5,10,11,12,12a,12b-Hexahydro-12b-hydroxyisoindolo[2,1-*a*]benz[*cd*]indol-5-one (4)——554 mg of 3 in 300 ml of acetone was irradiated with 500 W high-pressure mercury lamp for 25 min under a nitrogen atmosphere. Evaporation of the solvent gave solid which was recrystallized from ethanol to give colorless prisms, mp 254—256°, 425 mg (77%). *Anal.* Calcd. for $C_{18}H_{15}NO_2$: C, 78.00; H, 5.42; N, 5.06. Found: C, 77.93; H, 5.44; N, 5.18. IR ν_{max}^{Nujol} cm^{-1}: 3300 (OH), 1677 (C=O). UV λ_{max}^{EtOH} nm (ε): 230 (11110), 237 (sh, 10810), 284 (1910), 297 (5340). NMR (pyridine-d_5) δ: 3.06 (1H, C_{12a}–H), 9.00 (1H, O–H).

5,10,11,12-Tetrahydroisoindolo[2,1-*a*]benz[*cd*]indol-5-one (5)——Suspension of 4 (400 mg) in conc. HCl–EtOH (1: 10, v/v, 44 ml) was heated under refluxing for 0.5 hr to give a yellow solution. After standing the reaction mixture at room temperature overnight, precipitated yellow needles were collected by filtration (405.2 mg). Purification of the crude product by recrystallization from ethanol afforded bright yellow needles, mp 169—170°, 314.3 mg (83.5%). *Anal.* Calcd. for $C_{18}H_{13}NO$: C, 83.40; H, 5.02; N, 5.41. Found: C, 83.43; H, 4.95; N, 5.44. IR ν_{max}^{Nujol} cm^{-1}: 1714 (C=O). UV λ_{max}^{EtOH} nm (ε): 235 (28890), 242 (sh, 27220), 277 (30830), 294 (14720), 307 (16560), 370 (8890). NMR ($CDCl_3$) δ: 1.93—2.23 (2H, C_{11}–H), 2.72—2.98 (4H, C_{10}– and C_{12}–H), 6.8—7.7 (7H, aromatic protons).

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Studies on Ketene and Its Derivatives. LXXXVII.[1] Photoreaction of Diketene with 3-Acetoxy-5,5-dimethyl-2-cyclohexenone

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Photoreaction of diketene with 3-acetoxy-5,5-dimethyl-2-cyclohexenone (1) gives 6-acetoxy-7-hydroxy-4,4-dimethyl-*cis*-bicyclo[4.2.0]octan-2-one-7-acetic acid β-lactone (2 and 3). Treatment of 2 with dimethylamine affords 3-acetoxy-7-hydroxy-N,N,4,4-tetramethyl-*cis*-bicyclo[4.2.0]octan-2-one-7-acetamide (4), while similar treatment of 3 affords 1-acetoxy-N,N,4,4-tetramethylcyclooctane-2,6-dione-1-acetamide (5). This result suggests the spiro-configuration of 2 is the *trans* (acetoxy and oxetane O), while that of 3 being the *cis*.

Keywords——photoreaction; diketene; bicyclo[4.2.0]octane derivative; spiro compounds; acyl migration; configuration; shift reagent

In the preceeding paper[1] we have reported that photolysis of a solution of diketene and dimedone resulted in the [2+2]cycloaddition reaction accompanied with ring expansion to give the cyclooctane derivative. We now report the similar reaction of diketene with dimedone monoacetate, 3-acetoxy-5,5-dimethyl-2-cyclohexenone (1), to give the stereoisomers of the bicyclo[4.2.0]octanone, 2 and 3.

Irradiation of a solution of compound 1 and diketene in ethanol or acetonitrile gave crystalline products 2 and 3, to which we assigned the *cis*-bicyclo[4.2.0]octan-2-one-7-acetic acid β-lactone structures, where the juncture of acetoxy and oxetane oxygen of 2 is the *trans* while that of 3 is the *cis* configuration.

