Synthesis of N-Substituted 3-Aminomethylidenetetramic Acids

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Received 30 May 2005; revised 18 July 2005

Abstract: (*S*)-3-(Dimethylamino)methylidene-5-benzyltetramic acid derivatives **4a** and **4b** were prepared in three steps from N-protected (*S*)-3-phenylalanines **1a** and **1b**, respectively. Similarly, *N*-[*N*-(benzyloxycarbonyl)glycyl]glycine (**1c**) was transformed into the enaminone **4c**. Acid-catalysed coupling of enaminones **4a**–**c** with aliphatic, aromatic, and heteroaromatic primary amines **5**–**34** afforded the corresponding N(3′)-substituted 3-aminomethylidenetetramic acid derivatives **35**–**64** in 29–96% yields.

Key words: amines, chiral pool, coupling, heterocycles, enaminones

Tetramic acid (pyrrolidin-2,4-dione) derivatives have attracted scientific interest for several decades. A great deal of interest can be attributed to the fact, that the majority of naturally occurring tetramic acids exhibit biological activity, such as antibiotic and antiviral activity. Since many of naturally occurring tetramic acids exist as the 3-acyl derivatives, preparation of this type of compounds represents an important target in synthetic organic chemistry.[1] Such examples of naturally occurring 3-acyltetramic acids are tenuazonic acid,[2] equisetin,[3] α-cyclopiazonic acid,[4] and physarorubinic acid[5] (Figure 1).

In the last two decades, a series of 2-substituted alkyl 3-(dimethylamino)prop-2-enoates were prepared and used as versatile reagents for the preparation of various heterocyclic systems, functionalised heterocyclic compounds, and natural product analogues.[6] Just recently, the propenoate methodology has been employed in combinatorial synthesis of dehydroalanine derivatives and heterocycles.[7] In extension, various chiral 3-(dimethylamino)prop-2-enoate analogues were prepared from commercially available enantiopure starting materials, such as L-pyroglutamic acid, tetrahydrofuran-2-one-5-carboxylic acid, and (+)-camphor. These chiral enaminones were employed as the key intermediates in the preparation of functionalized heterocycles, such as β-heteroarylalanine, alaninol, and propane-1,2-diol derivatives, heterocyclic analogs of dipeptides, and terpene-functionalised heterocycles.[6,8] In continuation of our work in the field of chiral enaminones, we now report preparation of tetramic acid derived enaminones and coupling reactions with primary amines, which afforded the corresponding N(3′)-substituted 3-(aminomethylidene)pyrrolidine-2,4-dione derivatives **35**–**64** as aza-analogs of 3-formyl- (or 3-hydroxymethylidene)-substituted tetramic acids.

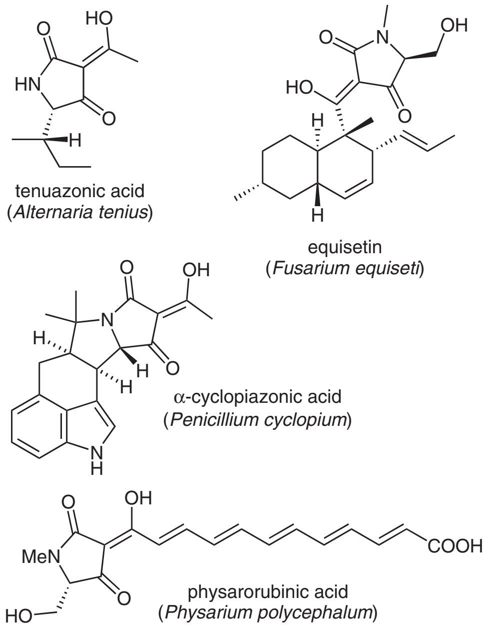

Figure 1 Some examples of naturally occurring 3-acyltetramic acid derivatives

First, (*S*)-5-benzyl-1-*tert*-butoxycarbonyl-4-hydroxy-2,5-dihydropyrrol-2-one (**3a**)[9a] and (*S*)-5-benzyl-1-benzyloxycarbonyl-4-hydroxy-2,5-dihydropyrrol-2-one (**3b**)[9b] were prepared according to literature procedures in two steps from (*S*)-*N*-*tert*-butoxycarbonyl-3-phenylalanine (**1a**) and (*S*)-*N*-benzyloxycarbonyl-3-phenylalanine (**1b**), respectively, via coupling of **1a**,**b** with Meldrum's acid in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP), followed by 'ring switching' transformation of the intermediates **2a**,**b** in refluxing ethyl acetate. Similarly, the analog **3c** was obtained in 93% overall yield from *N*-[*N*-(benzyloxycarbonyl)glycyl]glycine (**1c**). Finally, treatment of 1-acyltetramic acids **3a**–**c** with *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA) at 45–90 °C furnished the corresponding 1-acyl- and 1-alkoxycarbonyl-3-[(*E*)-(dimethylamino)methylidene]pyrrolidine-2,4-diones **4a**–**c** in 72–80% yields (Scheme 1).

