5α-Cholestan-3β-yl-2-acetamido-2-deoxy-β-D-glucopyranoside (VIIIb)——Yield 53%. mp 192—193°. $[\alpha]_D^{21}$ −10.0° (c=0.1, MeOH). *Anal.* Calcd. for $C_{35}H_{61}NO_6 \cdot 3/4H_2O$: C, 69.44; H, 10.41; N, 2.31. Found: C, 69.37; H, 10.39; N, 2.35. NMR (DMSO-d_6) δ: 0.64 (3H, s, 18-CH_3), 0.73 (3H, s, 19-CH_3), 0.84 (6H, d, J=7 Hz, 26- and 27-CH_3), 1.80 (3H, s, -$COCH_3$), 7.60 (1H, m, N-H).

5α-Cholestan-3α-yl-2-acetamido-2-deoxy-β-D-glucopyranoside (VIIIc)——Yield 73%. mp 190—191°. $[\alpha]_D^{21}$ +30.0° (c=0.1, MeOH). *Anal.* Calcd. for $C_{35}H_{61}NO_6 \cdot 1/2H_2O$: C, 69.96; H, 10.40; N, 2.33. Found: C, 69.75; H, 10.21; N, 2.44. NMR (DMSO-d_6) δ: 0.62 (3H, s, 18-CH_3), 0.74 (3H, s, 19-CH_3), 0.86 (6H, d, J=7 Hz, 26- and 27-CH_3), 1.76 (3H, s, -$COCH_3$), 7.58 (1H, m, N-H).

(6,7α,7β-d_3-Cholest-5-en-3β-yl-β-D-glucopyranosid)uronic Acid (IX)——6,7α,7β-d_3-Cholesterol (103 mg, 90% d_3), obtainable by the method of Wyllie *et al.*,[19] was treated in the manner as described for IIIa. mp 228—230° (dec.). Mixed melting point on admixture with a non-labeled authentic sample showed no depression. Mass spectrum (m/e 372[M-423]$^+$) showed the following isotopic composition: 0% d_0, 2% d_1, 11% d_2 and 87% d_3.

Gas Chromatography-Mass Spectrometry

Non-deuterated and deuterated cholesterol glucuronides (IIIa, IX) were analyzed as the methyl ester-trimethylsilyl (TMS) ether derivatives. IIIa or IX (100 μg) was dissolved in MeOH and methylated with diazomethane in the usual manner. The methyl ester was then treated with TMS imidazole (50 μl) in pyridine (50 μl) at 50° for 1 hr. The apparatus used for electron impact mass spectrometry was a JEOL JMS-01SG-2 g.c.m.s. system equipped with a JEOL JMA-2000 computer. A coiled glass column (1 m×2 mm i.d.) was packed with 3% OV-1 on Gas Chrom Q (100—120 mesh) and used at 300°. The temperatures of the separator and ion source were 280° and 270°, respectively. The electron energy was 75 eV.

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UDC 547.746.04 : 547.239.1.04

A Convenient Synthesis of α-Substituted Cyclic α-Imino Acids[1]

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Various α-substituted α-imino acids (**6**) were synthesized in good yields by the reaction of methyl α-substituted α-isocyanoacetates with alkylene bromides in the presence of sodium hydride, followed by cyclization and hydrolysis.

Keywords——methyl α-isocyanoacetates; alkylene bromides; α-substituted cyclic α-imino acid methyl esters; α-substituted cyclic α-imino acids; alkylation; ring transformation

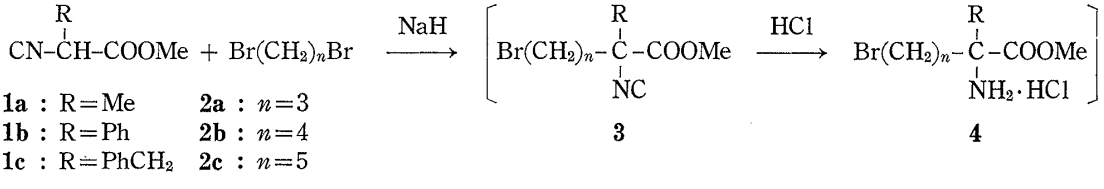
Various cyclic α-imino acids such as proline and pipecolic acid are not only important constituents of proteins but are also pharmacologically interesting as intermediates in the preparation of drugs. On the other hand, the corresponding α-substituted cyclic α-imino acids have hardly been investigated and only a few methods for their syntheses have been

1) This study was presented at the 28th Annual Meeting of the Kinki Branch of the Pharmaceutical Society of Japan, Nishinomiya, October 1978.

