[Chem. Pharm. Bull. 36(7)2647—2651(1988)]

Infrared Spectra of Conjugated Amides: Reassignment of the C=O and C=C Absorptions

NORIO NAKAMURA, FUMIYUKI KIUCHI, and YOSHISUKE TSUDA*

Faculty of Pharmaceutical Sciences, Kanazawa University, 13-1, Takara-machi, Kanazawa 920, Japan

(Received December 9, 1987)

Inspections of the infrared spectra of more than twenty tertiary and secondary amides and acid-induced shift experiments clarified that, in open chain amides, the carbonyl absorption shifts to lower frequency by 10—20 cm^{-1} when a conjugation is introduced and that, among the plural absorptions at 1600—1700 cm^{-1} in conjugated amides, the lowest absorption (usually the most intense one) should be attributable to the C=O and the higher absorptions are assignable to the C=C.

Keywords——conjugated amide; piperamide; IR; carbonyl absorption; acid-induced shift

Conjugated amides show several infrared (IR) absorption bands in the 1600—1700 cm^{-1} region; usually two in monoene-amides and three in diene-amides. Frequently the lower frequency band(s) was assigned to the C=C and the higher frequency band to the C=O stretching absorptions.[1] This assignment follows the literature,[2] which states that the carbonyl absorption frequency of amides is slightly raised by conjugation with a double bond as opposed to the more usual lowering.

Fujii *et al.*[3] showed that, in six-membered lactams, the above assignment is incorrect, proving that the carbonyl frequency is slightly (10—20 cm^{-1}) lowered by conjugation with a double bond, contrary to what has been proposed in the literature. This may also hold for open chain amides such as piperamides,[4] in which the assignment has been done according to the literature.[2] For example, among three absorptions at 1650, 1625, and 1600 cm^{-1} in piperylin (**7**) those at 1650 and 1625 cm^{-1} were assigned to the C=O and the C=C, respectively.[1a]

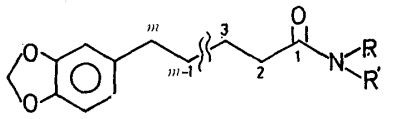
Since many kinds of open chain amides, conjugated or unconjugated, are in our hands as pepper constituents,[4] we have examined their IR spectra focusing on the above point. The structures of the amides used in this work are listed in Table I and Chart 1, and their IR absorptions in the 1600—1700 cm^{-1} region are listed in Table II. They can be classified into the following four groups.

Saturated amides (group 1) exhibit only one absorption at *ca.* 1620 cm^{-1} which is obviously attributable to the C=O.

Monoene-amides (group 2) exhibit two absorption bands at 1655 and 1600 cm^{-1} when they are tertiary, and at 1675—1665 and 1640—1620 cm^{-1} together with the amide-II band at *ca.* 1510 cm^{-1} when they are secondary. This is consistent with the generally accepted fact that a secondary amide absorbs at slightly higher frequency than a tertiary amide does. Of the above two absorptions, that at the lower frequency was more intense.

In diene-amides (group 3), tertiary amides exhibit three absorptions at *ca.* 1650, 1625, and 1590 cm^{-1}, the band at the lowest frequency being the most intense. Secondary amides also exhibit three absorptions at 1665—1650, 1630—1625, 1620—1610 cm^{-1} together with the amide II band at 1505 cm^{-1}. Again the absorption at the lowest frequency is the most intense.