Once the desired enamino tetramic acid derivatives **4a**–**c** were synthesized, dimethylamine substitution reactions were carried out with a variety of primary amines, such as anilines **5**–**14**, heteroarylamines **15**–**22**, α-amino acid es-

SYNTHESIS 2005, No. 17, pp 2969–2988
Advanced online publication: 23.09.2005
DOI: 10.1055/s-2005-916072; Art ID: T07105SS

Biographical Sketches

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David Bevk was born in Ljubljana, Slovenia, in 1977. In 2001, he obtained his BSc degree in chemistry, from the University of Ljubljana, Faculty of Chemistry and Chemical Technology. Since 2001 he is a PhD student under the supervision of Professor Branko Stanovnik.

Renata Jakše was born in Arbon, Switzerland, in 1975. She studied chemistry at the University of Ljubljana and received her Diploma in 1998, and her PhD in 2003 under the supervision of Professor Branko Stanovnik. She is currently working at Krka Pharmaceuticals d. d., Novo mesto, Slovenia.

Simon Rečnik was born in Maribor, Slovenia, in 1974. He studied chemistry at the University of Ljubljana and received his BSc in 1998. He continued his research under the supervision of Professor Jurij Svete and received his PhD in 2002. Since then, he is a Quality Manager at Lek Pharmaceuticals d. d., a new Sandoz company, Ljubljana, Slovenia.

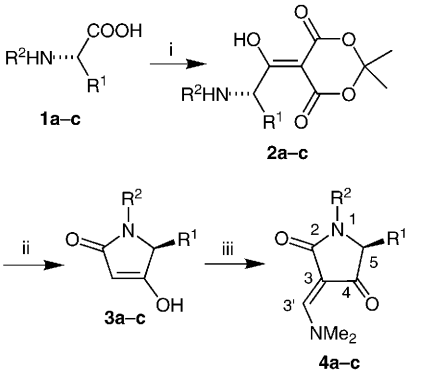
Ljubo Golič was born in 1932 in Vrenska gorca, Slovenia. He received his Diploma in chemistry in 1956 and his PhD in structural chemistry at the University of Ljubljana in 1965. He was a research student at the University of Glasgow in Professor Speakman's group. He continued his career at the University of Ljubljana, where he became a Full Professor in 1977. His research interests lie in the field of structural chemistry, with focus on compounds with short hydrogen bonds. Currently he is a Professor Emeritus at University of Ljubljana.

Amalija Golobič was born in Novo mesto, Slovenia, in 1969. She studied chemistry at the University of Ljubljana and received her Diploma in 1992 and PhD degree in 1996. Since 2004 she is an Assistant Professor at the University of Ljubljana. Her main research interests are structure determination of coordination and organic compounds in solid state by X-ray diffraction of single crystals and structural characterization of ceramics using powder diffraction.

Anton Meden was born in Ljubljana, Slovenia, in 1963. He studied Chemistry at the University of Ljubljana and received his PhD in 1994. In 1995/1996 he spent one year as a post-doc at the Laboratory of Crystallography at the ETH in Zurich. From 1995 to 2000 he was an Assistant Professor of Chemistry at the Faculty of Chemistry and Chemical Technology, University of Ljubljana. Since 2001 until present he is an Associate Professor and is responsible for the X-ray laboratory at the same institution.

Branko Stanovnik was born in Brezovica pri Ljubljani, Slovenia, in 1938. He received his Diploma in chemistry in 1960 and his PhD in organic chemistry at the University of Ljubljana in 1964. He became an Associate Professor at that university in 1967 and Full Professor in 1972. He was a postdoctoral fellow with the National Research Council in Canada and Visiting Professor in the USA and Australia. He is a member of many advisory boards and societies and the author of over 500 papers, reviews and books. His research interests lie in the field of heterocyclic chemistry, 1,3-dipolar cycloadditions, asymmetric synthesis, and natural products synthesis.

