from EtOH or EtOH–MeOH.

N,N'-diCH_3-AET: *Anal.* Calcd. for $C_5H_{15}N_3SBr_2$: C, 19.43; H, 4.89; N, 13.60. Found: C, 19.83; H, 4.98; N, 13.49. mp 158.5—159°.[10]

N',N'-diCH_3-AET: *Anal.* Calcd. for $C_5H_{15}N_3SBr_2$: C, 19.43; H, 4.89; N, 13.60. Found: C, 19.69; H, 5.01; N, 13.51. mp 212—214°.

N,N',N'-triCH_3-AET: *Anal.* Calcd. for $C_6H_{17}N_3SBr_2$: C, 22.30; H, 5.30; N, 13.01. Found: C, 22.44; H, 5.45; N, 12.84. mp 208—210°.

Measurements of IR and NMR Spectra——The IR spectra were measured in nujol mull with a JASCO-DS-301 spectrometer. The measurement of the NMR spectra was done in D_2O with a Varian HR-100 spectrometer.

The Rate of the Transguanylation——The rate of the transguanylation was measured potentiometrically with a Radiometer TTTIc titrator and SBR2c titrigraph. 0.8 ml of 0.1 N NaOH, corresponding to 0.5 equivalent with respect to AET molecule, was added rapidly into 20 ml of 8.00×10^{-3} M AET solution, which had been thermostatted at 15°. After standing for 10 min under mechanical stir, 0.8 ml of 0.1 N HCl was added into the reaction mixtures. Then, the solution was titrated with 0.1 N NaOH. The alkali titer, which is equimolar to the SH compound produced as the result of the transguanylation, indicate the extent of the reaction. A detailed procedure was described in a preceeding paper.[8]

The Ratio of the Cyclization Products——The ratio of the cyclization products from N,N'-diCH_3-AET was measured in D_2O at room temperature with a Varian HR-100 spectrometer. An aqueous solution of N,N'-diCH_3-AET, 84.7 mg in 5 ml ,was refluxed until no more starting material was recognized. After the the evaporation of water from the reaction mixtures under reduced pressure, the crude products were dissolved in D_2O and applied to the NMR measurement.

Acknowledgement We are grateful to Mr. M. Uoji and Mr. T. Kondo for the IR and NMR measurements, and to the members of the Analytical Center of Research Laboratories of Tanabe Seiyaku Co., Ltd. for the elemental analysis.

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10) All melting points described are uncorrected.

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Infrared Spectra of α-Bromoacylureas and Their N,N'-Deuterated Compounds

Toyozo Uno, Katsunosuke Machida
and Yutaka Saito

Faculty of Pharmaceutical Sciences, Kyoto University[1]

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This note is a continuation of the previous paper[2] dealing with the characteristic infrared absorption bands of the $-CONHCONH_2$ and $-CONDCOND_2$ groups of acylureas and deals with those of α-bromoacylureas. The infrared spectra of α-bromo-isovalerylurea and α-bromodiethylacetylurea, which were widely used as hypnotic, were reported,[3,4] but the absorptions due to the vibration of the $-CONHCONH_2$ group were not identified except a few like the C=O stretching bands. Both of these α-bromoacylureas show dimorphism and

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1) Location: *Shimoadachi-cho, Sakyo-ku, Kyoto.*
2) T. Uno, K. Machida, K. Hanai and Y. Saito, *Bull. Chem. Soc. Japan*, **42**, 619
3) C.J. Umberger and G. Adams, *Anal. Chem.*, **24**, 1309 (1952).
4) H. Satoh, *Tokyo Ika Daigaku Zasshi*, **21**, 311 (1963).

the difference of infrared spectra of α-bromo-isovalerylurea caused from the difference of the crystal form was already reported,$^{5)}$ but that of α-bromodiethylacetylurea has not been reported to date.

