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. $135\sim 136^\circ$. It colored red with FeCl_3 in EtOH. *Anal.* Calcd. for $\text{C}_{10}\text{H}_{15}\text{O}_2\text{Br}$: 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. $174\sim 175^\circ$, 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. $146\sim 147^\circ$; 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 $\text{C}_8\text{H}_9\text{O}_2\text{Br}_3$: 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 mono-enolate with N-bromosuccinimide was investigated. 1,3-Cyclohexanedione-3-mono-enolates, 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 mono-enolates 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.

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As reported in the previous papers of this series,^{1,2)} there are two types in the bromination reaction of cyclic 1,3-diketone mono-enolate 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 mono-enolates with the structural type (B) were brominated under the same condition at a 4- or 6-position in the conformational

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

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

enolates, (IIa) and (IIb), gave with simultaneous demethylation, an osazone (V), m.p. 270~272°(decomp.), $C_{20}H_{18}N_8O_9$. The same product (V) was also obtained from both (I) and bromodiketone (IV) by similar treatment with Brady's reagent.

The above series of reaction for bromo compound (I) reveals that the bromine was substituted at 6- rather than 4-position of this compound. Otherwise, the final product of the reaction must be tris(2,4-dinitrophenylhydrazone), because osazone formation via (IIa) and (IIb) must be preceded by demethylation. Thus, (I) must be 3-methoxy-5,5-dimethyl-6-bromo-2-cyclohexen-1-one.

As both bromohydrazone, (IIa) and (IIb), were isolated in crystalline form, these isomers are best interpreted as *cis* and *trans* isomers relative to C=N double bond of the hydrazone. Thus, (IIb) is convertible into (IIa) by its treatment with dilute sulfuric acid.

On methylation of the bromodiketone (VI), which was thought to have equatorial bromine,²⁾ an oily monobromo-enolate (VII), b.p.₅ 120°, was obtained, and on keeping at room temperature, the latter converted into (I).

As the boiling point of (VII) was lower than that of (I) (b.p.₅ 125°) and as the former was easily convertible into the latter, (VII) might possibly be a mixture of (I) contaminated with a small amount of its conformational pair of bromines.

With Brady's reagent under milder condition, (VII) was converted into the monohydrazone derivative (IIb) which was further isomerized into (IIa) by treatment with diluted sulfuric acid.

The results of the reactions reported in this paper reveal that in the case of 5,5-substituted 3-alkyl(or acyl)-2-cyclohexen-1-one, NBS attacked the 6-position to introduce bromine probably in axial conformation.

It is of interest that the two types of compounds having a common 1,3-diketone enolate system, (A) and (B), which differ in the substitution at 5-position, were proved to be brominated with NBS by different types of reaction. Thus, in the case of type (B) compounds, the reaction occurred at the methylene neighboring the carbonyl group.

The α,β -unsaturated carbonyl system is known to be attacked with NBS in two different ways, (1) and (2), which are shown in Chart 1, and the former type (1), which gives γ -brominated derivatives is more usual than the latter type (2) which results in α' -brominated product.⁶⁾ In the case of type (B) compound, therefore, NBS-bromination occurred in a similar mode as in (2) for the simple α,β -unsaturated carbonyl system, contrary to type (A) compounds which have already been shown¹⁾ to be brominated in a similar way as that for the simple enolate system.

Chart 1.

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Experimental

3-Methoxy-5,5-dimethyl-6-bromo-2-cyclohexen-1-one (VII)—To a suspension of 0.6 g. of (VI)²⁾ in 40 cc. of dehyd. Et_2O , an excess of the ether solution of CH_2N_2 was added and the mixture was

6) C. Djerassi : Chem. Revs., **43**, 271(1948).

kept in a refrigerator for 24 hrs. After evaporation of the solvent, the residual oil was distilled under diminished pressure to give 0.2 g. of a colorless liquid, b.p. 120~122°. *Anal.* Calcd. for $C_9H_{13}O_2Br$: C, 46.35; H, 5.57; Br, 34.34. Found: C, 46.59; H, 5.59; Br, 34.28.

