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Medium-Sized Cyclophanes. III. The Nitration Reaction of [2.2]Metacyclophane with Benzoyl Nitrate[1]

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The nitration reaction of [2.2]metacyclophane was carried out using dilute nitric acid or benzoyl nitrate under various conditions. Dilute nitric acid afforded 2-nitro-4, 5, 9, 10-tetrahydropyrene as the sole product, confirming Allinger's original experiments, whereas benzoyl nitrate furnished a complex mixture consisting of 4, 5, 9, 10-tetrahydropyrene, 4, 5-dihydropyrene and pyrene, together with the nitration product. A series of experiments established that 4, 5, 9, 10-tetrahydropyrene, which was formed by the 1, 4-elimination reaction of Allinger's intermediate, was the initial product of the reaction. Two competitive reactions, nitration and dehydrogenation reactions of the tetrahydropyrene, were assumed to be occurring, thus accounting for the experimental results.

Since the exact molecular structure of [2.2]-metacyclophane (I) was determined by X-ray measurements,[2] the compound was regarded as an ideal model for the calculation of transannular resonance effect between the two benzene rings, which have been reported to be held in a rigid, stepped arrangement and to be separated by only 2.689 Å (the distance between C_8 and C_{16}). Cram and Bauer[3a] have examined the 1 : 1 tetracyanoethylene-paracyclophane charge-transfer complexes and discussed the spectra in terms of ring size. More recently,[3b] it has been shown that the basicity of [2.2]cyclophanes as π-base increases in the order of [2.2]metaparacyclophane, [2.2]metacyclophane, and [2.2]paracyclophane, as is evidenced by the long wavelength charge-transfer bands, which occurred at 455, 486, and 521 mμ respectively. The theoretical treatment of cyclophane compounds has been extended by Allinger and co-workers,[4] who not only calculated the expected

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[1] Part II: T. Sato, S. Akabori, M. Kainosho and K. Hata, This Bulletin, **39**, 856 (1966).

[2] C. J. Brown, *J. Chem. Soc.*, **1953**, 3278.

[3] a) D. J. Cram and R. H. Bauer, *J. Am. Chem. Soc.*, **81**, 5971 (1959); b) D. J. Cram, R. C. Helgeson, K. Lock and L. A. Singer, *ibid.*, **88**, 1324 (1966).

[4] N. L. Allinger, M. A. Da Rooge and R. B. Hermann, *ibid.*, **83**, 1974 (1961).

position in the aromatic ring in compound I, at which substitution would occur, but who also carried out an electrophilic substitution reaction for the first time since it was prepared in 1899 by Pellegrin.[5] While the transannular ring closure of the ten-membered ring system in compound I had already been known to be effected by valence isomerization or cyclodehydrogenation reactions using aluminum chloride[6] or palladium-charcoal[6-8] respectively, Allinger and co-workers, by treating compound I with dilute nitric acid, clearly demonstrated the occurrence of double substitution reactions, accompanied by a transannular cyclization, eventually leading to 2-nitro-4, 5, 9, 10-tetrahydropyrene (VIII). Although this interesting work provided the first insight into the reaction mechanism and into the nature of the intermediate for this particular reaction, further experiments to determine the generality of the mechanism and to explore the scope and limitation of these types of reactions were desirable. It seemed particularly interesting to know the behavior of compound I toward aromatic electrophilic substitution reactions in general as well as toward radical reactions. The possibility of a reaction which effects only a simple substitution, without any transannular reaction, might also be examined. Unpublished results collected in a review article by Griffin[9] concern the attempted reactions of the compound with various reagents, such as alkyl metal, halogen and oxidants; these reagents were, however, selected mainly for the attack of the side chain.

A preliminary report from this laboratory[10] has described a homolytic transannular reaction with iodine under irradiation and an attempted iodination with iodine and silver perchlorate, both of which reactions afforded 4, 5, 9, 10-tetrahydropyrene (V) in a good yield. This paper will record the results obtained by the nitration reaction of [2.2]metacyclophane with benzoyl nitrate, a reaction which afforded products different from those of Allinger's work. By using benzoyl nitrate in a carbon tetrachloride solution, it was possible to attain stoichiometric control and also to eliminate the interference by the oxidizing reagent.