Namely, the infrared (IR) spectrum of 2 showed the β-lactone (1830 cm^{-1}), ester (1740 cm^{-1}), and ketone (1700 cm^{-1}) carbonyl absorptions. Nuclear magnetic resonance (NMR) spectrum showed three singlet methyl signals (0.97, 1.10 and 2.07 ppm), three singlet methylene signals (2.24, 2.58, and 3.32 ppm), and a multiplet signal (2.24—2.70 ppm, 3H) which was assignable to C_1-proton and C_8-methylene protons.

1) Part LXXXVI: T. Kato, M. Sato, and Y. Kitagawa, *J. Chem. Soc. Perkin I*, 1978, in press.
2) Location: *Aobayama, Sendai, 980, Japan.*

Similarly, IR spectrum of 3 indicated the maintenance of the β-lactone moiety (1840 cm^{-1}), and NMR spectrum showed a multiplet signal due to C_1-proton and C_8-methylene protons at 2.10—3.48 ppm.

These data were well consistent with the 7-hydroxybicyclo[4.2.0]octane-7-acetic acid β-lactone structure.

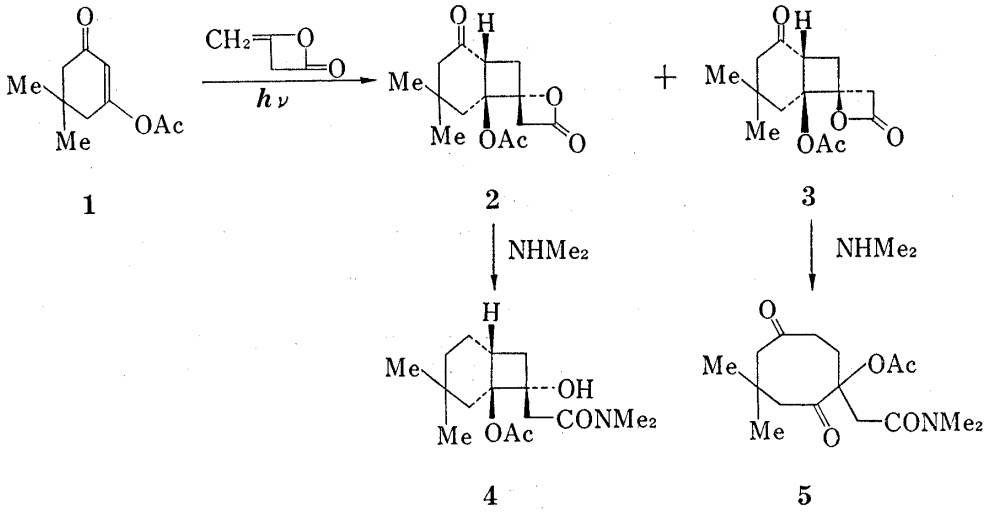
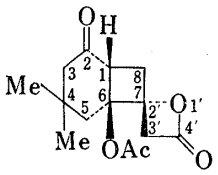
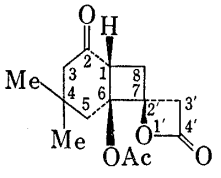