2) Location: *16-89 Kashima-3-chome, Yodogawa-ku, Osaka 532, Japan.*

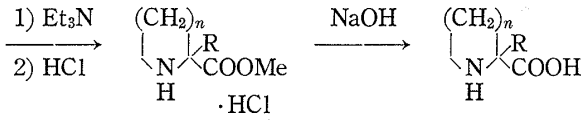
reported so far; *e.g.* the intramolecular cyclization of 5-methyl or 5-phenyl-5-(3-hydroxypropyl)hydantoins followed by hydrolysis[3] and the alkylation of 2-carbethoxycyclopentanone or 2-carbethoxycyclohexanone followed by ring expansion using the Schmidt or Beckmann rearrangement.[4] However, these methods are complicated and are not really suitable for practical use.

In our studies on the syntheses of amino acids and related compounds using isocyano compounds,[5] we previously reported syntheses of α-methyl-α-amino acids by the reaction of α-isocyanopropionates with alkylating reagents.[6] Schöllkopf *et al.* also described a similar alkylation.[7] Now, we wish to report a convenient method for the synthesis of various kinds



1a : R=Me **2a** : n=3
1b : R=Ph **2b** : n=4
1c : R=PhCH$_2$ **2c** : n=5

3 **4**



5a—i **6a—i**

a : n=2 R=Me **d** : n=3 R=Me **g** : n=4 R=Me
b : n=2 R=Ph **e** : n=3 R=Ph **h** : n=4 R=Ph
c : n=2 R=PhCH$_2$ **f** : n=3 R=PhCH$_2$ **i** : n=4 R=PhCH$_2$

TABLE I. α-Substituted Cyclic α-Imino Acid Methyl Ester Hydrochlorides (**5**)

Compd.	mp (°C) (dec.)	Yield (%) based on **1**	IR ν_{max}^{Nujol} cm^{-1}	NMR (D_2O), δ COOMe	NMR (D_2O), δ Other	Formula	Analysis (%) Calcd. (Found) C	H	N	Cl
5a	148—150	58	1730	3.75	1.43 (s, Me)	$C_7H_{14}ClNO_2$	46.78 (46.34	7.85 7.74	7.78 7.92	19.73 19.87)
5b	195—196	45	1735	3.73	7.30 (s, Ph)	$C_{12}H_{16}ClNO_2$	59.63 (59.72	6.67 6.28	5.80 5.80	14.67 14.72)
5c	169—171	52	1735	3.75	7.45 (br. s, Ph)	$C_{13}H_{18}ClNO_2$	61.04 (61.24	7.09 7.27	5.48 5.33	13.86 14.21)
5d	151—152	59	1735	3.80	1.60 (s, Me)	$C_8H_{16}ClNO_2$	49.61 (49.50	8.33 8.34	7.23 7.18	18.31 18.10)
5e	190—192	58	1730	3.80	7.40 (s, Ph)	$C_{13}H_{18}ClNO_2$	61.05 (60.75	7.09 7.03	5.48 5.49	13.86 14.23)
5f	>280	46	1735	3.73	7.30 (br. s, Ph)	$C_{14}H_{20}ClNO_2$	62.33 (61.86	7.47 7.45	5.19 5.16	13.14 13.37)
5g	171—174	73	1735	3.78	1.63 (s, Me)	$C_9H_{18}ClNO_2$	52.05 (51.82	8.74 8.51	6.74 6.89	17.07 17.52)
5h	155—157	56	1735	3.75	7.40 (s, Ph)	$C_{14}H_{20}ClNO_2$	62.33 (62.58	7.47 7.25	5.19 4.92	13.14 12.89)
5i	>280	50	1735	3.80	7.25 (br. s, Ph)	$C_{15}H_{22}ClNO_2$	63.48 (63.35	7.81 7.61	4.94 4.74	12.49 12.64)

