α,β-Unsaturated Carboxylic Acid Derivatives. XIII. The Synthesis and Configuration of Alkyl 2-Acylamino-2-alkenoates and Their Cyclized 2,5-Piperazinedione Derivatives[1]

Chung-gi SHIN, Masato HAYAKAWA, Takamichi SUZUKI, Akira OHTSUKA,* and Juji YOSHIMURA**

Laboratory of Organic Chemistry, Faculty of Technology, Kanagawa University, Rokkakubashi, Kanagawa-ku, Yokohama 221

***Laboratory of Chemistry for Natural Products, Faculty of Science, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152*

(Received June 24, 1977)

It is described that alkyl (*E*)- and (*Z*)-2-halo (Cl, Br, and I)-acetylamino-2-alkenoate (DHA), obtained by the condensation of alkyl 2-oxoalkanoate with chloro- or bromoacetamide and by halogen exchange from the chlorine of DHA to iodine, are cyclized with ammonia or hydroxylamine to give the (*E*)- and (*Z*)-isomers of unsymmetric 3-alkylidene-2,5-piperazinediones and their 1-hydroxy derivatives respectively. Alkyl (*E*)- and (*Z*)-2-iodoacetylamino-2-alkenoates were converted into the corresponding acetylamino- and phthalimidoacetylamino derivatives. The configurations of all the DHA and 2,5-piperazinedione derivatives were determined from the NMR spectra data.

Although there have been many works on the synthesis of 2-acylamino-2-alkenoic acids (α-dehydroamino acids; DHA), only a few papers have been recently reported on the geometric stereochemistry. Especially with regard to the chemical proof for the configurational assignment of the geometric isomers, only one example has been recently reported.[2] Austel and Steglich distingiushed the configuration of (*Z*)-3-methyl-5,5,5-trifluoro-2-trifluoroacetyl-4-trifluoroacetoxy-2-pentenoic acid by successfully converting it into the corresponding lactone, whereas the (*E*)-isomer did not cyclize. The NMR data of this compound indicated that methyl or methine protons *cis* to the trifluoroacetyl group appeared downfield relative to the occupied *trans* position. More recently, Srinivasan *et al.*[3] and another workers[4] have also commented that the low chemical shifts of 3-methyl groups *cis* to the alkoxycarbonyl group of DHA form a more reliable criterion for the assignment of stereochemistry than that of those *trans*.

Previously, Shin *et al.* reported briefly on the possibility of the available chemical determination of alkyl (*E*)- and (*Z*)-2-chloroacetylamino-2-alkenoates (**1**) on the basis of the chemical behavior of 3-alkylidene-2,5-piperazinediones (**6**), cyclization products of **1**, in acetylation.[5,6]

In this paper, we wish to report in detail an NMR method which can be used for the configurational determination of several DHA's and the stereochemistry of 3-alkylidene-(**6**)- and 3-alkylidene-1-hydroxy-2,5-piperazinediones (**7**), obtained by the cyclization of DHA with ammonia and hydroxylamine respectively.

Results and Discussion

Alkyl 2-Acylamino-2-alkenoates. The alkyl 2-chloroacetyl-(**1**)- and bromoacetylamino-2-alkenoate (**2**) were prepared in one step by the reaction of alkyl 2-oxoalkanoates with chloroacetamide or bromoacetamide in benzene under reflux for *ca.* 15 h, as has been reported previously.[5] Since the DHA thus obtained was found to be a mixture of (*E*)- and (*Z*)-isomers, the mixture was separated by chromatography on a silica gel column, using benzene as the eluent, to give, first, a colorless syrup and then crystals.

According to a method previously reported,[2-6] the geometric stereochemistry of the above DHA was readily determined by a comparison of the NH, vinyl, and 3-alkyl protons between (*E*)- and (*Z*)-isomers. The NMR data in Table 2 show that all the chemical shifts of the NH, vinyl, and 3-alkyl protons of **1** and **2** obtained in the oily state resonate at fields lower by 0.51—0.69, 0.26—0.54, and 0.33—0.76 ppm respectively than those of **1** and **2** in the crystalline state, indicating that the former syrup has the (*E*)-configuration, while the latter crystals have the (*Z*)-configuration.