Experimental

[2.2]Metacyclophane (I). The method of Müller and Röscheisen[11] was modified, and a 45% yield was attained by the slow addition (100 hr) of 1, 3-bis(bromomethyl)benzene (0.1 mol) in tetrahydrofuran to a solution of disodium tetraphenylethane, made up by the reaction of sodium with tetraphenylethylene in tetrahydrofuran, under a current of nitrogen at about −70°C. Final purification was achieved by sublimation under reduced pressure, followed by recrystallization from methanol-ethanol, colorless plates, mp 132—133°C. The details of the preparation of this compound and also its derivatives under various conditions will be published elsewhere.[12] The NMR spectra[13] are shown in Fig. 1; the spectra, including those at elevated temperatures have been briefly discussed in a recent paper.[1]

Nitration of [2.2]Metacyclophane (I) with Dilute Nitric Acid. Allinger's nitration reaction was reinvestigated using various concentrations of nitric acid. The results are tabulated in Table 1. Compound VIII was not obtained when the original procedure[4] was followed. It was found that heating the reaction mixture on a water bath was necessary when 6 N nitric acid was used. To a solution of 50 mg (0.25 mmol) of compound I in 4 m*l* of acetic acid, 2 m*l* of dilute nitric acid (9—12 N) was added. The solution was then kept at 25°C for 3 min and, if necessary, warmed on a water bath for 2 min. After the reaction was over, the solution was poured onto ice cubes. Compound VIII was the only product, as was proved by a combination of column chromatography (alumina-*n*-hexane) and NMR spectra (Fig. 1).

TABLE 1. THE REACTION OF [2.2]METACYCLOPHANE WITH DILUTE NITRIC ACID[a]

No.	Concn. of HNO_3, N	Temp. °C	Yield of VIII, %
1	9	25	0
2	10	25	0
3	11	25	0
4	11	48[b]	33
5	11	50[b]	92
6	12	25	100

a) Reaction time 3 min.
b) The reaction mixture was warmed further for 2 min at the temperature indicated.

Benzoyl Nitrate. According to the method of Francis,[14] benzoyl nitrate was prepared[15] by adding benzoyl chloride to a suspension of silver nitrate in carbon tetrachloride at −15—−20°C; the benzoyl nitrate was then kept in a refrigerator under −10°C. The benzoyl nitrate content was determined by weighing the silver chloride formed.

Nitration Reaction with Benzoyl Nitrate. *a) The Reaction with Compound I.* The reactions of compound

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[5] M. Pellegrin, *Rec. trav. chim.*, **18**, 457 (1899).
[6] W. Baker, J. F. W. McOmie and J. M. Norman, *J. Chem. Soc.*, **1951**, 1114.
[7] W. S. Lindsey, P. Stokes, L. G. Humber and V. Boekelheide, *J. Am. Chem. Soc.*, **83**, 943 (1961).
[8] W. Baker, J. F. W. McOmie and J. M. Norman, *Chem. & Ind.*, **1950**, 77.
[9] R. W. Griffin, Jr., *Chem. Revs.*, **63**, 45 (1963).
[10] T. Sato, E. Yamada, Y. Okamura, T. Amada and K. Hata, This Bulletin, **38**, 1049 (1965).
[11] E. Müller and G. Röscheisen, *Chem. Ber.*, **90**, 543 (1957).
[12] T. Sato *et. al.* to be published in this Bulletin.
[13] The NMR spectra were recorded by Varian Associate A-60 model using tetramethyl silane as an internal standard and were expressed in δ (ppm) value. Carbon tetrachloride was used as a solvent unless otherwise stated.
[14] F. Francis, *J. Chem. Soc.*, **89**, 1 (1906); *Ber.*, **39**, 3798 (1906).
[15] V. Gold, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, **1950**, 2467.