3) *a*) E.E. Smissman, P.L. Chien, and R.A. Robinson, *J. Org. Chem.*, **35**, 3818 (1970); *b*) J.J. Ellington and I.L. Honigberg, *ibid.*, **39**, 104 (1974).
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Table II. α-Substituted Cyclic α-Imino Acids (6)

Compd.	mp (°C) (dec.)	Yield (%)	6·HCl mp (°C) (dec.)	NMR (D_2O) δ	Formula	Analysis (%) Calcd. (Found) C	H	N	Cl
6a	263—265[a]	72							
6b	265—268[b]	88							
6c	>280	79	209—212	7.45 (br. s, Ph)	$C_{12}H_{16}ClNO_2$	59.63 (59.51	6.67 6.64	5.80 6.02	14.67 14.21)
6d	>280	88	253—255	1.40 (s, Me)	$C_7H_{14}ClNO_2$	46.80 (46.84	7.86 7.93	7.80 7.99	19.74 19.93)
6e	>280	75	254—256	7.50 (s, Ph)	$C_{12}H_{16}ClNO_2$	59.63 (59.89	6.67 7.02	5.80 5.61	14.67 14.69)
6f	>280[c]	61	>280	7.30 (br. s, Ph)	$C_{13}H_{18}ClNO_2$	61.05 (60.98	7.09 7.08	5.48 5.34	13.86 14.25)
6g	210—212	65	267—270	1.40 (s, Me)	$C_8H_{16}ClNO_2$	49.61 (50.08	8.32 8.79	7.23 6.92	18.31 18.05)
6h	>280	89	>280	7.35 (s, Ph)	$C_{13}H_{18}ClNO_2$	61.05 (61.09	7.09 7.12	5.48 5.74	13.86 13.71)
6i	>280	61	238—240	7.25 (br. s, Ph)	$C_{14}H_{20}ClNO_2 \cdot 1/2H_2O$	60.32 (60.62	7.59 7.93	5.02 5.21	12.72 12.61)

a) Lit.,[3a] 263—264.5° (dec.). *b*) Lit.,[3b] 260—265° (dec.). *c*) Lit.,[4] 380°(dec.).

of α-substituted cyclic α-imino acids by the alkylation of isocyano compounds, followed by cyclization.

The reaction of methyl α-substituted α-isocyanoacetates (**1a—c**), which are easily derived from the corresponding N-formylamino acid methyl esters,[8] with alkylene bromide (**2a—c**) was carried out in the presence of sodium hydride in tetrahydrofuran to obtain the α-alkylated products (**3**). Subsequently, compound **3** was treated with hydrochloric acid without purification to convert the isocyano group into an amino group, yielding ω-bromoalkyl-α-amino acid methyl esters (**4**). Next, **4** was derivatized to the corresponding α-substituted cyclic α-imino acid methyl esters (**5a—i**) by treatment with triethylamine, and these products were isolated as the hydrochlorides in good yields. Furthermore, saponification of **5a—i** gave the desired α-substituted α-imino acids (**6a—i**). The structures of these compounds **5a—i** and **6a—i** were confirmed by the spectral and analytical data, as summarized in Table I and II.

Experimental

Melting points are uncorrected and were measured with a Yamato melting point apparatus. Infrared (IR) spectra were recorded with a Shimadzu IR-27G spectrophotometer and nuclear magnetic resonance (NMR) spectra with a Hitachi Perkin-Elmer R-20A high resolution NMR spectrometer using tetramethylsilane as an internal standard.

General Procedure for the Preparation of α-Substituted Cyclic α-Imino Acid Methyl Ester Hydrochlorides (5)——A mixture of **1a—c** (0.1 mol), **2a—c** (0.15 mol) and tetrahydrofuran (50 ml) was added dropwise to a stirred suspension of sodium hydride (61% in oil, 5.9 g, 0.15 mol) in tetrahydrofuran (50 ml) at 25°. After stirring for 1 hr at room temperature, the mixture was neutralized with 10% AcOH under ice cooling and then concentrated under reduced pressure. The resulting residue was extracted with AcOEt and the extract was washed with H_2O, dried over Na_2SO_4, and evaporated down *in vacuo*. The oily products (crude **3**) thus obtained were dissolved in MeOH (50 ml) and conc. HCl (10 ml) was added dropwise below 15°. After stirring for 18 hr at 5—10°, the solvent was concentrated to dryness under reduced pressure to afford the crude compounds **4**. Subsequently, the products **4** (without purification) were heated under reflux in a mixture of triethylamine (0.2 mol) and tetrahydrofuran (200 ml) for 1 hr. The precipitates were filtered off, and the filtrate was evaporated down *in vacuo*. The resulting residue was extracted with AcOEt and the extract