Moreover, the syntheses of both alkyl (*E*)- and (*Z*)-2-iodoacetylamino-2-alkenoates (**3**) were readily achieved and in fairly good yields by the treatment of pure (*E*)- or (*Z*)-**1** with potassium iodide in acetone under reflux for 3 h (Table 1). The NMR spectrum shows a tendency similar to that described above, resonating the chemical shifts of the NH, vinyl, and 3-alkyl protons of the (*E*)-isomer at fields lower by 0.35—0.74, 0.26—0.35, and 0.30—0.68 ppm respectively than that of the (*Z*)-isomer. It is noteworthy that the chemical shifts of not only methylene but also of NH protons in the haloacetylamino groups in both (*E*)- and (*Z*)-isomers in the same series were lower by the order of **1**, **2**, or **3**, indicating that the substituent effect of halogen atoms reaches the nitrogen atom beyond the carbonyl function.

On the other hand, the configuration of one isomer of the alkyl 2-acetylamino-(**4**)- and 2-(phthalimidoacetylamino)-2-alkenoate (**5**),[7,8] obtained previously by the elimination of alkyl 2-(acetoxyamino)- or 2-(*N,O*-diacetylhydroxyamino)-2-alkenoates with a base, was confirmed unambiguously to have the (*Z*)-geometry by the agreement of the physical constants and spectral data with those derived here by the reaction of (*Z*)-**3** with zinc powder or potassium phthalimide. A similar treatment of (*E*)-**3** gave (*E*)-**4** and **5** in fairly good yields

* Present address: Kokusan Kagaku Co., Ltd., Itabashi-ku, Tokyo 174.

(Table 3). The NMR spectral pattern of **4** is very similar to those of **1**, **2**, and **3**, whereas in the case of **5** the chemical shifts of the NH and 3-alkyl protons of the (*E*)-isomer resonate at fields lower by 0.26—0.35 and 0.19—0.27 ppm respectively than that of the (*Z*)-isomer, while that of the vinyl proton of the (*E*)-isomer appears at field higher by 0.50—0.58 ppm, as has been reported recently.[3]

The evidence regarding the NMR data of DHA mentioned here can also be used to determine the configurations of other alkyl 2-(2-halopropionylamino)- and 2-(ethoxycarbonylamino)-2-alkenoate[1] and 2-azido-2-alkenoate[9] as well as 2-amino-2-alkenoate[10] by a comparison of the NH, vinyl, and 3-alkyl protons. These results will be reported and discussed elsewhere.

In the IR spectral data on **1**—**4** and **5**, the characteristic differences between the (*E*)- and (*Z*)-geometric isomers could not be recognized. The absorption bands of NH in the 3150—3350 cm^{-1} region, the ester carbonyl in the 1720—1735 cm^{-1} region, and the amide carbonyl in the 1645—1690 cm^{-1} region supported these structures, but that of the carbon-carbon double bond overlapped the amide carbonyl region.

The yields, physical constants, and spectral data of **1**—**4** and **5** are summarized in Tables 1, 2, and 3.

Cyclization Reactions. According to the method previously reported by us[5,6,8] and by Cook and Slater,[11] the cyclization reaction of individual (*E*)- and (*Z*)-**1** with ammonia and that of (*E*)- and (*Z*)-**2** and **3** with hydroxylamine were carried out. Pure (*E*)- or (*Z*)-**1** was treated with excess gaseous ammonia in ethanol to convert it into (*E*)- and (*Z*)-**6** respectively in *ca.* 50% yields. Since the cyclization of **1** with hydroxylamine in ethanol did not proceed, a similar treatment of the pure (*E*)- or (*Z*)-**2** with hydroxylamine under reflux in a stream of nitrogen for 18 h gave the expected (*E*)- and (*Z*)-**7** respectively as pinkish crystals, although the yields were low. However, in the case of **3**, it was found that the similar cyclization proceeded to give **7** in a comparatively good yield. The **7** thus obtained turned deep violet upon coloration with ferric chloride in methanol, indicating the presence of a hydroxamic acid structure. This seems to be the first example of the formation of unsymmetric cyclic monohydroxamic acid (**7**). This result offers many useful suggestions for the synthesis of antibiotics mycelianamide,[12] which has a cyclic dihydroxamic acid structure.