Chart 1



2



3

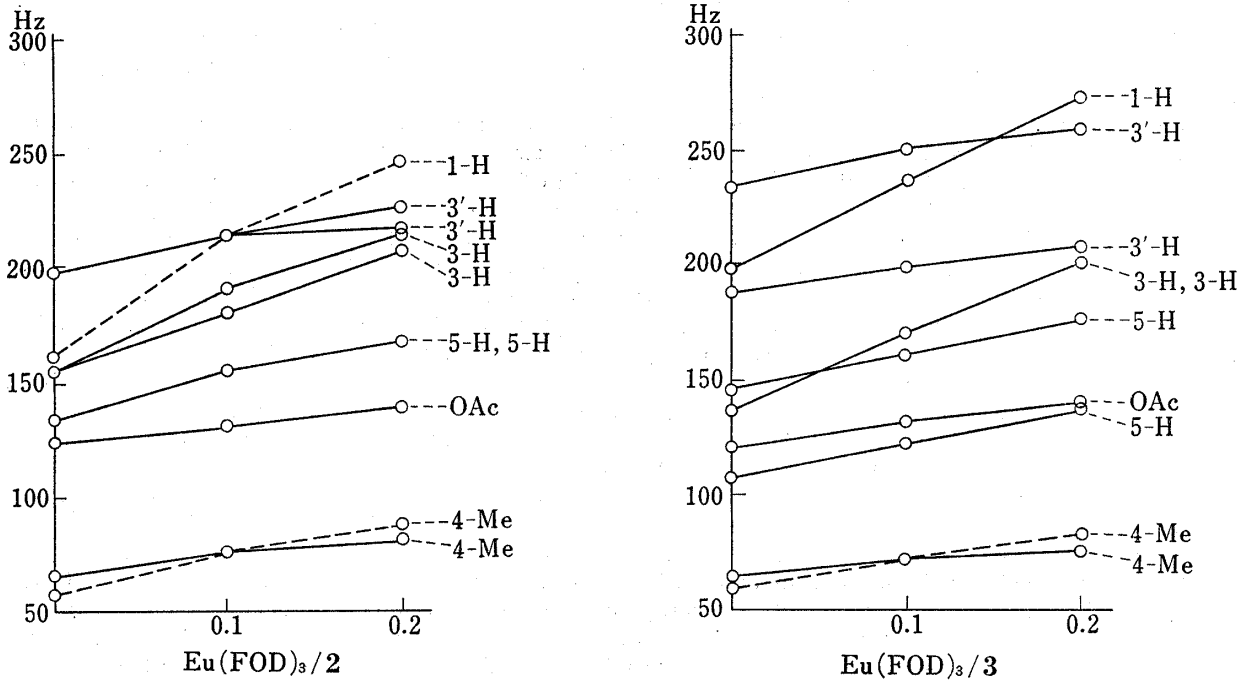
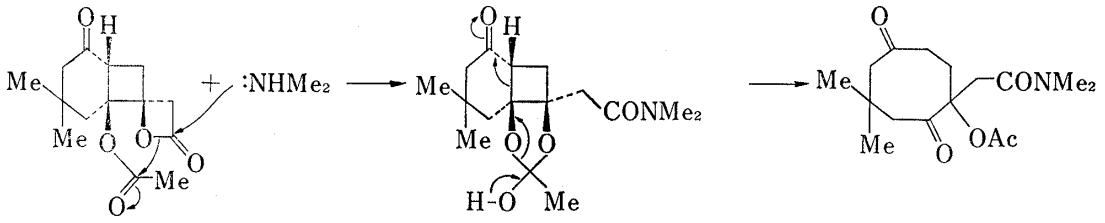


Fig. 1. The Relationship between Chemical Shifts and the Molar Ratio of $Eu(FOD)_3$/substrate (2 and 3)

Because of three asymmetric carbons several stereoisomers are possible. Of these, the *cis*-bicyclo[4.2.0]octane structure was assigned to both **2** and **3** on the basis of NMR spectroscopic study using europium shift reagent. As shown in Fig. 1, both C_1-protons show the largest paramagnetic shift, indicating the ring juncture of the bicyclooctane moiety of both **2** and **3** being the *cis* configuration.

Accordingly, compounds **2** and **3** should be the stereo isomers concerning the C_7-configuration which was determined by the chemical reactions as following: reaction of compound **2** with dimethylamine gave rise to the amide (**4**), which still maintained the bicyclooctane moiety. On the other hand, the same reaction of compound **3** resulted in the ring expansion to give the cyclooctane derivative (**5**). Structural assignment of the products **4** and **5** were made on the basis of elemental analyses and spectroscopic data detailed in the Experimental section. From the above reactions, we presumed that the acetoxy group and the oxetane ring oxygen of compound **2** should be the *trans* configuration while those of **3** being *cis*. That is to say, nucleophilic addition of dimethylamine results only the ring opening of the β-lactone to give the amide **4**. On the other hand, the ring opening of the β-lactone ring of compound **3** results in the acyl migration accompanied with the ring fission of the bicyclo structure to give the cyclooctane derivative (**5**) *via* the 1,3-dioxalane intermediate (**A**).



3 **A** **5**

Chart 2

Experimental

IR spectra were taken with a JASCO model IR-S spectrophotometer. NMR spectra were taken on a Hitachi R-20 instrument and a JEOL-JNM-PS-100. Chemical shifts are reported on the δ scale, parts per million downfield from tetramethylsilan as an internal standard. All melting points were uncorrected. The ultraviolet (UV) light source was a RIKO UVL-100HA watercooled high pressure mercury lamp (Pyrex filter).