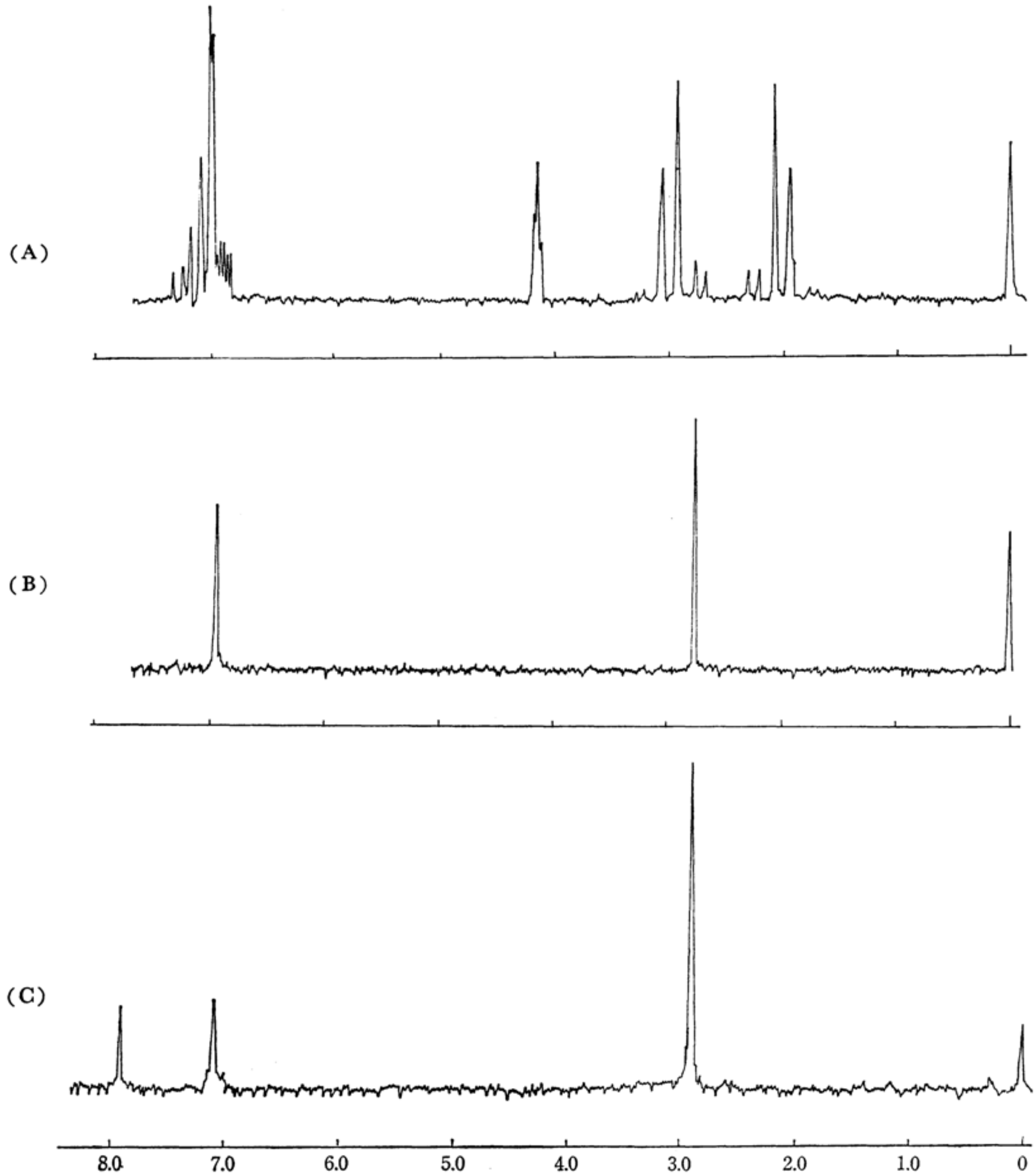

Fig. 1. NMR spectra of (A) 2.2 metacyclophane (I) in CS_2,
(B) 4, 5, 9, 10-tetrahydropyrene (V) in CS_2, and
(C) 2-nitro-4, 5, 9, 10-tetrahydropyrene (VIII) in CCl_4.

I with various amounts of benzoyl nitrate are summarized in Table 2. A typical reaction (Exp. No. 2) was carried out in the following way; to a solution of 208 mg (1 mmol) of compound I in 40 m*l* of carbon tetrachloride, a stock solution of benzoyl nitrate (2 mmol) in carbon tetrachloride was added. Under stirring it was kept at room temperature for 1 hr. After the reaction was over, the lower layer was washed twice with water, then with a sodium hydroxide solution, and again with water. The product in *n*-hexane was passed through a column of alumina and eluted successively with *n*-hexane containing increasing amounts of benzene. The recovered material (29.1%) came out first, followed by tetrahydropyrene, dihydropyrene and pyrene in that order. 4, 5, 9, 10-Tetrahydropyrene (V) was identified by means of its NMR spectra, which consisted of two singlets at δ 2.81 and 6.95 (Fig. 1), and also by a mixed melting point determination with an authentic sample, mp 138°C. 4, 5-Dihydropyrene (VI), mp 132°C, was confirmed by its identical infrared spectra and by a mixed melting point determination. Pyrene (VII) was identified by a direct comparison with the sample, mp 150°C, and also by the formation of picrate, mp 218—220°C, in addition to NMR spectra. The quantitative analysis of each hydrocarbon fraction was achieved by integrated NMR spectra. When the column