The yields, physical constants, and spectral data of **6** and **7** are summarized in Tables 4 and 5.

The NMR data of **6** and **7** may be summarized as follows:

1) Chemical shifts of NH and methylene protons of these cyclic compounds: **6** and **7** are lower, but those of vinyl protons are higher than those of **1**—**4**, reflecting

Table 1. The yields, physical constants, and elemental analyses of **1**, **2**, and **3**

Compound	R		Yield (%)	Bp °C/mmHg (Mp °C)[a]	Formula	Found (Calcd), % C	H	N
1a	CH_3	*E*	12.6	120—122/1				
		Z	37.7	(48—49)				
1b	C_2H_5	*E*	11.1	121—123/1				
		Z	34.9	(53—54)				
1c	*n*-C_3H_7	*E*	10.5	132—133/1				
		Z	31.5	(52—53)				
1d	*i*-C_3H_7[c]	*E*	11.2	133—135/1				
		Z	33.8	(68.5—69)				
1e	C_6H_5	*E*	14.1	178—181/1				
		Z	28.4	(103—104)				
2a	CH_3	*E*	8.5	123—125/1	$C_8H_{12}NO_3Br$	38.53	4.71	5.61
		Z	37.2	(71—73)		(38.42	4.80	5.60)
2b	C_2H_5	*E*	12.3	132—134/1	$C_9H_{14}NO_3Br$	40.81	5.23	5.40
		Z	40.7	(66—68)		(40.92	5.31	5.31)
2c	*n*-C_3H_7	*E*	9.8	139—141/1	$C_{10}H_{16}NO_3Br$	43.21	5.70	4.99
		Z	57.7	(75—76)		(43.20	5.76	5.04)
2d	*i*-C_3H_7[c]	*E*	10.7	125—128/1	$C_9H_{14}NO_3Br$	40.92	5.11	5.42
		Z	35.2	(68—69)		(40.92	5.31	5.31)
2e	C_6H_5	*E*	11.3	160—163/1	$C_{13}H_{14}NO_3Br$	50.11	4.50	4.32
		Z	28.9	(105—107)		(50.02	4.49	4.49)
3a	CH_3	*E*	90.2	(80—81)	$C_8H_{12}NO_3I$	33.76	4.02	4.76
		Z	93.4	(105—106)		(33.33	4.04	4.72)
3b	C_2H_5	*E*	88.5	(87—88)	$C_9H_{14}NO_3I$	34.62	4.44	4.25
		Z	92.7	(107—108)		(34.74	4.05	5.40)
3c	*n*-C_3H_7	*E*	87.9	(79—80)	$C_{10}H_{16}NO_3I$	36.81	4.93	4.17
		Z	81.1	(76—77)		(36.94	4.92	4.31)
3d	*i*-C_3H_7[c]	*E*	91.3	(64—65)	$C_9H_{14}NO_3I$	35.01	4.48	4.49
		Z	94.8	(70—71)		(34.71	4.05	4.50)
3e	C_6H_5	*E*	83.9	syrup	$C_{13}H_{14}NO_3I$	43.44	3.90	3.64
		Z	90.2	(137—138)		(43.43	3.90	3.90)

a) Colorless needles from dibutyl ether. b) Elemental analyses of the mixture of the (*E*)- and (*Z*)-isomers.
c) Methyl ester.

