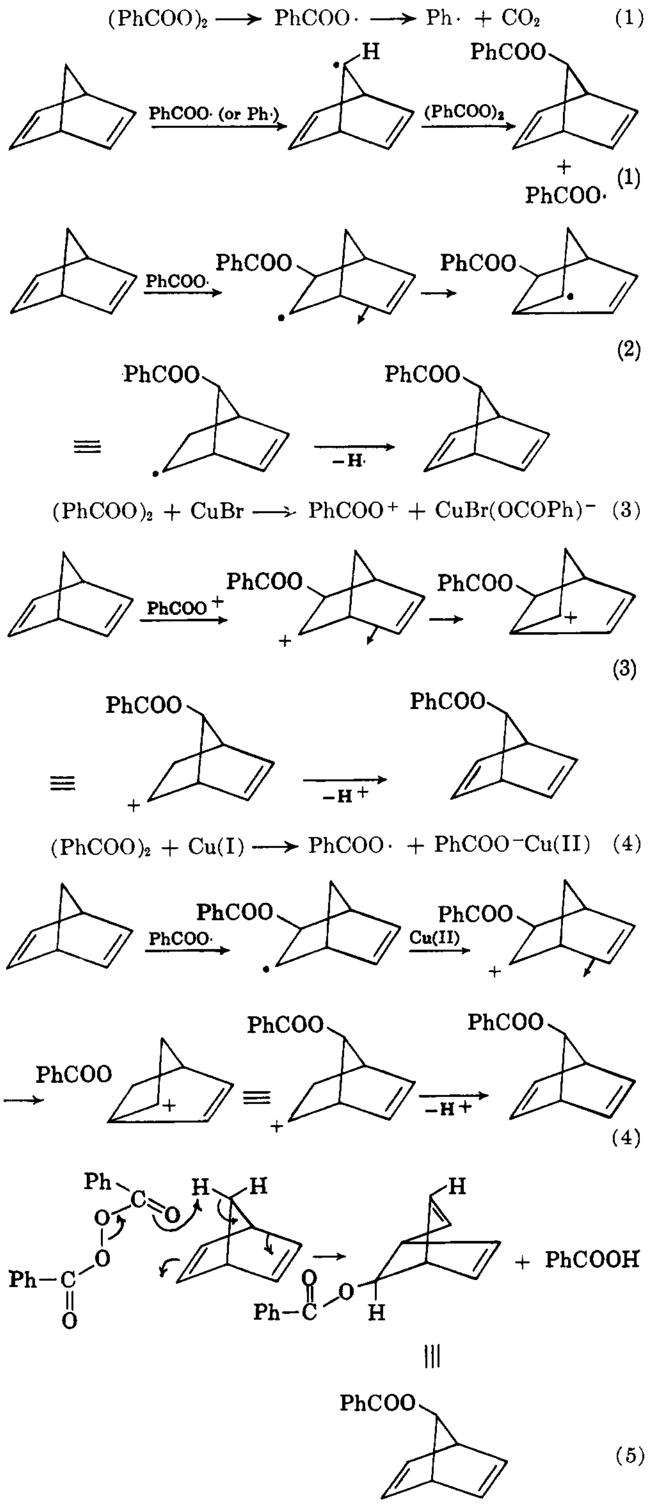
[6] H. Tanida and T. Tsuji, *Chem. Ind.* (London), 211 (1963).

[7] Phenylmagnesium bromide was better than methylmagnesium iodide previously used (refer to ref. 6), because III was more easily distilled, leaving trityl alcohol.

[8] G. Wittig and E. Knauss, *Ber.*, **91**, 895 (1958).

giving approximately same yields.[5] Even in the case of 4′-methylbenzonorbornadiene,[9] the product isolated was *anti*-7-benzoyloxy-4′-methylbenzonorbornadiene (VIII) without any attack of the benzoxy radical on the 4′-methyl group which was located in the benzyl position. None of the desired product was obtained in the case of benzonorbornene (IX), which suggested that the presence of an olefinic double bond was necessary for this reaction. (See Chart I.)

CHART II


$$(PhCOO)_2 \longrightarrow PhCOO\cdot \longrightarrow Ph\cdot + CO_2 \quad (1)$$
$$(PhCOO)_2 + CuBr \longrightarrow PhCOO^+ + CuBr(OCOPh)^- \quad (3)$$
$$(PhCOO)_2 + Cu(I) \longrightarrow PhCOO\cdot + PhCOO^-Cu(II) \quad (4)$$

On the basis of these results, we considered that the mechanism of this reaction would be one of the following five alternatives, which may be pictured and illustrated as shown in Chart II.