TABLE 2. THE REACTION OF [2.2]METACYCLOPHANE (I) AND 4, 5, 9, 10-TETRAHYDROPYRENE (V) WITH BENZOYL NITRATE

No.	Substrate	mmol	$BzONO_2$ mmol	Mol ratio[a]	Reaction time hr	Temp. °C	Yield,[b] %					
							I	V	VI	VII	VIII	Residue,[c] mg
1	I	2.5	6.9	2.8	3.3	20	11	7.7	5.5	1.3	24	59.3
2		0.50	1.0	2.0	1.0	25	29	5.1	13	4.7	7.2	+
3		0.50	0.50	1.0	1.01	25	52	17	10	1.7		
4		0.50	1.0	2.0	1.0	10—15	51	9.0	4.7		7.5	
5		0.50	0.50	1.0	1.0	10—15	73	6.7				
6	V	5.0	14	2.8	3.3	20		0.5	2.6	0.6	10	589.4
7		1.0	2.0	2.0	1.0	25		2.6	18	8.9	3.9	

a) Molar ratio of benzoyl nitrate to the substrate.
b) Yield is based on the starting material.
c) Insoluble matter in *n*-hexane.
d) The reaction mixture was warmed at 70°C for 10 min.

was further eluted with benzene, a new fraction, which contained 8.9 mg (7.2%) of 2-nitro-4, 5, 9, 10-tetrahydropyrene (VIII), mp 110—111°C, was obtained. The NMR spectra of this compound showed three absorptions at δ 2.93, 7.07 and 7.83 and was identified by comparing it with an authentic specimen.

b) The Reaction with Compound V. The results are summarized in Table 2. Exp. No. 6, a typical example, was conducted in the following way. A solution of 1.01 g (5 mmol) of compound V in 30 m*l* of carbon tetrachloride was treated, under stirring, with benzoyl nitrate solution (14 mmol) for 3.3 hr at room temperature. After the reaction mixture had been worked up as above, the products were analyzed by chromatography on alumina. The elution with *n*-hexane gave the starting material (0.5%), dihydropyrene (2.6%) and pyrene (0.6%), successively. Then the solvent was gradually switched to benzene to obtain 10.4% of compound VIII. All the materials were identified as in the above experiment.

c) The Reaction with Bibenzyl. To a solution of 455 mg (2.5 mmol) of bibenzyl in 50 m*l* of carbon tetrachloride, a benzoyl nitrate solution (5 mmol) and 15 mg of benzoyl peroxide were added under cooling. After the mixture had been allowed to react at room temperature for 1 hr, water was added and the mixture was worked up as usual. The product was chromatographed on alumina using *n*-hexane. After the starting material had been passed over (23% recovery), *trans*-stilbene was obtained in a 10% yield, contaminated with a small amount of the *cis*-isomer. Identification was made through olefinic signals in NMR spectra at δ 7.05 (*trans* CH=CH) and 6.54 (*cis* CH=CH) and by a mixed melting point determination with an authentic sample.

Results and Discussion

The nitration reaction of [2.2]metacyclophane (I) in acetic acid with dilute nitric acid has been shown to give 2-nitro-4, 5, 9, 10-tetrahydropyrene (VIII) as the sole product. Although the reaction was reported to be brought about by contact with 6 N nitric acid for 1 min, it turned out, on reexamination, that the compound VIII could be secured only after brief heating on a water bath. By carrying out the reaction using 9 to 12 N nitric acid, the results which are summarized in Table 1 were obtained. It was made clear that the reaction proceeded at room temperature when 12 N acid was used, yet not nitric acid weaker than 11 N, with which, however, a 92% yield of the nitro compound was obtained by warming it at 50°C.