TABLE 2. THE SPECTRAL DATA OF **1**, **2**, AND **3**

Compound	R		IR spectrum, cm^{-1} in KBr: NH	Ester	NCO C=C	NMR spectrum, δ in $CDCl_3$: 3-Alkyl (Phenyl)	Vinyl (J_{Hz})	-NH-	$-CH_2X$
1a	CH_3	*E*	3340—3260	1720	1678	2.16	7.30 (7.5)	8.57	4.12
		Z	3200—3160	1720	1658	1.81	6.90 (7.0)	7.88	4.17
1b	C_2H_5	*E*	3340—3260	1720	1665	2.65	7.18 (8.0)	8.57	4.14
		Z	3230	1720	1658	2.16	6.64 (7.5)	8.06	4.10
1c	n-C_3H_7	*E*	3350—3275	1730	1680	2.60	7.12 (7.5)	8.54	4.10
		Z	3250	1725	1660	2.16	6.70 (7.5)	7.85	4.10
1d	i-C_3H_7[a]	*E*	3260	1730	1678	3.40	6.94 (10.5)	8.45	4.11
		Z	3250	1740	1690	2.63	6.62 (10.5)	7.78	4.15
1e	C_6H_5	*E*	3290	1730	1680	(7.22)[b]	7.89	8.67	4.09
		Z	3240	1730	1670	(7.52—7.20)[c]		8.00	4.10
2a	CH_3	*E*	3300	1730	1680	2.14	7.22 (7.5)	8.46	3.96
		Z	3250	1720	1660	1.81	6.91 (7.5)	7.81	3.99
2b	C_2H_5	*E*	3300	1735	1690	2.63	7.16 (7.5)	8.36	3.91
		Z	3250	1730	1660	2.21	6.74 (7.5)	7.77	3.99
2c	n-C_3H_7	*E*	3250	1733	1675	2.56	7.03 (7.5)	8.49	3.96
		Z	3250	1720	1660	2.15	6.77 (7.5)	7.84	3.98
2d	i-C_3H_7[a]	*E*	3380	1730	1680	3.34	6.94 (10.0)	8.30	3.92
		Z	3250	1730	1670	2.58	6.60 (10.5)	7.68	3.96
2e	C_6H_5	*E*	3275	1720	1680	(7.23)[b]	7.94	8.60	3.90
		Z	3225	1728	1670	(7.52—7.20)[c]		7.92	3.90
3a	CH_3	*E*	3250	1718	1660	2.12	7.10 (7.5)	7.98	3.77
		Z	3250	1720	1660	1.82	6.83 (7.0)	7.60	3.83
3b	C_2H_5	*E*	3250	1730	1662	2.59	7.02 (7.5)	7.90	3.77
		Z	3260	1730	1662	2.20	6.67 (7.5)	7.55	3.81
3c	n-C_3H_7	*E*	3250	1733	1662	2.56	7.04 (7.5)	7.93	3.77
		Z	3260	1733	1668	2.17	6.70 (7.5)	7.50	3.80
3d	i-C_3H_7[a]	*E*	3250	1730	1670	3.32	6.81 (10.0)	7.86	3.77
		Z	3250	1735	1645	2.64	6.55 (10.0)	7.38	3.77
3e	C_6H_5	*E*	3225	1730	1660	(7.21)[b]	7.68	8.36	3.80
		Z	3225	1728	1662	(7.52—7.20)[c]		7.62	3.76

a) Methyl ester. b) Sharp singlet. c) Multiplet.