TABLE I. Structures of Piperamides **1**—**23**



	Piperamide[a]	*m*	Double bond posit. and config.	–NRR′
1	A5:0	5		Piperidino
2	B5:0	5		Isobutylamino
3	C5:0	5		Pyrrolidino
4	C5:1 (2*E*)	5	2*E*	Pyrrolidino
5	A5:2 (*E*,*E*)	5	2*E*, 4*E*	Piperidino
6	B5:2 (*E*,*E*)	5	2*E*, 4*E*	Isobutylamino
7	C5:2 (*E*,*E*)	5	2*E*, 4*E*	Pyrrolidino
8	C7:0	7		Pyrrolidino
9	C7:1 (6*E*)	7	6*E*	Pyrrolidino
10	C7:2 (2*E*,6*E*)	7	2*E*, 6*E*	Pyrrolidino
11	A7:3 (*E*,*E*,*E*)	7	2*E*, 4*E*, 6*E*	Piperidino
12	C9:0	7		Pyrrolidino
13	A9:1 (8*E*)	9	8*E*	Piperidino
14	C9:1 (8*E*)	9	8*E*	Pyrrolidino
15	A9:2 (2*E*,8*E*)	9	2*E*, 8*E*	Piperidino
16	B9:2 (2*E*,4*E*)	9	2*E*, 4*E*	Isobutylamino
17	B9:2 (2*E*,8*E*)	9	2*E*, 8*E*	Isobutylamino
18	C9:2 (2*E*,8*E*)	9	2*E*, 8*E*	Pyrrolidino
19	A9:3 (2*E*,4*E*,8*E*)	9	2*E*, 4*E*, 8*E*	Piperidino
20	B9:3 (2*E*,4*E*,8*E*)	9	2*E*, 4*E*, 8*E*	Isobutylamino
21	C9:3 (2*E*,4*E*;8*E*)	9	2*E*, 4*E*, 8*E*	Pyrrolidino
22	B11:3 (2*E*,4*E*,10*E*)	11	2*E*, 4*E*, 10*E*	Isobutylamino
23	B13:3 (2*E*,4*E*,12*E*)	13	2*E*, 4*E*, 12*E*	Isobutylamino

a) The following systematic nomenclature is adopted, *i.e.*, "piperamide-A, -B, or -C *m*:*n*," where A, B, and C indicate piperidin-, *N*-isobutyl-, and pyrrolidin-amide, respectively, *m* indicates the number of carbon atoms between nitrogen and the aromatic nucleus, and *n* is the number of double bonds. For details, see ref. 4.

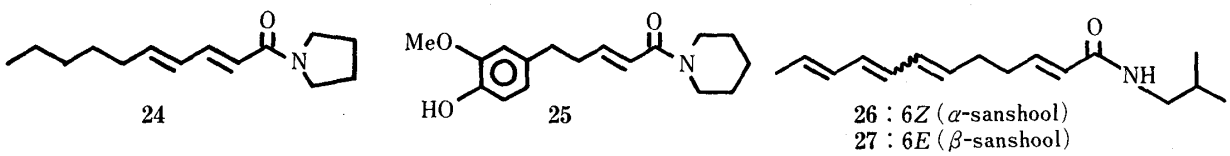


Chart 1

When the number of conjugations increases (group 4), the most intense band shifts to lower frequency, and a new additional absorption appears in the higher frequency region. Thus, piperamide-A7:3 (*E*, *E*, *E*) (piperettine) (**11**) exhibits four bands, the absorption at 1575 cm^{-1} being the most intense.

In all groups the most intense absorption appeared at the lowest frequency, which shifted successively to lower frequency with increase of conjugation; this implies that this absorption is attributable to the C=O. This assignment was confirmed by the following experiments, proposed by Fujii *et al.*[3]

Piperamide-C9:2 (2*E*, 8*E*) (**18**) (a group 2 amide) shows two peaks at 1655 and 1600 cm^{-1}. On addition of an equimolar amount of monochloroacetic acid, the intensity of the latter band markedly decreased and a new absorption at 1570 cm^{-1} appeared, while the former band was almost unchanged. On increase of the amount of the acid the band at

