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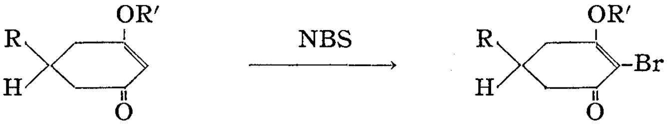
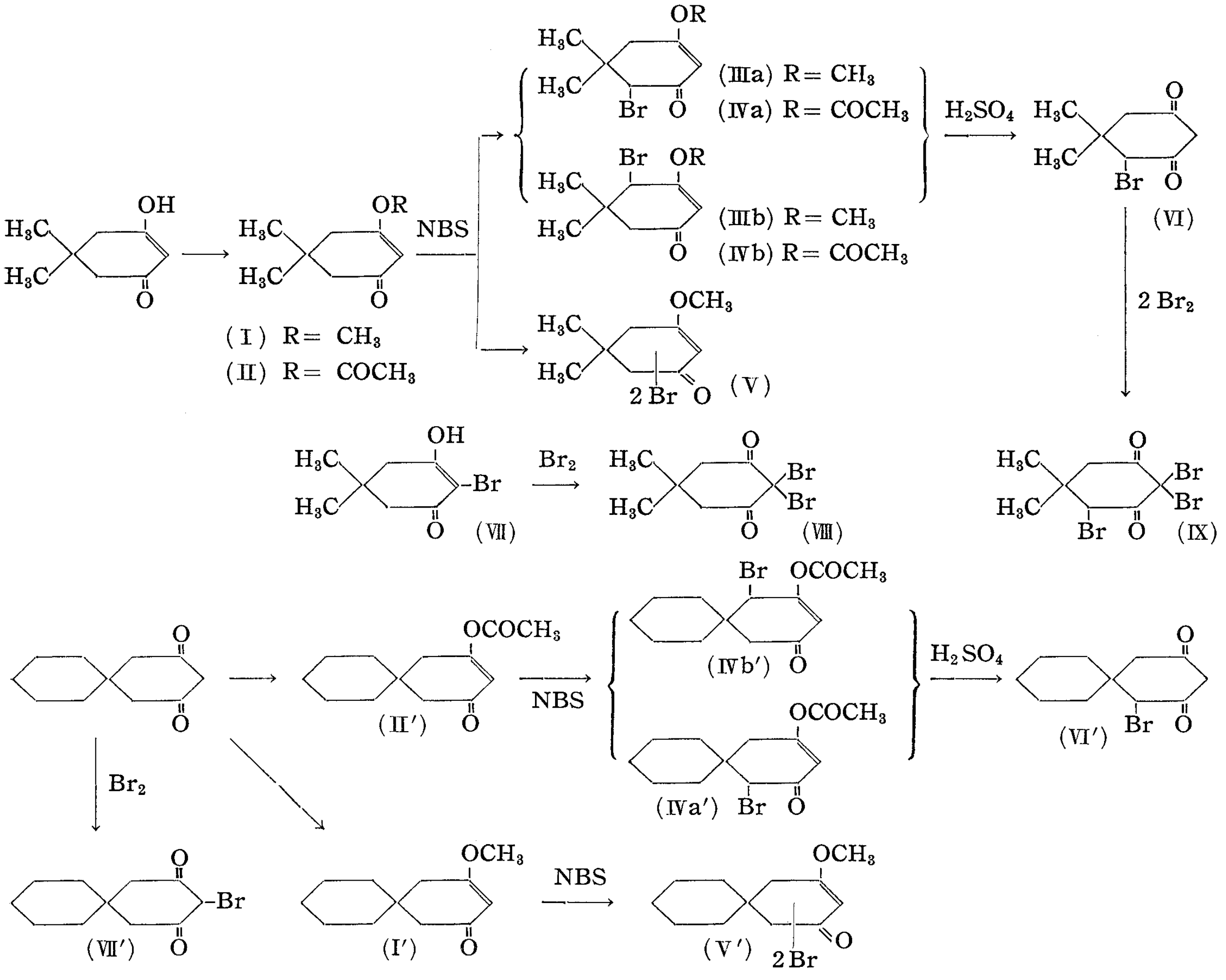
90. **Kiichi Arakawa**: Bromination of Cyclic 1,3-Diketone Monoenolates with N-Bromosuccinimide. II.