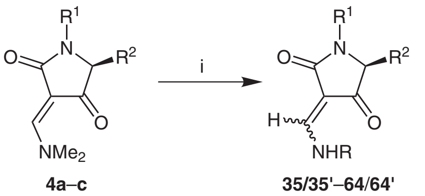
Jurij Svete was born in Ljubljana, Slovenia in 1962. He received his Diploma in chemistry in 1986 and his PhD in 1990 under supervision of Professor Stanovnik. He continued to work as a researcher with the group of Professor Stanovnik. In 1997 he spent one year as a Humboldt Fellow at the University of Stuttgart, Germany, working with Professor Jäger on the synthesis of iminopolyols from furannitrile oxide cycloadducts. In 1996, he became an Assistant Professor at the University of Ljubljana and an Associate Professor in 2001. His research interests include synthesis of heterocyclic compounds with emphasis on chiral functionalized heterocycles, stereoselective synthesis, chemistry of enaminones, 1,3-dipolar cycloadditions, and combinatorial synthesis.



Compound	R^1	R^2	Yield (%) 3	Yield (%) 4
1a–4a	CH$_2$Ph	COOBu^t	94[a]	72
1b–4b	CH$_2$Ph	COOBn	89[b]	72
1c–4c	H	COCH$_2$NHCOOBn	93	80

[a] Ref 9a. [b] Ref. 9b.

Scheme 1 *Reagents and conditions*: (i) Meldrum's acid, DMAP, DCC, CH$_2$Cl$_2$, 0–20 °C, then washing with 1 M aq NaHSO$_4$ (Ref.[9]); (ii) EtOAc, reflux (Ref.[9]); (iii) DMFDMA, toluene, 80–90 °C (**3a** → **4a**) or DMFDMA, CH$_2$Cl$_2$, reflux (**3b** → **4b**)



Compound	R^1	R^2	Isomer (major or minor)
35a–64a	CH$_2$Ph	COO^{t}Bu	major
35'a–64'a	CH$_2$Ph	COO^{t}Bu	minor
35b–64b	CH$_2$Ph	COOBn	major
35'b–64'b	CH$_2$Ph	COOBn	minor
35c–64c	H	COCH$_2$NHCOOBn	major
35'c–64'c	H	COCH$_2$NHCOOBn	minor

Scheme 2 *Reagents and conditions*: (i) RNH$_2$ (**5**–**34**), EtOH, 37% HCl (1 equiv), 20–80 °C

ters **23**–**29**, alkylamines **30**–**33**, and hydroxylamine **34**. In this manner, a series of N-substituted 1-acyl-3-aminomethylidenetetramic acid derivatives **35**–**64** were prepared in 29–96% yields. All these couplings of enaminones **4a**–**c** with primary amines proceeded under relatively mild conditions. Typically, reactions were carried out in ethanol with amine hydrochlorides or with free amines in the presence of one equivalent of 37% hydrochloric acid at 20–80 °C to afford the corresponding substitution products as the *E*/*Z*-mixtures of the major isomers **35**–**64** and the minor isomers **35′**–**64′** isomers (Scheme 2, Table 1).

Table 1 Experimental and Physical Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′**

Reactants	Product	Method	Temp (°C)	Time (h)	CC	Yield (%)	*E*:*Z*	Mp (°C)
–	**2′c**	–	–	–	–	93	–	145–147
–	**2c**	–	–	–	–	~100	–	84–85
–	**3c**	–	–	–	–	~100	–	133–136
–	**4a**	–	–	–	–	72	100:0	128–130
–	**4b**	–	–	–	–	72	100:0	oil
–	**4c**	–	–	–	–	80	100:0	148–149
4a + PhNH$_2$·HCl (**5**)	**35/35′a**	A	20	48	1:2[a]	83	52:48	57–60
4b + PhNH$_2$·HCl (**5**)	**35/35′b**	A	20	48	2:1[a]	83	53:47	98–104
4c + PhNH$_2$·HCl (**5**)	**35/35′c**	B	80	3	–	95	56:44	184–186
4b + 4-MeC$_6$H$_4$NH$_2$·HCl (**6**)	**36/36′b**	B	20	48	–	71	93:7	136–139
4c + 4-MeC$_6$H$_4$NH$_2$·HCl (**6**)	**36/36′c**	B	80	1.5	–	95	84:16	196–198
4a + 4-NO$_2$C$_6$H$_4$NH$_2$ (**7**)	**37/37′a**	B	20	18	–	77	85:15	165–166
4b + 4-NO$_2$C$_6$H$_4$NH$_2$ (**7**)	**37/37′b**	B	20	48	–	79	44:56	181–183
4c + 4-NO$_2$C$_6$H$_4$NH$_2$ (**7**)	**37/37′c**	B	80	3	–	90	55:45	212–214[b]
4c + 2-MeOC$_6$H$_4$NH$_2$ (**8**)	**38/38′c**	B	80	3	–	87	60:40	200–202
4c + 3-MeOC$_6$H$_4$NH$_2$ (**9**)	**39/39′c**	B	80	3	–	87	58:42	179–182
4a + 4-MeOC$_6$H$_4$NH$_2$ (**10**)	**40/40′a**	A	20	24	1:2[a]	71	54:46	56–61