TABLE II. IR Absorption Frequencies of Amides in the Carbonyl Region

Group	Compound[a]	Amide		Absorption frequency (cm^{-1}) $CHCl_3$	KBr
1	PA-A5:0	**1**	*tert*	1620	1640[b]
	PA-A9:1 (8*E*)	**13**	*tert*	1620	1640[b]
	PA-C5:0	**3**	*tert*	1615	1640[b]
	PA-C7:0	**8**	*tert*	1620	1635[b]
	PA-C7:1 (6*E*)	**9**	*tert*	1620	1635[b]
	PA-C9:0	**12**	*tert*	1620	1640[b]
	PA-C9:1 (8*E*)	**14**	*tert*	1620	1635[b]
	PA-B5:0	**2**	*sec*	1660	
2	PA-A9:2 (2*E*,8*E*)	**15**[5]	*tert*	1655, 1600	
	PA-C5:1 (2*E*)	**4**	*tert*	1655, 1600	
	PA-C7:2 (2*E*,6*E*)	**10**	*tert*	1655, 1600	
	PA-C9:2 (2*E*,8*E*)	**18**	*tert*	1655, 1600	
		25[1c]	*tert*	1655, 1605[c]	
	PA-B9:2 (2*E*,8*E*)	**17**[5]	*sec*	1675, 1640	
	α-Sanshool	**26**[6]	*sec*		1668, 1626[c]
	β-Sanshool	**27**[6]	*sec*		1667, 1623[c]
3	PA-A9:3 (2*E*,4*E*,8*E*)	**19**[7]	*tert*		1650, 1625, 1590[c]
	PA-C9:3 (2*E*,4*E*,8*E*)	**21**	*tert*	1650, 1625, 1590	1650, 1625, 1590
		24	*tert*	1650, 1620, 1600	
	PA-B9:2 (2*E*,4*E*)	**16**[8]	*sec*		1660, 1630, 1618[c]
	PA-B9:3 (2*E*,4*E*,8*E*)	**20**	*sec*		1660, 1630, 1615
	PA-B11:3 (2*E*,4*E*,10*E*)	**22**	*sec*		1655, 1625, 1610
	PA-B13:3 (2*E*,4*E*,12*E*)	**23**	*sec*	1665, 1630, 1615	1650, 1625, 1610
4	PA-A5:2 (*E*,*E*)	**5**	*tert*	1635, 1615, 1585	1635, 1610, 1585
	PA-C5:2 (*E*,*E*)	**7**	*tert*	1635, 1615, 1585	1640, 1615, 1590
	PA-A7:3 (*E*,*E*,*E*)	**11**	*tert*	1630, 1615, 1590, 1575	1625, 1600, 1585, 1570
	PA-B5:2 (*E*,*E*)	**6**	*sec*	1655, 1610	1655, 1610

a) PA = piperamide. For structures, see Table I. *b*) Liquid film. *c*) Data from the reference cited.

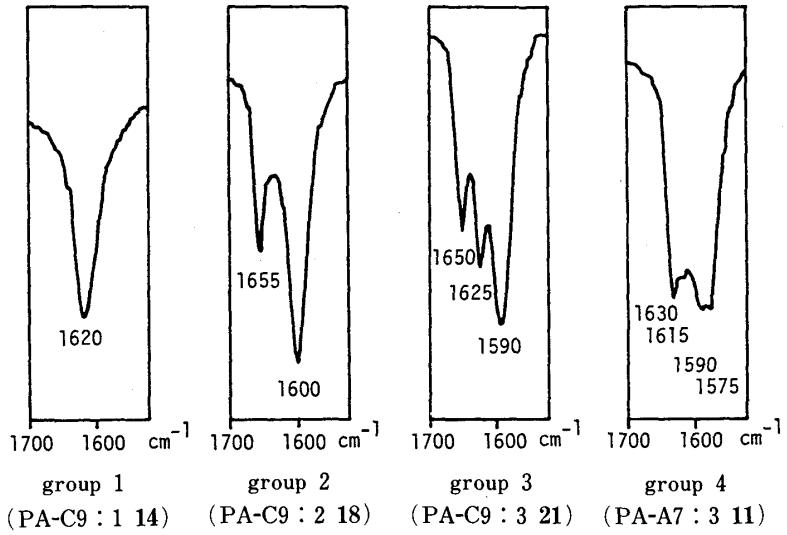


Fig. 1. Carbonyl Region Frequencies of Amides in Chloroform Solution

1600 cm^{-1} was diminished and only the band at 1570 cm^{-1} remained. Therefore the band at 1600 cm^{-1} should be attributable to the carbonyl and the new band at 1570 cm^{-1} to the association band between the carbonyl and monochloroacetic acid. Piperamide-C9:3 (2*E*,