Experimental

Bromoacetyl-, α-bromopropionyl-, α-bromo-isobutyryl- and α-bromo-*n*-butyrylureas were prepared by heating a mixture of urea and corresponding α-bromoacylbromide.$^{6,7)}$ Chloroacetylurea was prepared similarly by heating a mixture of urea and chloroacetylchloride. α-Bromodiethylacetyl- and α-bromo-isovalerylureas were those of commercial source. These materials were recrystallized several times from ethanol. The β-form crystal of α-bromodiethylacetylurea and the α-form crystal of α-bromo-isovalerylurea were obtained by usual crystallization from ethanol.$^{8,9)}$ The α-form crystal of the former was obtained by very slow crystallization from a saturated solution$^{8)}$ and the β-form crystal of the latter was obtained by heating the α-form crystal at 120° for 5 hr.$^{9)}$ N,N′-Deuterated α-bromoacylureas and chloroacetylurea were prepared by crystallization from a mixture of heavy water and dioxane. The β-form crystal of N,N′-deuterated α-bromo-isovalerylurea was obtained by heating its α-form crystal at 120° for 5 hr in a sealed tube. The α-form crystal of N,N′-deuterated α-bromodiethylacetylurea was not obtained.

The infrared spectra were recorded on a Koken DS 301 infrared spectrophotometer equipped with NaCl and KBr prisms. The samples were subjected to the measurement in the form of solid dispersed in Nujol and hexachlorobutadiene (H.C.B.). The α-form crystal of α-bromo-isovalerylurea is stable, but its β-form crystal is converted into the α-form crystal on mulling with H.C.B. Therefore, the infrared speotra of this crystal were obtained only on Nujol mulls.

Results and Discussion

The infrared spectra of α-bromoacylureas and chloroacetylurea and their N,N′-deuterated compounds are shown in Fig. 1. By comparing with the previously reported spectra of acylureas and by referring to the frequency shift on N,N′-deuteration, most of the characteristic frequencies of the $-CONHCONH_2$ and $-CONDCOND_2$ groups of α-bromoacylureas can be easily assigned. The observed frequencies and the assignments are summarized in Tables I and II.

Chloroacetyl-, bromoacetyl-, α-bromopropionyl- and α-bromo-*n*-butyrylureas and the β-form crystal of α-bromo-isovalerylurea show three bands in the region between 3450 and 3200 cm^{-1}. From analogy to acylureas,$^{2)}$ the bands near 3400 and 3220 cm^{-1} can be assigned to the NH_2 *antisym* and *sym* stretching vibrations and the band near 3330 cm^{-1} to the NH stretching vibration. These bands are replaced by the bands near 2550, 2380 and 2450 cm^{-1} on N,N′-deuteration. The β-form crystal of α-bromodiethylacetylurea shows only two bands in the region between 3450 and 3200 cm^{-1}. From the spectral change on N,N′-deuteration it is suggested that the NH stretching absorption of this compound overlaps with the NH_2 *antisym* stretching absorption. For α-bromo-isobutyrylurea, the α-form crystal of α-bromo-isovalerylurea and the α-form crystal of α-bromodiethylacetylurea, it is rather difficult to assign the individual bands to the specific groups.

The bands due to the C=O stretching vibrations of α-bromoacylureas are observed near 1710 and 1680 cm^{-1}. These frequencies are 50 cm^{-1} higher than that of fatty acid amides$^{10)}$ and are comparable with that of acylureas$^{2)}$ and imides.$^{11)}$ The band in the region between 1620 and 1570 cm^{-1} which disappears on N,N′-deuteration is assigned to the NH_2 bending

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5) T. Oba, Y. Tada and Y. Koide, ***Eisei Shikensho Hokoku*, 82, 33 (1964).**

6) K. Nishizaki and S. Nishihara, ***Yakugaku Zasshi*, 35, 1143 (1915).**

7) K. Nishizaki and S. Nishihara, ***Yakugaku Zasshi*, 36, 21 (1916).**

8) A. Watanabe, ***Yakugaku Zasshi*, 60, 416 (1940).**

9) A. Watanabe, ***Yakugaku Zasshi*, 58, 565 (1938).**

10) L.J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Edition, Methuen & Co., Ltd. London, John Wiley & Sons, Inc. New York, 1958, p. 203.