In considering the mechanism of this facile reaction it has been suggested[4] that nitrotetrahydropyrene arose through an intermediate II, which resulted from two simultaneous substitution reactions by nitronium and phenonium ions on the benzene rings. The extrusion of the proton *via* structure III to form the intermediate IV, followed by the oxidation reaction with an excess of nitric acid, would afford compound VIII. Even in cases where the conversion was incomplete, the rest of the starting material was found to be recoverable by a careful examination with alumina chromatography and even a trace amount of tetrahydropyrene V was not detectable; Thus, the alternative mechanism,[16] postulating the intermediacy of the tetrahydropyrene V formed by the nitric acid oxidation of compound I prior to the nitration, was disproved. In fact, the nitration of compound V was also known to afford compound VIII, but this latter was obtained much more efficiently from [2.2]metacyclophane itself.

On the other hand, in a recent communication[10] we have reported that the attempted iodination of compound I with iodine and silver perchlorate in ether resulted in the formation of 4, 5, 9, 10-tetrahydropyrene (V) in a 60% yield. In this reaction the intermediate corresponding to IV was suggested to be IX. The compound V could also be obtained as the main product in the photochemical reaction of compound I with iodine in cyclohexane.

From these conflicting results, one was lead to assume that the fate of the intermediate IV, would

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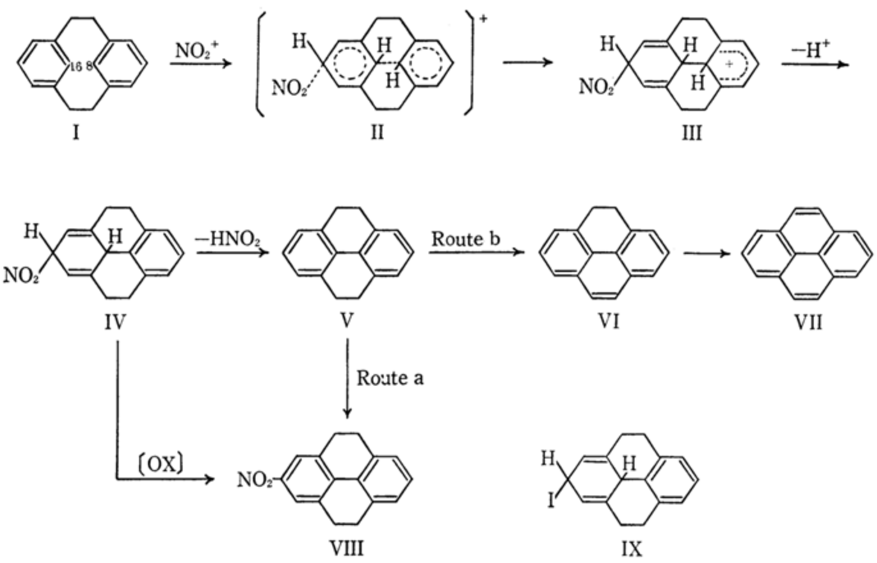
[16] B. H. Smith, "Bridged Aromatic Compounds," Academic Press Inc., New York, N. Y. (1964), p. 236.



be dependent on the nature of the reagent. In order to test this idea, studies of the nitration of compound I avoiding the participation of an oxidant seemed to be necessary. In this connection, the reaction of [2.2]metacyclophane with benzoyl nitrate was extensively studied with various amounts of the latter reagent under several conditions.

Benzoyl nitrate was first used by Francis(14) for the nitration of aromatic compounds. A variety of compounds, including hydrocarbons, phenols, phenol ethers and acetanilide, have been nitrated so far.(17) Kinetic studies of this reagent have revealed that the nitration proceeded through dinitrogen pentoxide, which was formed by the following equilibrium.(15,16,18)

$$2C_6H_5COONO_2 \rightleftarrows N_2O_5 + (C_6H_5CO)_2O$$

It has been shown that the order of reactivity for the series of nitration agents concerned was as follows.(15)