(1) A hydrogen abstraction from the homoconjugated bridge methylene (C-7) in the initial step of the reaction by the benzoyloxy or phenyl radical, which was formed by the decomposition of benzoyl peroxide. If this mechanism operates, the Wagner–Meerwein rearrangement will not occur.

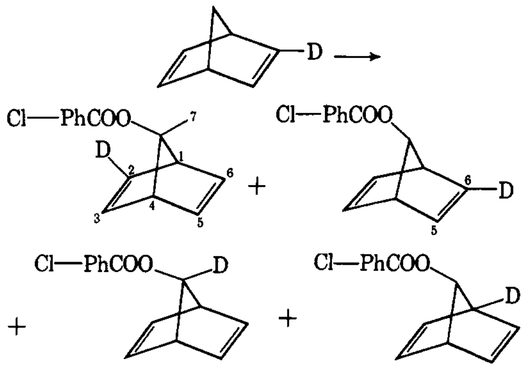
(2) An all-radical mechanism, which would involve the addition of a benzoyloxy radical to the double bond, followed by a radical type of Wagner–Meerwein rearrangement, and then elimination of a hydrogen radical.

(3) An all-ionic mechanism, which would be initiated by the addition of a benzoyloxy cation formed by a copper salt-catalyzed ionic decomposition of benzoyl peroxide,[10] followed by the Wagner–Meerwein rearrangement, and proton loss to form a double bond.

(4) A mechanism, which, initially radical and becoming ionic in mid-course, starts as the addition of a benzoyloxy radical like mechanism 2, but involves the change of the resulting radical into a carbonium ion intermediate by the oxidative action of copper ions, followed by the Wagner–Meerwein rearrangement, and finally proton loss to form a double bond. It is substantially a modification of the general olefin–benzoyl peroxide mechanism proposed by Kochi.[11]

(5) A concerted cyclic mechanism, which might be attractive, but does not appear to assign any function to the cuprous bromide. Perhaps cuprous bromide may coordinate loosely with the olefinic bond and with the peroxide and thus may serve to bring the reagents together.

Deuterium-Labeling Experiment.—Occurrence of a rearrangement in the reaction path was evidenced by deuterium-labeling experiments carried out by essentially the same methods as Story used in the case of the *t*-butyl perbenzoate reaction.[12] 2-Deuterionorbornadiene was prepared by the method of Streitweiser.[13] Analysis by n.m.r. spectra showed that 25.0% of the olefinic hydrogens were replaced by deuterium. The deuterated norbornadiene was treated with bis(*p*-chlorobenzoyl) peroxide, which gave the product in the best yield as mentioned below, in the presence of



---

[9] For the preparation of this compound refer to H. Tanida, R. Muneyuki, and T. Tsuji, *Bull. Chem. Soc. Japan*, **37**, 40 (1964).

[10] Ionic mechanisms involving peroxide are well-known, for example, in the 9-decalyl perbenzoate solvolysis (E. S. Gould, "Mechanism and Structure in Organic Chemistry" Henry Holt and Co., New York, N. Y., 1959, p. 633).

[11] J. K. Kochi, *J. Am. Chem. Soc.*, **84**, 1572 (1962).

[12] P. R. Story, *Tetrahedron Letters*, **No. 9**, 401 (1962).

[13] A. Streitweiser and R. A. Caldwell, *J. Org. Chem.*, **27**, 3360 (1962).

cuprous bromide to yield deuterated 7-*p*-chlorobenzoyloxynorbornadiene which was examined by n.m.r. Careful investigation of the peak areas and comparison with an authentic undeuterated sample showed deuterium at all skeletal positions in an approximately statistical distribution as shown in Table I. These data and the formation of the stereospecific product from benzonorbornadiene (IV) will rule out mechanism 1.

TABLE I

DISTRIBUTION OF THE DEUTERIUM IN 7-*p*-CHLOROBENZOYLOXYNORBORNADIENE PREPARED FROM 2-DEUTERIONORBORNADIENE

Position of hydrogen	Distribution of D	Calcd. value[a]
C-2 and C-3	0.32	0.25
C-5 and C-6	0.20	0.25
C-7	0.23	0.25
C-1 and C-4	0.32	0.25

[a] Calculated on the assumption that the Wagner–Meerwein rearrangement would occur.