11) T. Uno and K. Machida, *Bull. Chem. Soc. Japan*, 34, 551 (1961).

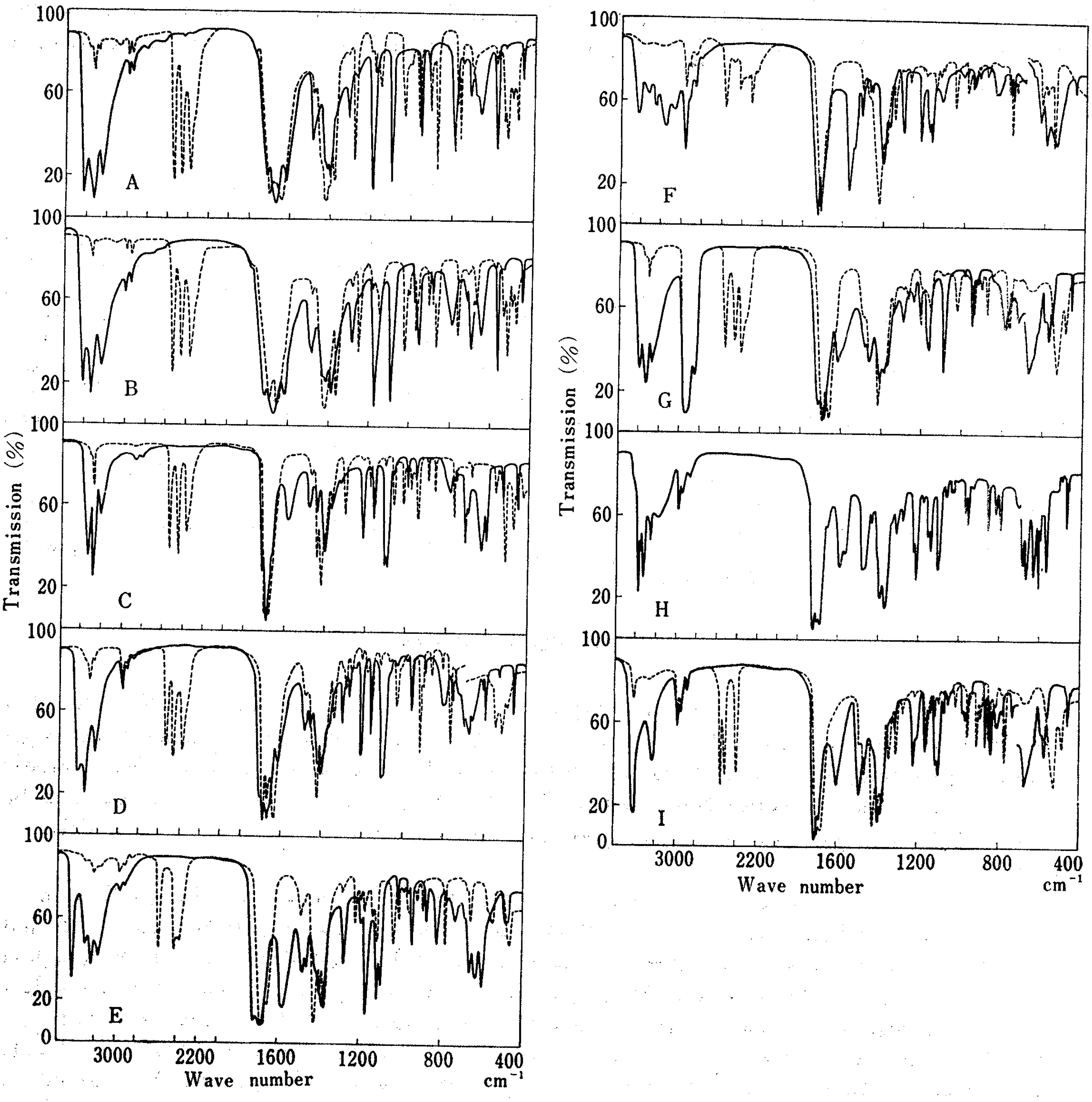

Fig. 1. Infrared Spectra of Chloroacetyl- and α-Bromoacylureas, —— shows the Infrared Spectra of the Non-deuterated Compounds, ------ shows that of the N,N′-deuterated Compounds