TABLE 3. THE YIELDS, PHYSICAL CONSTANTS, AND SPECTRAL DATA OF **4** AND **5**

Compound	R		Yield (%)	Mp °C[a] (Bp °C/mmHg)	IR spectrum, cm^{-1} δ in KBr: NH	Ester	NCO C=C	NMR spectrum, δ in $CDCl_3$: 3-Alkyl (3-Phenyl)	Vinyl (J_{Hz})	-NH-	$-COCH_3$ $-CH_2-X$
4a	CH_3	*E*	83.9	syrup[b]	3260	1738	1670	2.10	6.99 (7.5)	7.76	2.16
		Z	90.2	66—66.5	3260	1740	1672	1.80	6.80 (7.0)	7.32	2.14
4b	C_2H_5	*E*	65.0	syrup[b]	3270	1740	1675	2.58	6.93 (8.0)	7.56	2.12
		Z	81.0	(115—118/1)	3260	1740	1675	2.19	6.65 (7.0)	7.32	2.12
4c	n-C_3H_7	*E*	78.5	syrup[b]	3260	1735	1670	2.55	6.96 (7.5)	7.96	2.28
		Z	87.3	syrup[b]	3260	1735	1670	2.16	6.66 (7.5)	7.45	2.12
4d	i-C_3H_7[c]	*E*	80.7	syrup[b]	3260	1738	1670	3.26	6.66 (10.0)	7.55	2.10
		Z	84.5	syrup[b]	3250	1738	1670	2.60	6.52 (10.0)	7.38	2.19
4e	C_6H_5	*E*	75.3	syrup[b]	3260	1730	1670	(7.55)[d]		8.00	2.12
		Z	82.8	97—98	3248	1725	1665	(7.60—7.24)[e]			2.04
5a	CH_3	*E*	73.4	161—162.5	3260	1740	1680	1.90	6.04 (7.5)	9.82	4.32
		Z	74.5	180.5—181.5[f]	3250	1738	1680	1.71	6.57 (7.0)	9.56	4.36
5b	C_2H_5	*E*	73.6	158—158.5	3260	1730	1678	2.31	5.94 (7.5)	9.83	4.32
		Z	75.8	173—173.5	3250	1740	1680	2.12	6.46 (7.5)	9.58	4.36
5c	n-C_3H_7	*E*	77.6	160—160.5	3250	1730	1675	2.31	5.95 (8.0)	9.77	4.32
		Z	78.3	174—174.5	3250	1735	1675	2.12	6.45 (7.5)	9.50	4.36
5d	i-C_3H_7[c]	*E*	70.0	181.5—183	3250	1740	1680	2.92	5.80 (10.5)	9.87	4.32
		Z	81.1	162—165[i]	3250	1738	1670	2.65	6.31 (10.0)	9.52	4.36
5e	C_6H_5	*E*	77.1	190—191.5	3260	1738	1670	(7.30)[k]	6.71	10.35	4.40
		Z	82.5	191—193[j]	3260	1725	1690	(7.80—7.38)[l]	7.29	10.00	4.42

a) **4**; Colorless needles from dibutyl ether, **5**; colorless needles from ethanol. b) Colorless, purified on a silica gel column using benzene as the eluent. c) Methyl ester. d) Sharp singlet (phenyl and vinyl protons). e) Multiplet (phenyl, vinyl, and NH protons). f) Lit,[7] mp 176—179 °C. g) Lit,[7] mp 173—174 °C. h) Lit,[14] mp 196—197 °C. i) Lit,[14] mp 164—165 °C. j) Lit,[7] mp 191—193 °C. k) Sharp singlet (phenyl protons). l) Multiplet (phenyl protons).