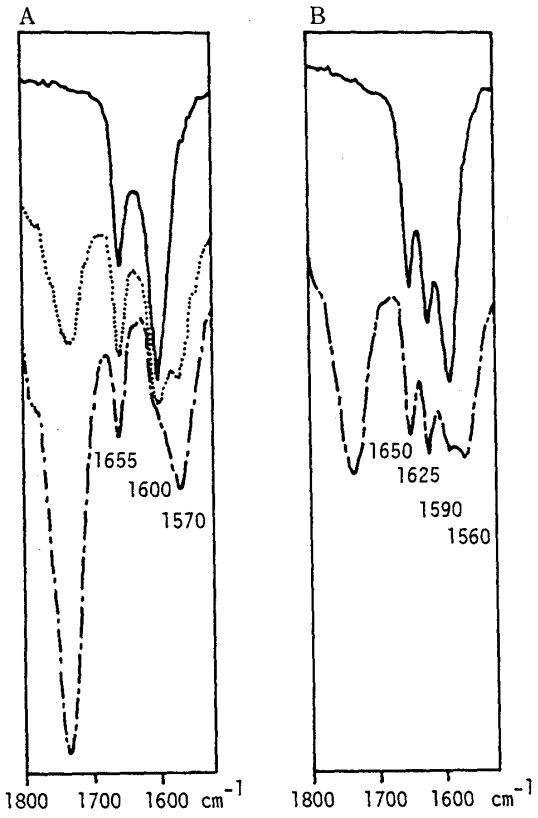


Fig. 2. Effect of Monochloroacetic Acid on the CO and Related Absorptions of Conjugated Amides

(A) Piperamide-C9 : 1(8*E*) (**18**): ——, **18** in 0.02 M solution in $CHCl_3$; ------, **18** + equimolar of $CH_2ClCOOH$ in $CHCl_3$; — · —, **18** + excess $CH_2ClCOOH$ in $CHCl_3$.

(B) Piperamide-C9 : 3 (2*E*,4*E*,8*E*) (**21**): ——, **21** in 0.02 M solution in $CHCl_3$; — · —, **21** + excess $CH_2ClCOOH$ in $CHCl_3$.

4*E*, 8*E*) (**21**) (a group 3 amide), in a similar experiment, showed a decrease of the intensity of the lowest absorption at 1590 cm^{-1} and the appearance of a new association band at 1560 cm^{-1}. For the amide of group 4, piperamide-A7 : 3 (*E*, *E*, *E*) (piperettine) (**11**), the lowest absorption at 1575 cm^{-1} was decreased and a new absorption at 1555 cm^{-1} due to the association appeared.

In conclusion, in open chain amides the carbonyl absorption shifts to lower frequency by 10—20 cm^{-1} when a conjugation is introduced, as suggested[3] in cyclic amides. Among the plural absorptions at 1600—1700 cm^{-1} in conjugated amides, the lowest absorption (usually the most intense one) should be attributable to the C=O and the higher absorptions are assignable to the C=C.

Experimental

General——Melting points were taken on a Yanagimoto micro hot-stage apparatus, and are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were measured in $CDCl_3$ solution with tetramethylsilane as an internal standard on a JEOL FX-100 spectrometer, and are given in δ. Mass spectra (MS) and high-resolution mass spectra (HRMS) were obtained on a Hitachi M-80 machine at an ionization voltage of 20 or 70 eV, respectively.