A: chloroacetylurea B: bromoacetylurea C: bromopropionylurea D: bromo-*n*-butyrylurea
E: bromo-isobutyrylurea F: the α-form crystal of bromo-isovalerylurea
G: the β-form crystal (only on Nujol mulls, * the bands due to Nujol)
H: the α-form crystal of bromodiethylacetylurea I: the β-form crystal

vibration. Previously, the infrared spectra of acylureas were classified into the types I and II by the feature of the C=O stretching and the NH_2 bending bands.[2] This classification is also applicable to the presently studied α-bromoacylureas. The type I spectrum is shown by chloroacetyl-, bromoacetyl- and α-bromo-*n*-butyrylureas and the β-form crystal of α-bromo-isovalerylurea and the type II spectrum by α-bromopropionylurea, α-bromo-isobutyrylurea, the α-form crystal of α-bromo-isovalerylurea, the α-form and β-form crystals of α-bromodiethylacetylurea. It is interesting that the type of the α-form crystal of α-bromo-isovalerylurea is different from that of the β-form crystal but both of the α-form and β-form crystals of α-bromodiethylacetylurea show the same type. On N,N′-deuteration of α-bromoacylureas, the C=O stretching bands shift to about 1690 and 1645 cm^{-1} for the type I and about 1690 and

Table I. Infrared Characteristic Frequencies of the $-CONHCONH_2$ Group of α-Bromoacylureas

Cl- acetyl-	Br- acetyl-	Br- propionyl-	Br-*n*- butyryl-	Br-iso- butyryl-	Br-isovaleryl- (α-form)	Br-isovaleryl- (β-form)	Br-diethylacetyl- (α-form)	Br-diethylacetyl- (β-form)	Assignment
1710 s	1714 vs	1716 s	1710 sh 1694 vs	1717 vs	1731 vs	1715 sh	1707 vs	1725 vs 1707 vs	C=O stretching
1672 vs	1675 vs	1694 vs	1670 vs	1686 vs	1709 vs	1688 vs	1685 sh	1691 vs	C=O stretching
1619 s	1620 vs	1596 m	1623 m	1580 s	1573 s	1617 m	1605 m	1598 m 1570 m	NH_2 bending
1493 m	1483 m	1486 w	1485 m	1486 m	1503 m	1481 w	1488 s	1476 m	imide II
1402 s	1390 vs	1406 m	1408 s	1384 s	1400 s	1407 s	1396 vs	1393 s	CN stretching (?)
1196 vs	1178 vs	1166 m	1164 m	1172 s	1163 m	1170 m	1161 m	1147 m	imide III
1101 vs	1098 vs	1103 s 1096 s	1105 s	1113 s 1097 m	1106 m	1095 s	1099 m	1107 m	NH_2 rocking
962 m	959 m	956 w	967 m	947 m	954 w	957 m	965 m	959 m	CN stretching
789 m	795 m	782 w	810 w 801 w	818 m	845 m 833 m	791 m	809 w	799 m	CO out-of-plane def.
660 mb	650 mb	642 mb	683 mb	630 m	550 ?	675 m	628 m	662 sb	NH_2 wagging or NH out-of-plane def.
582 m	568 s	526 m	595 m	598 m	568 m	586 m	574 m	608 m	C=O in- or out-of-plane def.

vs : very strong, s : strong, m : medium, w : weak, vw : very weak

Table II. Infrared Characteristic Frequencies of the $-CONDCOND_2$ Group of N,N′-Deuterated α-Bromoacylureas