(*Department of Chemistry, Institute for Infectious Diseases,* University of Tokyo*)

In the preceding paper of this series,[1] the present author reported on the mode of N-bromosuccinimide (NBS) bromination reaction for some cyclic 1,3-diketone monoenolates. Thus, several 5-monosubstituted 3-alkyl- or -acyloxy-2-cyclohexen-1-ones were proved to be brominated with NBS at their 2-position.



This paper deals with the result of the same reaction for the analogous cyclic 1,3-diketone monoenolates having two substituents at their 5-position, because these compounds showed different type of reaction from that reported in the preceding paper.[1]



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* Shiba, Minato-ku, Tokyo (荒川基一).

[1] Part I: This Bulletin, **5**, 524(1957).

5,5-Dimethyl-1,3-cyclohexanedione and sprio[5.5]undecane-2,4-dione were derived to their methyl (I) and (I′) and acetyl enolates (II and II′).

The brominations of (I and I′) with equimolar amount of NBS occurred under irradiation of the reaction mixture with ultraviolet ray, giving both monobromo (IIIa or IIIb) and dibromo derivatives (V) from (I), and only dibromo derivatives (V′) from (I′).

In the cases of (II) and (II′), although a prolonged irradiation was necessary to complete the reaction, the products isolated were monobromo derivatives, (IVa or IVb) and (IV′a or IV′b), respectively.

The monobromo derivatives (III, IV, and IV′) thus obtained were hydrolysed to give the respective monobromo diketones (VI and VI′). On mixed fusion of the monobromo dimedone (VI) with 2-bromodimedone (VII), which was synthesised according to the method reported by Vorländer[2] and Norris,[3] a remarkable depression was observed.

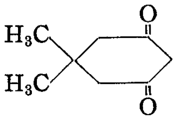
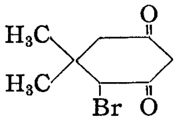
Therefore, (VI) and (VII) must be isomers relative to the position of bromine substitution.

In order to know the position of substituted bromine in both (VI) and (VII), these were further brominated with molecular bromine in acetic acid. By these reactions, (VII) gave 2,2-dibromodimedone with m.p. 146~147° as reported by Norris,[3] but the product from (VI) was a tribromo derivative of dimedone (IX).

Because the bromination of dimedone with molecular bromine in glacial acetic acid is well known to furnish 2,2-dibromodimedone as the final product,[2,3] it is obvious that the original bromine in (VI), accordingly in (III) and (IV), was attached at 4- or 6-position.

Further information for the substituted bromine in (VI) was obtained from the analysis of its infrared absorpion spectra.

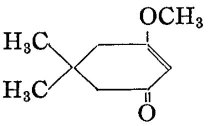
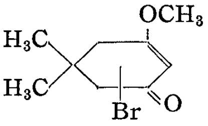
Table I. Infrared Absorption (in $CHCl_3$) (cm^{-1})

	$\nu_{C=O}$	1733 , 1710	⊿ 18
	$\nu_{C=O}$	1751 , 1720	

As shown in Table I, the position of absorption for C=O streching in compound (VI) showed a hypsochromic deviation of ca. 18 cm^{-1} from that of dimedone.

Many instances have been reported on a similar hypsochromic effect (ca. 20 cm^{-1})[4,5] for C=O streching absorptions when the bromine substitution occurred at the α-sosition of the carbonyl group, with the exception of α-axial substituted bromoketones in

Table II. Infrared Absorption (in $CHCl_3$) (cm^{-1})

	$\nu_{C=O}$	1648 ,	$\nu_{C=C}$	1613	⊿ 4
	$\nu_{C=O}$	1652 ,	$\nu_{C=C}$	1612	

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[2] D. Vorländer, M. Kohlmann : Ann., **322**, 239(1902).

[3] G. P. Norris, J. F. Thorpe : J. Chem. Soc., **1921**, 1119.

[4] R. N. Jones, D. A. Ramsay, F. Herling, K. Dobriner : J. Am. Chem. Soc., **74**, 2828(1952).

[5] E. T. Corey : *Ibid.*, **75**, 2301, 3297, 4832(1953).

hydroaromatic ring. From such a point of view, the substituted bromine in (VI) is obviously in the carbon atom at 4- or 6-position with possible equatorial conformation.

Table II shows the comparison of C=O streching absorption for dimedone methyl monoenolate with (IIIa) and (IIIb). In this case, tha latter shows only a slight hypsochromic shift (Δ 4 cm^{-1}) of C=O streching absorption from that of the former. From these data, according to the generalized relationship between conformational structure of hydroaromatic α-bromoketones and their C=O streching absorptions[4,5] the 4-position adjacent to the enolate group, in both axial and equatorial conformations, or at 6, adjacent to the carbonyl group, in axial conformation, is possible for the substituted bromine in the compound (VII).