8) I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer, and K. Offermann, *Angew. Chem.*, **77**, 492 (1965).

was washed with H_2O, dried over Na_2SO_4, and concentrated under reduced pressure. The oily residue was treated with 10% HCl–MeOH and the resulting crystals were recrystallized from ether–EtOH to afford **5** as hydrochlorides. These results are summarized in Table I.

General Procedure for the Preparation of α-Substituted Cyclic α-Imino Acids (6)——A mixture of **5** (0.01 mol), 10% NaOH (10 ml) and EtOH (50 ml) was heated under reflux for 30 min with stirring, then EtOH was evaporated off *in vacuo*. The resulting residue was applied to a strong cation exchange resin (Amberlite IR 120) and eluted with 4 N NH_4OH. After removal of the eluent by evaporation, the residue was recrystallized from aqueous EtOH to obtain the desired cyclic α-imino acids **6**. Furthermore, treatment with 10% HCl–dioxane, followed by recrystallization from EtOH–ether gave analytically pure **6**·HCl as colorless prisms. These results are summarized in Table II.

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Sulfonoglycolipid from the Sea Urchin *Anthocidaris crassispina* A. Agassiz

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On the basis of chemical and physicochemical evidence, a sulfonoglycolipid isolated from the shell of the sea urchin *Anthocidaris crassispina* A. Agassiz has been shown to be a 96:4 mixture of 1′-O-palmitoyl-3′-O-(6-sulfo-α-D-quinovopyranosyl)glycerol and its myristoyl counterpart.

Keywords——sea urchin; *Anthocidaris crassispina*; sulfonoglycolipid; ^{1}H-NMR; ^{13}C-NMR; FD-MS

Among five classes in the phylum Echinodermata, *Holothuroidea* (sea cucumber) and *Asteroidea* (starfish) are of particular interest in view of their oligoglycosidic metabolites, which exhibit various biological activities. We have already elucidated the chemical structures of some of those: *e.g.* thornasteroside A (from *Acanthaster planci* L.),[2] holotoxins A and B (from *Stichopus japonicus* Selenka),[3] and holothurins A[4] and B[5] (from *Holothuria leucospilota* Brandt). As a continuing study on the metabolites of Echinodermata, we have been examining the chemical constituents of the sea urchin *Anthocidaris crassispina* A. Agassiz (Japanese name, "murasaki-uni") and have isolated a sulfonoglycolipid (designated as Ant-1) from the shell. This paper deals with a structural study of Ant-1 (**1**) showing that it consists of 1′-O-palmitoyl-3′-O-(6-sulfo-α-D-quinovopyranosyl)glycerol and the myristoyl counterpart in a 96:4 ratio.

The aqueous methanolic extract of the shell of *A. crassispina* was subjected to solvent partition, column chromatography, and droplet counter-current chromatography (DCC) (Chart 1). A fraction containing Ant-1 thus obtained was purified by silica gel column chromatog-

1) Location: *133-1, Yamada-kami, Suita, Osaka 565, Japan.*
2) *a*) I. Kitagawa, M. Kobayashi, and T. Sugawara, *Chem. Pharm. Bull.* (Tokyo), **26**, 1852 (1978); *b*) I. Kitagawa and M. Kobayashi, *ibid.*, **26**, 1864 (1978).
3) I. Kitagawa, H. Yamanaka, M. Kobayashi, T. Nishino, I. Yosioka, and T. Sugawara, *Chem. Pharm. Bull.* (Tokyo), **26**, 3722 (1978).
4) I. Kitagawa, T. Nishino, and Y. Kyogoku, *Tetrahedron Lett.*, **1979**, 1419.
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