Cl- acetyl-	Br- acetyl-	Br- propinyl-	Br-*n*- butyryl-	Br-iso- butyryl-	Br-isovaleryl- (α-form)	Br-isovaleryl- (β-form)	Br-diethylacetyl- (β-form)	Assignment
1702 vs	1698 vs	1698 vs	1693 vs 1675 s	1686 vs	1714 vs	1690 vs	1694 vs	C=O stretching
1643 vs	1651 vs	1680 vs	1638 vs	1649 vs	1690 sh	1656 vs	1680 vs	C=O stretching
1421 vs	1420 vs	1424 s	1426 vs	1421 vs	1421 vs	1416 vs	1420 vs	CN stretching (?)
1380 s	1367 vs	1306 m	1347 m	1371 s	1345 m	1341 m	1343 m	imide II′
1156 w	1157 w	1166 w	1155 w	1175 w	1145 w	1160 w	1155 m	ND_2 bending
1035 m	1028 m	1020 w	1036 w	1031 m	1041 m	1033 w	1014 w	imide III′
968 m	967 m	949 m	966 m	948 w	951 w	945 w	955 m	CN stretching
874 m	872 s	858 m	864 w	888 w	887 w	878 w	891 w	ND_2 rocking
766 m	766 m	767 m	771 m	774 m	764 m	771 m	769 m	C=O out-of-plane def.
531 m	524 m	514 m	550 m	549 m	549 m	534 s	560 m	C=O in- or out-of-plane def.
480 m	575 m	572 m	490 w	470 w	?	485 m	580 s	ND_2 wagging or ND out-of-plane def.

vs : very strong, s : strorg, m : medium, w : weak, vw : very weak

1680 cm^{-1} for the type II. Such a large frequency shift is different from the case of fatty acid amides[10)] and imides[11)] and is comparable with biuret-hydrate[12)] and acylureas.[2)] For the ND_2 bending band near 1155 cm^{-1}, the difference between the type I and II was not observed.

α-Bromoacylureas show the bands near 1490 and 1160 cm^{-1} which disappear on N,N′-deuteration. These bands can be assigned, respectively, to the imide II and III bands resulting from the coupling between the NH in-plane deformation and the CN stretching vibrations of the -CONHCO- group.[13)] The imide II frequencies of α-bromoacylureas and acylureas are close to each other, but the imide III frequencies of α-bromoacylureas are 50—100 cm^{-1} lower than that of acylureas.[2)] Since the imide III frequencies are affected by alkyl-framework as seen in Table I, the C=O and NH bonds of the RCONH- group may be in the trans position

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12) T. Uno, K. Machida and Y. Saito, *Bull. Chem. Soc. Japan*, **42**, 1539 (1969).

from analogy to acylureas.[2)] On N,N′-deuteration these bands are replaced by the imide II′ and III′ bands near 1340 and 1030 cm^{-1}, respectively. The former is mainly contributed by the CN stretching vibration and the latter by the ND in-plane deformation.[13)]

α-Bromoacylureas show a band at 1100 cm^{-1} which disappears on N,N′-deuteration, but is not affected by the change of alkyl-framework. This band was also observed for acylureas[2)] and was assigned to the NH_2 rocking vibration. On N,N′-deuteration this band is replaced by the ND_2 rocking band near 880 cm^{-1} which is slightly affected by the change of alkyl-framework. From analogy to acylureas,[2)] the band near 950 cm^{-1} observed for non-deuterated compounds can be assigned to the CN stretching vibration. It is difficult to identify the remaining CN stretching absorption expected near 1400 cm^{-1} because of the interference of the CH deformation bands of alkyl group. The bands in the region below 850 cm^{-1} are tentatively assigned as shown in Table I and II from anlogy to acylureas.[2)]

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13) T. Uno and K. Machida, *Bull. Chem. Soc. Japan,* **36,** 427 (1963).