Infrared (IR) Spectra——Unless otherwise noted, IR spectra were taken in $CHCl_3$ solution at a concentration of 0.1—0.3 M on a JASCO A-202 spectrometer and are given in cm^{-1}.

Chemicals——Unless otherwise mentioned, all chemicals were of spectro-grade, purchased from Nakarai Chemicals Ltd.

Piperamides——Unless otherwise noted, piperamides were obtained from pepper and purified as described in a previous paper.[4]

Piperamide-A5 : 0 (Tetrahydropiperine) (1)——Piperine (**5**) was hydrogenated in ethanol over 5% Pd–C under a pressure of hydrogen at 4.5 kg/cm^2 for 3 h to give **1**, as an oil. ^{1}H-NMR: 1.36—1.76 (10H), 2.33 (2H, m, $COCH_2$), 2.56 (2H, m, $ArCH_2$), 3.28—3.62 (4H, CH_2NCH_2), 5.92 (2H, s, OCH_2O), 6.54—6.76 (3H, ArH). MS *m/z* (%): 289 (M^+, 84), 204 (40), 154 (38), 148 (37), 141 (40), 140 (70), 135 (39), 127 (100), 126 (18), 112 (35), 86 (24), 85 (19), 84 (50), 70 (19). HRMS: *m/z* Calcd for $C_{17}H_{23}NO_3$ (M^+): 289.1676. Found: 289.1671.

Piperamide-C5 : 0 (Tetrahydropiperylin) (3)——Piperylin (**7**) was hydrogenated as described above to give **3** as an

oil. ^{1}H-NMR: 1.44—2.12 (8H), 2.27 (2H, m, $COCH_2$), 2.56 (2H, m, $ArCH_2$), 3.31—3.58 (4H, CH_2NCH_2), 5.94 (2H, s, OCH_2O), 6.56—6.76 (3H, ArH). MS *m/z* (%): 275 (M^+, 56), 204 (17), 148 (27), 140 (19), 135 (34), 127 (36), 126 (62), 113 (100), 99 (15), 98 (19), 85 (18), 70 (19). HRMS: *m/z* Calcd for $C_{16}H_{21}NO_3$ (M^+): 275.1519. Found: 275.1514.

Piperamide-C7:0 (8)——Piperamide-C7:2 (**10**) was hydrogenated as described above to give **8** as an oil. ^{1}H-NMR: 1.28—2.06 (12H), 2.29 (2H, m, $COCH_2$), 2.56 (2H, m, $ArCH_2$), 3.35—3.58 (4H, CH_2NCH_2), 5.96 (2H, s, OCH_2O), 6.57—6.81 (3H, ArH). MS *m/z* (%): 303 (M^+, 26), 168 (29), 135 (27), 126 (56), 113 (100), 70 (11). HRMS: *m/z* Calcd for $C_{18}H_{25}NO_3$ (M^+): 303.1833. Found: 303.1836.

Piperamide-C9:0 (12)——Piperamide-C9:3 (**21**) was hydrogenated as described above to give **12**, as an oil. ^{1}H-NMR: 1.24—2.03 (16H), 2.26 (2H, m, $COCH_2$), 2.52 (2H, m, $ArCH_2$), 3.32—3.56 (4H, CH_2NCH_2), 5.93 (2H, s, OCH_2O), 6.54—6.77 (3H, ArH). MS *m/z* (%): 331 (M^+, 30), 196 (20), 135 (31), 126 (61), 113 (100), 70 (12). HRMS: *m/z* Calcd for $C_{20}H_{29}NO_3$ (M^+): 331.2145. Found: 331.2129.