The final decision of the bromo substitution of (III) must be reached by more chemical research which is now under progress and the result will be reported in the next paper of this series.

The author wishes to express his deep appreciation to Prof. T. Ukita for helpful advices and encouragement. Thanks are due to Miss R. Ota and Mr. B. Kurihara for carrying out the microanalyses. The author also wishes to thank the Sankyo Co., Ltd. for the measurement of infrared spectra.

Experimental

3-Methoxy-5,5-dimethyl-2-cyclohexen-1-one (I) and 4-Methoxyspiro[5.5]undec-3-en-2-one (I′)—These were obtained from 5,5-dimethyl-1,3-cyclohexanedione or spiro[5.5]undecane-2,4-dione and dehyd. MeOH according to the method reported in the preceding paper.[1] (I), $b.p_{1.5}$ 80~81°; yield, 80%. (I′), $b.p_{1.5}$ 128~131°, and m.p. 51~52.5° (recrystallized from EtOH). *Anal.* Calcd. for $C_{12}H_{18}O_2$: C, 74.23; H, 9.27. Found: C, 73.96; H, 9.18. Yield, ca. 80~85%.

3-Acetyl-5,5-dimethyl-2-cyclohexen-1-one (II) and 4-Acetoxyspiro[5.5]undec-3-en-2-one (II′)—These compounds were also synthesized by the method reported in the preceding paper.[1] (II), $b.p_2$ 97~99°, gave reddish brown color reaction with $FeCl_3$ in EtOH. (II′), $b.p_1$ 143~146°, colored reddish brown with $FeCl_3$ in EtOH. Yield, ca. 70~80%.

NBS-Bromination of (I)—To a solution of 1.5 g. of (I) dissolved in 20 cc. of CCl_4, 1.8 g. of NBS was added and the mixture was refluxed for 20 mins. under irradiation of ultraviolet ray. Irradiation was stopped when succinimide began to separate out on the surface of the solution and the refluxing was continued until all succinimide was separated. The latter was removed by filtration. On evaporation of the solvent, the filtrate gave colorless sandy crystals (III) which were recrystallized from diluted EtOH to the pure product melting at 90~91°; yield, 70%. It gave no color reaction with $FeCl_3$ in EtOH. *Anal.* Calcd. for $C_9H_{13}O_2Br$: C, 46.35; H, 5.62; Br, 34.34. Found: C, 46.78; H, 5.46; Br, 34.69.

The longer irradistion of ultraviolet ray gave the dibromo derivatives besides the monobromide. Recrystallization of the former from EtOH afforded colorless sandy crystals, m.p. 129~130°, which gave no marked change of color with $FeCl_3$ in EtOH. *Anal.* Calcd. for $C_9H_{12}O_2Br_2$: C, 34.61; H, 3.84; Br, 51.28. Found: C, 34.37; H, 3.72; Br, 51.18.

Bromination of (I′) with NBS—A mixture of 2.8 g. of (I′) and NBS in dry CCl_4 was refluxed for 20 mins. under irradiation of ultraviolet ray. The succinimide separated was removed by filtration and the filtrate was distilled to dryness under reduced pressure. Trituration of the residue with MeOH afforded 1.4 g. of a yellow solid. After repeated recrystallization from EtOH, it gave colorless crystals (V′) with m.p. 125~126°. *Anal.* Calcd. for $C_{12}H_{16}O_2Br_2$: C, 40.90; H, 4.55; Br, 45.45. Found: C, 41.27; H, 4.56; Br, 44.81.

Hydrolysis of 3-Methoxy-5,5-dimethyl-4(or 6)-bromo-2-cyclohexen-1-one—A mixture of 2 g. of methyl enolate (IIIa or IIIb) and 15 cc. of 50% H_2SO_4 was warmed on a steam bath for 10 mins., the reaction mixture was poured into ice water, the precipitate was extracted with Et_2O, and the ethereal solution was again extracted with 5% Na_2CO_3. The alkaline solution was neutralized with HCl to separate the demethylated product. The white amorphous precipitate thus obtained was recrystallized from hot water to colorless crystals (VI), m.p. 150~151°(decomp.); yield, 1.2 g. It colored reddish brown with $FeCl_3$ in EtOH. *Anal.* Calcd. for $C_8H_{11}O_2Br$: C, 43.83; H, 4.93; Br, 36.50. Found: C, 43.94; H, 4.72; Br, 36.60.