On standing, this oil solidified into crystals which was identified with (I) reported in the preceding paper.²⁾

3-Methoxy-5,5-dimethyl-6-bromo-2-cyclohexen-1-one Dinitrophenylhydrazone (IIa or IIb)—a) 0.46 g. of bromoketone (I) dissolved in the minimum amount of MeOH was treated at room temperature with freshly prepared Brady's reagent⁷⁾ containing 0.4 g. of 2,4-dinitrophenylhydrazine (DNPH). The precipitated hydrazone was filtered within 5~10 mins. and washed thoroughly with cold hydr. MeOH. The crude product was extracted with boiling EtOH and EtOH solution was evaporated to afford reddish sandy crystals which were recrystallized from EtOH to the pure product (IIb), melting at 143~144°. *Anal.* Calcd. for $C_{15}H_{17}O_5N_4Br$: C, 43.58; H, 4.11; N, 13.56; Br, 19.37. Found: C, 44.12; H, 4.29; N, 13.31; Br, 19.31.

The substance which was not extracted with EtOH was recrystallized from EtOAc to reddish needles (IIa), m.p. 196~197°. *Anal.* Calcd. for $C_{15}H_{17}O_5N_4Br$: C, 43.58; H, 4.11; N, 13.56; Br, 19.37; CH_3O , 7.51. Found: C, 43.54; H, 4.32; N, 13.80; Br, 19.13; CH_3O , 7.95.

b) The oily bromodiketone methyl-enolate (VII) was treated with DNPH by the method similar to a). The reaction of (VII) with DNPH gave only dinitrophenylhydrazone, m.p. 143~144°, which showed no depression when mixed with the sample (IIb) obtained from a).

Rearrangement of (IIb) to (IIa)—To a suspension of 0.1 g. of (IIb) in 5 cc. of MeOH, 0.5 cc. of H_2SO_4 was added, the mixture was kept over night in a refrigerator, and the reddish solution was poured into ice water. The precipitate was collected by filtration and on recrystallization from EtOH the product gave 0.05 g. of reddish needles, m.p. 196~197°, which showed no depression when mixed with (IIa).

3-Methoxy-5,5-dimethyl-6-(1-pyridyl)-2-cyclohexen-1-one 2,4-Dinitrophenylhydrazone (III)—A mixture of 0.2 g. of bromohydrazone (IIa or IIb) and 4 cc. of pyridine was warmed for 20 mins. on a steam bath. After cool, the separated precipitate was collected by filtration, pressed, and dried on a porcelain plate. Recrystallization from EtOH gave 0.15 g. of reddish needles, m.p. 225~227° (decomp.). *Anal.* Calcd. for $C_{20}H_{22}O_5N_5Br$: C, 48.68; H, 4.66; N, 14.20; Br, 16.22. Found: C, 48.74; H, 4.83; N, 14.03; Br, 17.19.

3-Methoxy-5,5-dimethyl-6-(1-piperidyl)-2-cyclohexen-1-one 2,4-Dinitrophenylhydrazone (IV)—A mixture of 0.2 g. of bromohydrazone (IIa or IIb) and 0.5 cc. of piperidine was kept at the room temperature for 1 hr., the piperidine hydrogen bromide that separated was removed by filtration, and the filtrate was distilled to dryness under reduced pressure. Trituration of the residue with dil. EtOH afforded reddish brown solid, recrystallization of which from EtOH gave 0.12 g. of reddish brown crystals, m.p. 138~139°. *Anal.* Calcd. for $C_{20}H_{27}O_5N_5$: C, 57.54; H, 6.52; N, 16.78; CH_3O , 7.43. Found: C, 57.32; H, 6.44; N, 17.13; CH_3O , 7.44.

5,5-Dimethyl-1,3,6-cyclohexanetrione 1,6-Osazone (V)—a) A mixture of 0.2 g. of bromohydrazone (IIa or IIb) was refluxed for 3 hrs. with excess of Brady's reagent. After cool, the separated crystals were recrystallized from pyridine to reddish sandy crystals, m.p. 270~272°(decomp.); yield, 0.12 g. *Anal.* Calcd. for $C_{20}H_{18}O_9N_8$: C, 46.67; H, 3.50; N, 21.78. Found: C, 46.82; H, 3.67; N, 21.45.

b) A mixture of 0.2 g. of bromodiketone methyl enolate (I) or 5,5-dimethyl-6-bromo-1,3-cyclohexanedione (VI) was refluxed with excess of Brady's reagent. After cool, the reaction mixture was treated by a similar procedure as in a). In either case reddish sandy crystals, m.p. 270~272°, were obtained which showed no depression when mixed with the product obtained in a).

Summary

The position of substituted bromine in the product obtained by bromination with N-bromosuccinimide of 1,3-cyclohexanedione 3-monoenolates having two alkyl substituents at the 5-position was established as 6, probably in axial conformation.

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7) O. L. Brady: J. Chem. Soc., 1931, 757.