Piperamide-B5:2 (*E,E*) (Piperlonguminine) (6)——Piperine (**5**) was hydrolyzed with 10% ethanolic NaOH to piperic acid, mp 220—222 °C (lit. mp 216 °C).[1a] A mixture of piperic acid (182 mg) and triethylamine (170 mg, 2 eq) in CH_2Cl_2 was stirred for 15 min at 0 °C, then methanesulfonyl chloride (105 mg, 1.5 eq) was added and the whole was stirred for a further 30 min. Isobutylamine (90 mg, 1.5 eq) was added to the mixture and stirring was continued for 1 h at 0 °C and 1 h at room temperature. The reaction mixture was taken up in CH_2Cl_2, and washed with 5% HCl, saturated aqueous $NaHCO_3$, and water. The organic layer, on concentration after drying, gave **6** (127 mg), mp 170—172 °C (lit. mp 166—168 °C),[9] as yellow needles from ethanol. ^{1}H-NMR: 0.93 [6H, d, J=6.0 Hz, $(CH_3)_2$], 1.82 (1H, m, CH), 3.16 (2H, t, J=6.0 Hz, NCH_2), 5.58 (1H, br s, NH), 5.88 (1H, d, J=15.0 Hz, =CHCO), 5.92 (2H, s, OCH_2O), 6.59—6.96 (5H, ArH, 2× =CH–), 7.12—7.45 (1H, –CH=C–CO). MS *m/z* (%): 273 (M^+, 72), 216 (20), 201 (100), 174 (27), 173 (72), 172 (27), 171 (15), 143 (25), 115 (57), 96 (24).

Piperamide-B5:0 (2)——Piperamide-B5:2 (**6**) was hydrogenated as described for **1** to give **2**, as colorless prisms, mp 61—62 °C (from hexane–benzene). ^{1}H-NMR: 0.90 [6H, d, J=6.6 Hz, $(CH_3)_2$], 1.48—1.90 (5H, 2×CH_2, CH), 2.18 (2H, m, $COCH_2$), 2.55 (2H, m, $ArCH_2$), 3.07 (2H, t, J=6.6 Hz, NCH_2), 5.74 (1H, br s, NH), 5.92 (2H, s, OCH_2O), 6.52—6.74 (3H, ArH). MS *m/z* (%): 277 (M^+, 86), 204 (55), 148 (67), 142 (24), 135 (92), 128 (47), 115 (100), 86 (31), 74 (26), 72 (27), 60 (78), 57 (24). HRMS: *m/z* Calcd for $C_{16}H_{23}NO_3$ (M^+): 277.1677. Found: 277.1677.

Acknowledgement The authors thank Prof. T. Fujii of our Faculty for valuable discussions.

References and Notes

1) *a*) R. Grewe, W. Freist, H. Newmann, and S. Kersten, *Chem. Ber.*, **103**, 3752 (1970); *b*) O. P. Vig, R. C. Aggarwal, C. Shekher, and S. D. Sharma, *Indian J. Chem.*, **17B**, 560 (1979); *c*) R. Inatani, N. Nakatani, and H. Fuwa, *Agric. Biol. Chem.*, **45**, 667 (1981).
2) *a*) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed., Methuen, London, 1958, pp. 213—215; *b*) K. Nakanishi, P. H. Solomon, and N. Furutani, "Infrared Absorption Spectroscopy—Practical—," Qualitative Data Part, 19th ed., Nankodo, Tokyo, 1983, p. 46.
3) T. Fujii, Y. Takai, M. Ohba, H. Kogen, and M. Ohki, *Chem. Pharm. Bull.*, **33**, 2697 (1985).
4) F. Kiuchi, N. Nakamura, Y. Tsuda, K. Kondo, and H. Yoshimura, *Chem. Pharm. Bull.*, **36**, 2452 (1988).
5) These were recently synthesized in our laboratory. Details to be published.
6) L. Crombie and J. L. Tayler, *J. Chem. Soc.*, **1957**, 2760.
7) W. Tabuneng, H. Bando, and T. Amiya, *Chem. Pharm. Bull.*, **31**, 3562 (1983).
8) B. G. Pring, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 1493.
9) A. Chatterjee and C. P. Dutta, *Tetrahedron*, **23**, 1769 (1967).