Table 4. The yields, physical constants, and spectral data of **6**

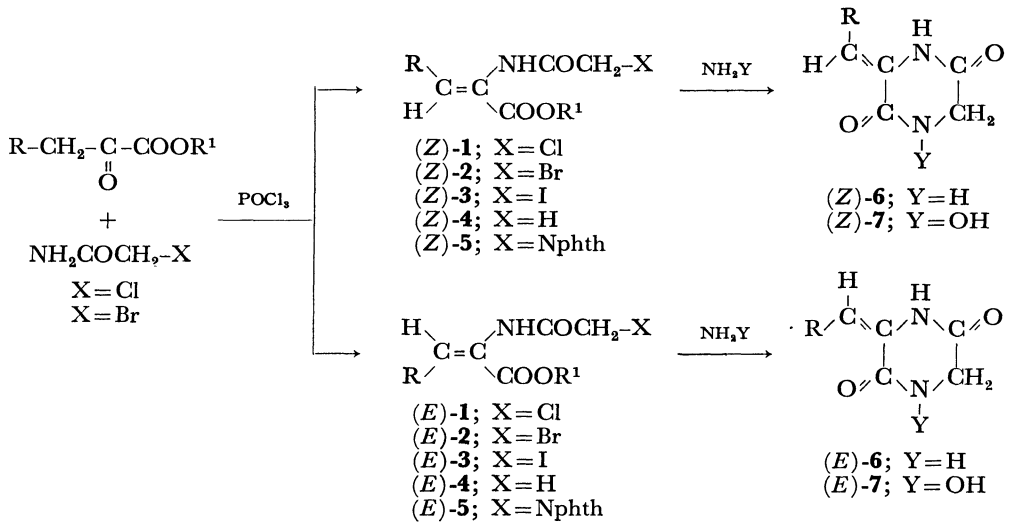
Compound	R		Yield (%)	Mp °C[a] (dec)	IR spectrum, cm^{-1} in KBr				NMR spectrum, δ in CF_3COOH				
					NH	NCO		C=C	3α-Alkyl (3α-Phenyl)	Vinyl (J_{Hz})	NH		Methylene
6a	CH_3	*E*	43.8	263—264	3180	1700	1668	1640	2.27	6.11 (7.5)	8.16	9.70	4.42
		Z	55.0	294—295	3190	1710	1685	1640	2.00	6.60 (7.5)	8.40	9.70	4.48
6b	C_2H_5	*E*	45.6	258—259	3185	1700	1660	1632	2.83	6.08 (7.5)	8.24	9.76	4.46
		Z	58.0	275—276	3190	1715	1690	1645	2.41	6.56 (7.5)	8.48	9.78	4.50
6c	*n*-C_3H_7	*E*	43.1	257—258	3190	1700	1668	1635	2.76	6.05 (7.5)	8.18	9.67	4.41
		Z	53.0	270—271	3175	1705	1685	1640	2.38	6.59 (8.0)	8.43	9.79	4.51
6d	*i*-C_3H_7	*E*	47.9	258—259	3200	1700	1680	1640	3.75	5.90 (10.0)	8.26	9.72	4.46
		Z	57.0	269—271	3200	1720		1645	2.84	6.44 (10.8)	8.46	9.78	4.52
6e	C_6H_5	*E*	55.8	270—271	3194	1700	1690	1620	(7.24)[b]	6.96	8.14	9.84	4.46
		Z	65.0	260—262	3220	1700		1635	(7.50)[c]	7.41	8.44	9.31	4.54

a) Colorless prisms from boiling water. b) Broad singlet. c) Sharp singlet.