Bromination of (II) with NBS—A solution of 3.6 g. of the enol acetate (II) in 50 cc. of dry CCl_4 was refluxed with 3.5 g. of NBS for 30 mins. under irradiation of ultraviolet ray. On removal of the solvent from the filtrate after removal of succinimide, a brown oily product was obtained. Because of the unstability of the product to liberate the acetyl group, this was directly hydrolized with dil. H_2SO_4 to give the desired brominated product. The bromo derivative thus obtained was identified by mixed fusion with the 4- or 6-bromo derivative which was obtained by the hydrolysis of (III) (a or b).

Bromination of (II′) with NBS—A mixture of 4 g. of (II′) in 30 cc of CCl_4 and 3.2 g. of NBS was refluxed for 4.5 hrs. under irradiation of ultraviolet ray. After cooling of the reaction mixture, the succinimide separated was removed by filtration. On evaporation of the solvent from the filtrate, an oily substance was obtained. The unstable product was deacetylated with dil. Na_2CO_3 to give crude deacetylated product which upon crystallization from benzene-petr. ether gave 1.8 g. of the diketobromo derivative (VI′), m.p. 135～136°. It colored red with $FeCl_3$ in EtOH. *Anal.* Calcd. for $C_{10}H_{15}O_2Br$: C, 50.95; H, 5.79. Found : C, 51.35; H, 5.89.

2-Bromo-5,5-dimethyl-1,3-cyclohexanedione (VII)—To a solution of 0.25 g. of 5,5-dimethyl-1,3-cyclohexanedione dissolved in 30 cc. of CCl_4, 0.32 g. of NBS was added and the mixture was refluxed for 5 mins. After cool, the separated succinimide was removed by filtration and the filtrate was concentrated under reduced pressure to about 15 cc. On cooling, colorless crystals separated out. Recrystallization from CCl_4 yielded colorless crystals, m.p. 174～175°, which showed no depression when mixed with the authentic specimen synthesized by the method of Vorländer.[2]

2,2-Dibromo-5,5-dimethyl-1,3-cyclohexanedione (VIII)—A solution of 0.5 g. of monobromide (VII) in 20 cc. of dry CCl_4 was refluxed with 0.33 g. of NBS for 20 mins. The reaction mixture was treated as above. Recrystallization of the product from dil. EtOH gave colorless needles, m. p. 146～147°; yield, 0.37 g. It showed no depression when mixed with the authentic specimen synthesized by the method of Vorländer.[2]

2,2,6-Tribromo-5,5-dimethyl-1,3-cyclohexanedione (IX)—To a solution of 0.5 g. of (VI) in glacial AcOH, a solution of Br_2 in glacial AcOH was added dropwise until the solution showed a faint yellow color. The reaction mixture was poured into ice water, and separate white crystals were recrystallized from EtOH to colorless crystals, m.p. 141°(decomp.). EtOH solution of the product colored reddish brown with $FeCl_3$ solution and liberated Br_2 from KI solution. *Anal.* Calcd. for $C_8H_9O_2Br_3$: C, 25.46; H, 2.38; Br, 63.66. Found : C, 25.73; H, 2.50; Br, 63.94.

Summary

The position of the substituted bromine in bromination of 1,3-cyclohexanedione monoenolate with N-bromosuccinimide was investigated. 1,3-Cyclohexanedione-3-monoenolates, which have two alkyl substituents at their 5-position, were found to be brominated at positions other than 2. From the data obtained in infrared spectra, the stereochemical situations of the bromo substitution were discussed.

In this reaction dibromo compounds were obtained as by-products which were not found in a similar reaction for 1,3-cyclohexanedione monoenolates having no or one aryl substituent at their 5-positions.

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91. **Kiichi Arakawa** : Bromination of Cyclic 1,3-Diketone Monoenolates with N-Bromosuccinimide. III.

(*Department of chemistry, Institute for Infectious Diseases,* University of Tokyo*)

As reported in the previous papers of this series,[1,2] there are two types in the bromination reaction of cyclic 1,3-diketone monoenolate with N-bromosuccinimide (NBS).

Thus for the compounds with general structural type (A), the bromination occurred at their 2-position, while the 1,3-diketone monoenolates with the structural type (B) were brominated under the same condition at a 4- or 6-position in the conformational

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* Shiba, Minatoku, Tokyo (荒川基一).

[1] Part I : This Bulletin, **5**, 524(1957).

[2] Part II : This Bulletin, **5**, 528(1957).