Reaction of 3-Acetoxy-5,5-dimethyl-2-cyclohexen-1-one (1) with Diketene to give 6-Acetoxy-7-hydroxy-4,4-dimethyl-*cis*-bicyclo[4.2.0]octan-2-one-7-acetic Acid β-Lactone (2 and 3)——1) A solution of dimedone acetate (**1**) (3.7 g, 0.02 mol) and diketene (17 g, 0.2 mol) in ethanol (30 ml) was irradiated with ice-cooling under nitrogen for 12 hr. The solvent and excess diketene were removed by vacuum distillation on a water bath. Vacuum distillation was continued on an oil bath at 130° and 1.7 g of compound **1** was recovered. The residue was adsorbed on a silica gel (Wakogel C-200, 130 g) column. Elution with benzene (4 l) gave compound **3** as prisms (from ether) (0.6 g, 12%). mp 114—116°. *Anal.* Calcd. for $C_{14}H_{18}O_5$ (**3**): C, 63.14; H, 6.81. Found: C, 63.22; H, 6.58. IR ν_{max}^{KBr} cm^{-1}: 1840 (β-lactone), 1740 (ester), 1695 (ketone). NMR ($CDCl_3$) ppm: 0.97 (3H, s, 4-CH_3), 1.07 (3H, s, 4-CH_3), 1.63—2.60 (2H, ABq, J=15.5 Hz, 5-CH_2), 2.04 (3H, s, OAc), 2.28 (2H, s, 3-CH_2), 2.10—3.48 (3H, m, 1-CH, 8-CH_2), 3.00—4.07 (2H, ABq, J=16 Hz, oxetane CH_2). Subsequent elution with chloroform gave compound **2** as needles (from ether) (0.2 g, 4%), mp 149—150°. *Anal.* Calcd. for $C_{14}H_{18}O_5$ (**2**): C, 63.14; H, 6.81. Found: C, 63.22; H, 6.70. IR ν_{max}^{KBr} cm^{-1}: 1830 (β-lactone), 1740 (ester), 1700 (ketone). NMR ($CDCl_3$) ppm: 0.97 (3H, s, 4-CH_3), 1.10 (3H, s, 4-CH_3), 2.07 (3H, s, OAc), 2.24 (2H, s, 5-CH_2), 2.24—2.70 (3H, m, 1-CH, 8-CH_2), 2.58 (2H, s, 3-CH_2), 3.32 (2H, s, oxetane CH_2).

2) A solution of compound **1** (1.8 g) and diketene (9 g) in acetonitrile (12 ml) was irradiated under the same condition as above to give 0.2 g (7%) of compound **3** and 0.3 g (11%) of compound **2**.

6-Acetoxy-7-hydroxy-N,N,4,4-tetramethyl-*cis*-bicyclo[4.2.0]octan-2-one-7-acetamide (4)——A mixture of compound **2** (106 mg, 0.4 mmol), 40% dimethylamine (80 mg, 0.8 mmol), and chloroform (2 ml) was stirred at room temperature for 2 hr. The mixture was diluted with chloroform (10 ml), and the chloroform layer was washed with water, dried over magnesium sulfate, and filtered. The filtrate was condensed. The residue was convered with a small amount of *n*-hexane and kept in a refrigerator overnight. Crystals separated were collected, and recrystallized from ethyl acetate–*n*-hexane (1: 3) to give the amide (**4**) (98 mg, 80%)

as leaves, mp 124—126°. *Anal.* Calcd. for $C_{16}H_{25}NO_5$ (**4**): C, 61.71; H, 8.09; N, 4.50. Found: C, 62.12; H, 8.16; N, 4.43. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3380, 1735, 1700, 1628. NMR ($CDCl_3$) ppm; 0.94 (3H, s, CH_3), 1.11 (3H, s, CH_3), 1.84—2.53 (2H, ABq, $J=11.5$ Hz, CH_2), 1.96—2.32 (2H, ABq, $J=10$ Hz, CH_2), 2.03 (3H, s, OAc), 2.14—2.85 (3H, m), 2.64 (2H, s, CH_2), 2.96 (3H, s, NCH_3), 3.04 (3H, s, NCH_3), 5.25 (1H, broad, OH).