Table 5. The yields, physical constants, and spectral data of **7**

Compound	R		Yield[a] (%)	Yield[b] (%)	Mp °C	Formula	Found (Calcd), %			IR spectrum[c]		NMR spectrum, δ in DMSO-d_6			
							C	H	N	NH (OH)	NCO (C=C)	NH	Vinyl (J_{Hz})	3α-Alkyl (3α-Phenyl)	CH_2
7a	CH_3	*Z*	19.8	30.5	263—265	$C_6H_8N_2O_3$	46.11 (46.15)	5.23 (5.16)	17.96 (17.94)	3210, (2760)	1680 (1640)	10.00,	5.85 (7.6),	1.66,	4.26
7b	C_2H_5	*Z*	20.5	41.1	237—240	$C_7H_{10}N_2O_3$	49.86 (49.41)	5.93 (5.92)	16.41 (16.46)	3180, (2760)	1690 (1640)	9.94,	5.74 (7.6),	2.18,	4.25
7c	*n*-C_3H_7	*Z*	21.1	42.0	233—235	$C_8H_{12}N_2O_3$	52.12 (52.17)	6.49 (6.57)	15.16 (15.21)	3195, (2760)	1680 (1640)	9.99,	5.80 (8.2),	2.18,	4.27
7d	*i*-C_3H_7	*E*	—	38.9	249—251	$C_8H_{12}N_2O_3$[e]	52.09 (52.17)	6.48 (6.57)	15.05 (15.21)	3060, (2790)	1695 (1620)	10.12,	5.32 (9.5),	3.72,	4.22
		Z	15.9	57.1	250—251					3200, (2760)	1690 (1625)	10.00,	5.67 (10.5),	2.88,	4.29
7e	C_6H_5	*E*	—	46.5	244—245	$C_{11}H_{10}N_2O_3$[e]	60.93 (60.55)	4.57 (4.62)	12.97 (12.84)	3040, (2930)	1670 (1625)	10.47,	6.43,	(7.52—7.16)[d]	4.33
		Z	10.7	80.0	245—247					3050, (2780)	1690 (1630)	9.98,	6.78,	(7.56—7.28)[d]	4.39

a) From Compound **2**. b) From Compound **3**. c) cm^{-1} in KBr. d) Multiplet. e) Elemental analyses of the mixture of the (*E*)- and (*Z*)-isomers.



a; R=CH_3, **b**; R=C_2H_5, **c**; R=*n*-C_3H_7, **d**; R=*i*-C_3H_7, **e**; R=C_6H_5
R^1=C_2H_5 (excepting R^1=CH_3 in the case of R=*i*-C_3H_7)

Scheme 1.

the change in the coplanarity of the molecules.

2) The chemical shifts of the methylene, vinyl, and 3α-alkyl protons of **7** are higher than those of **6**, indicating the introduction of an electron-releasing hydroxyl group into **6**.

3) The vinyl and methylene protons of the (*Z*)-isomer of **6** and **7** resonate at a lower magnetic field ($\Delta\delta$ 0.35—0.54 and 0.04—0.10 ppm respectively) compared with that of the (*E*)-isomer, whereas 3α-alkyl protons of (*Z*)-isomer resonate at a higher magnetic field ($\Delta\delta$ 0.27—0.91 ppm). These facts seem to indicate a flattened boat-conformation[13] for these cyclic compounds (**6** and **7**).

The IR spectrum of **7** showed a characteristic absorption band in the 2760—2930 cm^{-1} region due to a hydroxamic acid, supporting the structure of **7**.

Experimental

All the boiling and melting points are uncorrected. The IR spectra were recorded with a Hitachi EPI-G3 Spectrometer. The NMR spectra were measured with a JNM-PS-100 Spectrometer (Japan Electron Optics Laboratory Co., Ltd.), using tetramethylsilane as the internal standard.

Materials. The (*E*)- and (*Z*)-isomers of **1** were prepared by the method previously reported.[5] The mixture of (*E*)- and (*Z*)-isomers thus obtained was separated by chromatography on a silica gel column using benzene; the earlier eluted one was an oil thought to be the (*E*)-isomer, and the latter, crystals thought to consist of the (*Z*)-isomer.

Preparation of ***2***. According to the above method, when a solution of ethyl or methyl 2-oxoalkanoate (0.10 mol) and bromoacetamide (0.12 mol) in benzene (100 ml) in the presence of phosphoryl chloride (0.02 mol) was refluxed for *ca.* 15 h, a colorless syrup was obtained in *ca.* a 40% yield after the removal of the benzene and the subsequent distillation of the residue under reduced pressure. The mixture syrup of (*E*)- and (*Z*)-isomers thus obtained was similarly worked up to give an oil ((*E*)-isomer) and crystals ((*Z*)-isomer).