$$N_2O_5 > C_6H_5COONO_2 > HNO_3$$

The results of the nitration with this reagent are shown in Table 2. When excess benzoyl nitrate (2.8 equiv.) was used, the reaction gave a complex mixture consisting of 7.7% 4, 5, 9, 10-tetrahydropyrene (V) and 24% 2-nitro-4, 5, 9, 10-tetrahydropyrene (VIII), plus 4, 5-dihydropyrene (VI) and pyrene (VII). The analyses were performed by using alumina column chromatography, each fraction being examined spectroscopically; by studies of the NMR spectra, quantitative analyses of compounds I, V and VIII were made. The NMR spectra of compounds I, V, and VIII are shown in Fig. 1. The disappearance of a triplet at δ 4.23, which was assignable to intra-annular protons at the 8 and 16 positions in compound I, was taken as an indication of the occurrence of the transannular reaction. Compound V had only two singlets, at δ 2.81 and 6.95, in an expected ratio of 4 : 3, whereas compound VIII had three absorptions, at δ 2.93, 7.07 and 7.83, in 8 : 3 : 2. The infrared spectra were also indicative of the structure. In the 700—800 cm^{-1} region, compound I showed two bands, at 710 and 790 cm^{-1}, while compound V had absorptions at 730 and 780 cm^{-1}. Although a quantitative analysis of these two compounds in a mixture was possible, it was not as straightforward as when integrated NMR spectra were used.

Experiments 1 through 5, which were arranged in approximately decreasingly forced reaction conditions, revealed that the recoverable metacyclophane increased in this order, and that compound V was formed throughout the experiments, whereas compound VIII was detected only in Experiments 1, 2 and 3. Compound V was found to be formed in 17, 42, 59 and 100% (conversion) respectively in Experiments 2 through 5. Comparing the experiments made under the same temperature, it was noticed that compound VIII was not formed when less benzoyl nitrate was used, and that the conversion rate to compound V increased by a factor of about 3. Under mild conditions (*e. g.*, Exp. No. 5), compound V was found to be the sole product. From these results, coupled with nitration studies of 4, 5, 9, 10-tetrahydropyrene itself, one was lead to conclude that compound V, which was formed by the 1, 4-elimination reaction of the intermediate IV, was the initial product of this reaction. 2-Nitro-4, 5, 9, 10-tetrahydropyrene (VIII) was obtained by the further nitration reaction according to route a.

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17) For historical description of the use of this reagent, see papers cited in Ref. 15.

18) See however, H. Burton and P. F. G. Praill, *J. Chem. Soc.*, **1955**, 729.

The formation of dihydropyrene and pyrene needs to be mentioned. Apparently they may be considered to arise by the dehydrogenation of tetrahydropyrene according to route b. This dehydrogenation reaction persists through Exp. No. 4, where compound VIII was no longer detected. It may be inferred that, of the decay processes of compound V through two competitive routes, a and b, the latter is favored. The dehydrogenation reaction was further investigated by using tetrahydropyrene V and bibenzyl. Dihydropyrene was formed, together with a nitrated product, when the formed compound was subjected to the reaction conditions cited in Table 2 (Exps. No. 6 and 7). Bibenzyl gave about 10% of *trans*-stilbene, contaminated with a small amount of the *cis* isomer.

A hydrogen abstraction reaction at the benzylic position of these compounds, a reaction initiated by the radical derived from benzoyl nitrate, was thus shown to be taking place. Besides the aromatic substitution reactions, acyl nitrates, including acetyl nitrate, are known to give addition products from olefins.[19) The formation of benzoyl quinolinium salt by the reaction of benzoyl nitrate with quinoline *N*-oxide has also been reported.[20) No radical reaction by means of acyl nitrate has been described to date. Related reactions using simple model compounds are now being studied. Gill and Williams[21) recently investigated the decomposition of benzoyl peroxide in benzene in the presence of nitrogen dioxide, thereby obtaining results which indicated the formation of benzoyl nitrate by the reaction of the benzoyloxy radical and the NO_2 radical.

It may be concluded that the nitration reaction with benzoyl nitrate proceeds through an addition elimination process which assumes the intermediacy of IV. Nitrotetrahydropyrene (VIII) is obtained *via* V, but not directly from IV. This mechanism is also applicable to the case of iodination reactions carried out in our laboratory.[10) It has also become clear that the reaction is accompanied by a radical reaction, which is responsible for the formation of dihydropyrene and pyrene.

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19) F. G. Bordwell and E. W. Garbisch, Jr., *J. Org. Chem.*, **28**, 1765 (1963); A. A. Griswold and P. S. Starcher, *ibid.*, **31**, 357 (1966).

20) E. Ochiai and C. Kaneko, *Chem. Pham. Bull.*, **7**, 267 (1957) and literatures cited therein.

21) G. B. Gill and G. H. Williams, *J. Chem. Soc.*, **1965**, 5756.