1-Acetoxy-N,N,4,4-tetramethylcyclooctane-2,6-dione-1-acetamide (**5**)——A mixture of compound **3** (133 mg, 0.5 mmol), 40% dimethylamine (100 mg, 1 mmol) and chloroform (2 ml) was stirred at room temperature for 2 hr. The mixture was diluted with chloroform (10 ml). The chloroform layer was washed with water, dried over magnesium sulfate, and condensed. The resulting residue was kept in a refrigerator overnight giving a crystalline solid. Recrystallization from *n*-hexane gave compound **5** as prisms (110 mg, (71%), mp 103—104°. *Anal.* Calcd. for $C_{16}H_{25}NO_2$ (**5**): C, 61.71; H, 8.09; N, 4.50. Found: C, 61.65; H, 8.27; N, 4.62. IR ν_{max}^{KBr} cm^{-1}: 1730 (ester), 1710 (ketone), 1690 (ketone), 1635 (amide). NMR ($CDCl_3$) ppm: 1.09 (3H, s, CH_3), 1.20 (3H, s, CH_3), 1.88—3.10 (8H, m, $4\times CH_2$), 2.16 (3H, s, OAc), 2.88 (3H, s, NCH_3), 2.97 (3H, s, NCH_3), 3.28 (2H, s, $CH_2CON<$).

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Syntheses of Apogalanthamine Analogs as α-Adrenergic Blocking Agents. III.[1] 5,6,7,8-Tetrahydrodibenz[*c*,*e*]azocine and Its 6-Substituted Derivatives[2]

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The apogalanthamine analogs, 5,6,7,8-tetrahydrodibenz[*c*,*e*]azocine (**10**) and its N-substituted derivatives (**11**—**15**) were synthesized. Boron tribromide was found to be effective for cleavage and bromination of the lactone ring in diphenide (**25**). This is the first time it has been employed as a cleaving and brominating agent for a lactone.

Keywords——apogalanthamine analog; α-adrenergic blocking agent; tetrahydrodibenz[*c*,*e*]azocine; intramolecular cyclization; diphenide; boron tribromide; cyanohydroxyphenanthrene

Recently Ishida, *et al.* reported[4] that the 6-β-bromoethylated derivative (**1**)[5] of 10,11-methylenedioxy-5,6,7,8-tetrahydrodibenz[*c*,*e*]azocine (**2**) has an irreversible α-adrenergic blocking action and blocks the response of rat aortic strips to adrenaline rather than their response to 5-hydroxytryptamine (5-HT). On the other hand, tests on the apogalanthamine analogs,[1] compound **2** and its 6-alkylated derivatives (**3** and **4**), 10,11-dimethoxy- and 11,12-dimethoxydibenz[*c*,*e*]azocine (**5** and **6**, respectively) and their 6-alkylated derivatives (**7**, **8**, and **9**), and 5,6,7,8-tetrahydrodibenz[*c*,*e*]azocine (**10**) and its 6-substituted derivatives (**11**—**13**) showed

1) *a*) Part I: S. Kobayashi, M. Kihara, S. Shizu, S. Katayama, H. Ikeda, K. Kitahiro, and H. Matsumoto, *Chem. Pharm. Bull.* (Tokyo), **25**, 3312 (1977) *b*) Part II: M. Kihara and S. Kobayashi, *ibid.*, **26**, 155 (1978).
2) This forms Part XVIII of "Studies on the Syntheses of Benzoheterocyclic Compounds" by S. Kobayashi, Part XVII: ref. Ib.
3) Location: *1-78, Sho-machi, Tokushima, 770, Japan.*
4) Y. Ishida, K. Watanabe, S. Kobayashi, and M. Kihara, *Jpn. J. Pharmacol.*, **26**, 607 (1976).
5) S. Kobayashi, M. Kihara, K. Yamasaki, Y. Ishida, and K. Watanabe, *Chem. Pharm. Bull.* (Tokyo), **23**, 3036 (1975).