Preparation of ***3***. The purely isolated (*E*)- and (*Z*)-isomers of **1** (0.01 mol) were treated separately with potassium iodide (0.02 mol) in acetone (50 ml) under reflux for 3 h to convert it into the (*E*)- and (*Z*)-isomers of **3** respectively as colorless crystals in an almost quantitative yield, after the removal of the potassium chloride deposited and the acetone.

Preparation of ***4***. A mixture of the (*E*)- or (*Z*)-isomer of **3** (0.01 mol) and zinc powder (6.54 g, 0.1 mol) in ethanol (50 ml) was stirred at room temperature for 5 h. After the subsequent removal of the zinc and the ethanol, the residue was distilled under reduced pressure to give a colorless oil or crystals ((*E*)- and (*Z*)-isomers of **4** respectively).

Preparation of ***5***. A solution of the (*E*)- or (*Z*)-isomer of **3** (0.01 mol) and potassium phthalimide (0.01 mol) in dimethyl sulfoxide (30 ml) was stirred at room temperature for 5 h. When the reaction solution was then poured into ice water (100 ml), colorless crystals (**5**) were separated out.

Preparation of ***6***. According to the method previously reported,[5] the individual (*E*)- and (*Z*)-isomer of **6** was prepared by the reaction of the (*E*)- or (*Z*)-isomer of **1** with ammonia.

Preparation of ***7***. A solution of the individual (*E*)- and (*Z*)-isomer of **2** or **3** (0.005 mol) and hydroxylamine (made from hydroxylamine hydrochloride (0.02 mol) and sodium (0.02 mol) in dry ethanol (5 ml)) in dry ethanol (50 ml) was refluxed under nitrogen gas for 18 h. The reaction solution was then evaporated to dryness under reduced pressure, the residue obtained was dissolved in water (1000 ml), and the aqueous solution was passed successively through columns of Dowex 50 WX-12 cation-exchange regin and Dowex 1-X8 anion-exchange regin (acetate form). The aqueous fraction thus eluted evaporated under reduced pressure to give faint pinkish crystals (**7**).

References

1) Part XII: C. Shin, Y. Sato, H. Sugiyama, K. Nanjo, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **50**, 1786 (1977). This work was presented at the 33rd and the 35th National Meetings of Chemical Society of Japan, Fukuoka, October, 1975; Sapporo, September, 1976.

2) V. Austel and W. Steglich, *Chem. Ber.*, **108**, 2361 (1975).

3) A. Srinivasan, K. D. Richards, and R. K. Olsen, *Tetrahedron Lett.*, **1976**, 891.

4) D. Hoppe and R. Follmann, *Chem. Ber.*, **109**, 3062 (1976).

5) C. Shin, M. Fujii, and J. Yoshimura, *Tetrahedron Lett.*, **1971**, 2499; C. Shin, K. Sato, A. Ohtsuka, K. Mikami, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **46**, 3876 (1973).

6) C. Shin, M. Hayakawa, K. Mikami, and J. Yoshimura, *Tetrahedron Lett.*, **1977**, 863.

7) C. Shin, K. Nanjo, E. Ando, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **47**, 3109 (1974).

8) C. Shin, K. Nanjo, M. Kato, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **48**, 2584 (1975).

9) C. Shin, Y. Yonezawa, and J. Yoshimura, *Chem. Lett.*, **1976**, 1063.

10) C. Shin, Y. Yonezawa, and J. Yoshimura, *Chem. Lett.*, **1976**, 1095.

11) A. H. Cook and C. A. Slater, *J. Chem. Soc., C*, **1956**, 4130.

12) W. K. Anslow and H. Raistrick, *Biochem. J.*, **25**, 39 (1931).

13) J. Yoshimura, Y. Sugiyama, and H. Nakamura, *Bull. Chem. Soc. Jpn.*, **46**, 2850 (1973); J. Yoshimura, H. Nakamura, and K. Matsunari, *ibid.*, **48**, 605 (1975).

14) C. Shin, M. Masaki, and M. Ohta, *Bull. Chem. Soc. Jpn.*, **43**, 3219 (1970).