TABLE II

SUBSTITUENT EFFECTS

Substituent[a]	Reaction time required, hr.	Products, %[b]				Ratio	
		XI	II	XII	XIII	XI:II	XII:XIII
CN	11.5	12.8	13.0	21.3	23.7	0.98	0.90
Cl	9	26.5	24.6	24.3	31.0	1.08	0.78
H	9		25.4		62.8		
MeO	8	17.3	19.9	34.1	30.9	0.87	1.10

[a] In the case of *p*-NO_2, a very low yield was obtained with a large amount of tarry products. [b] Calculated from the peroxide used.

TABLE III

EFFECTS OF COPPER ION AND SOLVENTS

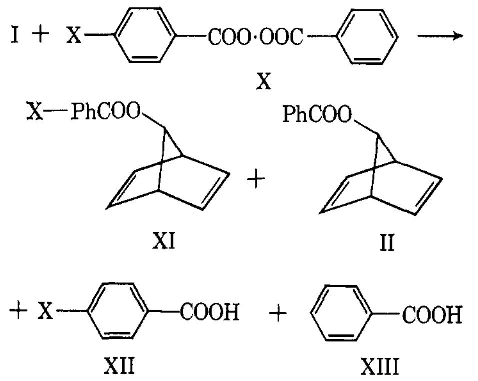
(with 7.11 g. of IV and 3.03 g. of benzoyl peroxide)

Runs	CuBr, mg.	Solvents	Temp., °C.	Time, hr.	Ph-COOH, %	V, %[a]	High mol. products, g.
1	0	Benzene	Reflux	25	22.3	0	
2	5	Benzene	Reflux	6.33	78.2	29.7	2.75
3	10	Benzene	Reflux	5.33	87.3	37.7	1.89
4	25	Benzene	Reflux	5.66	92.4	48.0	1.78
5	25	Chlorobenzene	100°	4.0	84.6	44.8	2.20
6	40	Chlorobenzene	110°	4.0	84.0	47.9	1.85
7	25	CH_3CN	Reflux	11.0	62.8	*b*	2.61
8	25	CH_3COOH (1) Benzene (3)	Reflux	5.0		*c*	2.83

[a] Yields of crude V from the peroxide. [b] Vapor phase chromatography showed a mixture of two products. [c] Besides the 7-benzoyloxy derivative, other kinds of compounds having carbonyl were found by infrared.

The possibility that all paths are radical would be rejected by the following considerations. Berson and his co-workers[14] reported that the thermal decomposition of 2-azobornane at temperatures above 250° gave a mixture of hydrocarbons, among which is 2,3,3-trimethylnorbornane, resulting from a free-radical Wagner–Meerwein rearrangement. However, the yield of the rearranged product in his experiments was lower than 2%, under a variety of reaction conditions, and his conditions were very drastic. To the best of our knowledge, there is no other example of a free-radical Wagner–Meerwein rearrangement reported in the literature. Thus we can reasonably assume that such a high yield of the substitution product as ours would not be obtained under milder conditions from a reaction involving a radical rearrangement.

Reactions with Substituted Benzoyl Peroxides.—In order to investigate whether the decomposition of benzoyl peroxide is heterolytic or homolytic, some experiments were carried out using *p*-monosubstituted benzoyl peroxide (X). As shown in Table II, the product ratio of *p*-substituted and unsubstituted benzoyloxynorbornadienes and of *p*-substituted and unsubstituted benzoic acid (XI : II and XII : XIII in Table II) was approximately unity within experimental errors, although their total yields were dependent upon the kind of benzoyl peroxides used. The heterolytic decomposition of benzoyl peroxide would not be preferred owing to the lack of substituent effects observed here. Thus mechanism 3 would be eliminated. In addition, the variation of total yields (XI + II) of the esters suggests the usefulness of *p*-substituted benzoyl peroxides in this reaction.



Effects of the amounts of cuprous bromide added and of the solvents were investigated in order to decide whether or not a concerted cyclic mechanism operated. As clearly shown in Table III, increasing the amount of the added copper salt increased the yield. None of the desired product was obtained in the absence of copper salt. Employment of such a nucleophilic solvent as acetic acid or acetonitrile gave some by-products, indicating solvolysis participation in a kind of ionic

---

(14) J. A. Berson, C. J. Olsen, and J. S. Walia, *J. Am. Chem. Soc.*, **84**, 3337 (1962).

intermediate in this reaction. The important role of copper catalyst would not be explained by the idea of a cyclic mechanism.

Thus, all our observations, indicating the homolytic cleavage of benzoyl peroxide, the radical addition of the olefinic double bond, the significant role of copper ion, and the evidence of a carbonium ion Wagner–Meerwein rearrangement, are most satisfactorily interpreted by mechanism 4.

Finally, we wish to state that the use of bis(*p*-chlorobenzoyl) peroxide gives the best yield of the desired benzoyl esters, as expected from the above-described experiments of substituted benzoyl peroxides.

Experimental[15]

7-Benzoyloxynorbornadiene (II).—To a stirred mixture of 101 g. (1.10 moles) of norbornadiene (I) and 1.6 g. of freshly prepared cuprous bromide in 500 ml. of benzene, there was added, in a nitrogen atmosphere, a solution of 203 g. (0.84 mole) of benzoyl peroxide in 600 ml. of benzene over a period of 2 hr. at 40°. After the addition was completed, the reaction mixture was heated gradually to boiling and then refluxed for 3 days. Qualitative analysis by potassium iodide–starch paper indicated that no benzoyl peroxide remained after this period. During the course of the reaction, the color of the solution changed gradually from blue to green. After cooling to room temperature, the reaction mixture was extracted with 10% aqueous sodium carbonate to remove 70 g. of benzoic acid, washed with water, and dried over anhydrous sodium sulfate. Removal of the solvent left 185 g. of an oily residue. Vacuum distillation of this residue gave 78.0 g. of crude II, b.p. 100–102° (0.6 mm.), which was further purified by column chromatography on 1 kg. of Merck standard alumina using hexane to give 64.5 g. (36.2% from the peroxide) of pure II as colorless prisms, m.p. 53–54°.

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.22; H, 5.78.

7-Norbornadienol (III).—To a solution of phenylmagnesium bromide in ether, which was prepared from 76.0 g. of bromobenzene and 11.7 g. of magnesium turnings in 300 ml. of anhydrous ether, there was added slowly a solution of 41.0 g. of the benzoyl ester (II) in 200 ml. of anhydrous ether in a nitrogen atmosphere. After refluxing for 2 hr., the mixture was poured into a saturated aqueous solution of ammonium chloride. The ether layer which separated was dried over anhydrous sodium sulfate. After removal of the solvent, the triphenylcarbinol was filtered as it precipitated by an addition of *n*-pentane. The filtrate was concentrated, and the residue was distilled to give 17.0 g. (83.2%) of 7-norbornadienol (III), b.p. 78–80° (56 mm.), $n^{26}D$ 1.5097, which was identified with an authentic sample.[4]

anti-**7-Benzoyloxybenzonorbornadiene** (V).—Essentially the same procedure as above was applied for the reaction of 7.11 g. (0.05 mole) of benzonorbornadiene (IV) with 3.03 g. (0.013 mole) of benzoyl peroxide and 25 mg. of cuprous bromide in 50 ml. of benzene. The reaction required 6 hr., and the color of the solution was blue. After removal of 1.41 g. (92.4%) of benzoic acid, 4.46 g. (62.8%) of IV was recovered by distillation under reduced pressure leaving 3.11 g. of an oily residue. High vacuum distillation of the residue gave 1.57 g. (48.0% from the peroxide) of crude V, b.p. 150° (0.25 mm.), and left 1.78 g. of viscous high molecular products. Crude V was purified by recrystallization from hexane to yield 1.10 g. (33.6%) of pure V as colorless needles with m.p. 95–96°.

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.56; H, 5.50.

anti-**7-Benzonorbornadienol** (VI).—A solution of 262 mg. (0.001 mole) of the benzoyl ester (V) in 10 ml. of anhydrous ether was added dropwise to an ether solution of methylmagnesium iodide which was prepared from 852 mg. of methyl iodide and 146 mg. of magnesium turnings in 20 ml. of anhydrous ether. After refluxing for 2.5 hr., the mixture was poured into a saturated aqueous solution of ammonium chloride, washed with 10% aqueous sodium thiosulfate, and dried over anhydrous sodium sulfate. After removal of phenyldimethylcarbinol by vacuum distillation at about 110–120° (5 mm.), the residue (200 mg.) was recrystallized from hexane to yield 120 mg. (76.3%) of VI as colorless prisms with m.p. 105–106°, lit.[3b] m.p. 106.3–108.2°.

anti-**7-Benzonorborneol** (VII).—A catalytic reduction of the dienol (VI) with palladium on charcoal yielded colorless prisms, m.p. 104–105°, lit.[3b] m.p. 104.1–105.7°, which were recrystallized from hexane and identified with an authentic sample.[3b]

7-*p*-Chlorobenzoyloxynorbornadiene (XIV).—With 35.9 g. (0.39 mole) of norbornadiene (I), 41.3 g. (0.13 mole) of bis(*p*-chlorobenzoyl) peroxide (97.5% of purity), and 300 mg. of cuprous bromide in 650 ml. of benzene, the above procedure was carried out. A color change in the reaction mixture was from green to blue. After removal of 9.8 g. (48.1%) of *p*-chlorobenzoic acid and the solvent, 46.7 g. of the oily residue was chromatographed on 200 g. of Merck standard alumina using hexane. The hexane eluate (29 g.) was vacuum distilled to give 14.4 g. (44.1% from the peroxide) of XIV at b.p. 108° (0.1 mm.), which was immediately crystallized forming colorless needles with m.p. 82–83°.

Anal. Calcd. for $C_{14}H_{11}ClO_2$: C, 68.18; H, 4.46. Found: C, 68.39; H, 4.76.

anti-**7-*p*-Chlorobenzoyloxybenzonorbornadiene** (XV).—With 100 g. (0.703 mole) of benzonorbornadiene (IV), 75 g. (0.234 mole) of bis(*p*-chlorobenzoyl) peroxide, and 745 mg. of cuprous bromide in 1600 ml. of benzene, the above procedure was carried out. The reaction mixture was washed with 10% aqueous sodium carbonate to remove *p*-chlorobenzoic acid. After removal of the solvent, *n*-hexane was added to the residue to precipitate 16.3 g. of crystals as the first crop of crude XV, m.p. 115–127°. After removal of the solvent, the mother liquor was chromatographed on alumina using 15% benzene–hexane to yield 10.7 g. of crystals. Both sets of crystals collected (39.1% yield) were recrystallized from hexane to give 24.7 g. of pure XV as colorless needles with m.p. 126–127°. The yield of the pure crystals was 35.8% from the peroxide.

Anal. Calcd. for $C_{18}H_{13}ClO_2$: C, 72.85; H, 4.15. Found: C, 73.13; H, 4.52.

Reaction in the Absence of Cuprous Bromide.—To a stirred solution of 13.8 g. (0.15 mole) of benzonorbornadiene (IV) in 100 ml. of benzene was added 12.1 g. (0.05 mole) of benzoyl peroxide in 100 ml. of benzene during 2.5 hr. under reflux. The mixture was refluxed with stirring for an additional 25 hr. until the peroxide disappeared. After removal of 1.36 g. (22.3%) of benzoic acid, nonacidic products were distilled to yield 790 mg. of an oil at b.p. 70–75° (0.22 mm.), which was chromatographed on 30 g. of alumina using hexane. None of the desired 7-benzoyloxynorbornadiene was obtained.

Reactions with *p*-Monosubstituted Benzoyl Peroxide.—*p*-Methoxy-, *p*-chloro-, *p*-cyano-, and *p*-nitrobenzoyl peroxides were prepared from the corresponding *p*-substituted benzoyl chloride, perbenzoic acid, and potassium hydroxide, according to the method of Wieland and Rasuwajew.[16]

The standard procedure was carried out with 12.8 g. (0.139 mole) of norbornadiene (I), *p*-monosubstituted benzoyl peroxide (0.035 mole), and 75 mg. of cuprous bromide. The work-up procedure yielded the acidic and nonacidic products. The former were methylated by absolute methanol containing 5% dry hydrogen chloride and were separated into methyl benzoate and methyl *p*-substituted benzoate by distillation or vapor phase chromatography. The latter nonacidic products were chromatographed on 200 g. of alumina using 10% benzene–hexane to remove the high molecular products. The eluate was distilled again. The distillate obtained was chromatographed on alumina using hexane, 10% benzene–hexane, and finally 30% benzene–hexane. By careful separation, biphenyl and 7-benzoyloxynorbornadiene were obtained.

7-*p*-Methoxybenzoyloxynorbornadiene had m.p. 82–83°.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.52; H, 5.81.

7-*p*-Cyanobenzoyloxynorbornadiene had m.p. 120°.

Anal. Calcd. for $C_{15}H_{11}NO_2$: C, 75.93; H, 4.67; N, 5.90. Found: C, 75.97; H, 4.74; N, 5.79.

Acknowledgment.—We wish to thank Prof. J. F. Bunnett and Prof. H. Hart for helpful discussions and Prof. E. Ochiai and Dr. K. Takeda for their encouragement. Our thanks go also to Dr. S. Sumimoto for the preparation of a deuterio compound.

---

(15) All melting points and boiling points are uncorrected.

(16) H. Wieland and G. Rasuwajew, *Ann.*, **480**, 168 (1930).