Table 1 Experimental and Physical Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′** (continued)

Reactants	Product	Method	Temp (°C)	Time (h)	CC	Yield (%)	*E*:*Z*	Mp (°C)
4b + 4-MeOC$_6$H$_4$NH$_2$ (**10**)	**40/40′b**	A	80	2	80:1[c]	82	54:46	151–152
4c + 4-MeOC$_6$H$_4$NH$_2$ (**10**)	**40/40′c**	B	80	3	–	84	59:41	190–191
4c + 2-BrC$_6$H$_4$NH$_2$ (**11**)	**41/41′c**	B	80	2	–	85	60:40	196–200
4c + 3-BrC$_6$H$_4$NH$_2$ (**12**)	**42/42′c**	B	80	2	–	88	62:38	206–208
4b + 4-BrC$_6$H$_4$NH$_2$ (**13**)	**43/43′b**	B	80	3	–	89	84:16	174–175
4c + 4-BrC$_6$H$_4$NH$_2$ (**13**)	**43/43′c**	B	80	2	–	90	86:14	247–250
4b + 1-naphthylamine (**14**)	**44/44′b**	A	80		60:1[c]	93	49:51	115–125
4c + 1-naphthylamine (**14**)	**44/44′c**	B	80	3	–	84	60:40	159–166
4a + 3-amino-5-methyl-1*H*-pyrazole (**15**)	**45/45′a**	A	20	18	2:1[a]	48	46:54	95–98
4a + 5-amino-1*H*-tetrazole (**16**)	**46a**	B	20	18	–	48	0:100	145–153
4b + 5-amino-1*H*-tetrazole (**16**)	**46b**	B	20	48	–	74	0:100	187–198
4a + 3-amino-5-methylisoxazole (**17**)	**47/47′a**	A	20	18	1:1[a]	63	42:58	67–70
4c + 3-amino-1*H*-indazole (**18**)	**48/48′c**	B	80	1.5	–	91	58:42	210–212[b]
4a + 2-aminopyridine (**19**)	**49/49′a**	A	20	48	2:1[a]	46	45:55	67–69
4c + 2-aminopyridine (**19**)	**49/49′c**	A	80	9	2:1[a]	43	57:43	160–161
4a + aminopyrazine (**20**)	**50/50′a**	A	50	1	1:0[a]	76	42:58	75–81
4b + aminopyrazine (**20**)	**50/50′b**	B	20	48	–	77	30:70	153–155
4c + aminopyrazine (**20**)	**50c**	A	80	2.5	1:0[a]	29	100:0	198–202[b]
4a + 2-amino-4-methylpyrimidine (**21**)	**51/51′a**	A	60	2	1:0[a]	73	42:58	56–64
4b + 2-amino-4-methylpyrimidine (**21**)	**51/51′b**	A	20	48	1:0[a]	43	51:49	51–57
4b + 3-aminoquinoline (**22**)	**52/52′b**	B	80	2	–	79	44:56	170–173
4c + 3-aminoquinoline (**22**)	**52/52′c**	B	80	3	–	93	56:44	195–197[b]
4a + HCl·H-Gly-OMe (**23**)	**53/53′a**	B[d]	20	24	–	88	76:24	115–125
4c + HCl·H-Gly-OMe (**23**)	**53/53′c**	B	50	4	–	35	60:40	194–198
4a + HCl·H-L-Ala-OEt (**24**)	**54/54′a**	A	60	4	1:0[a]	53	19:81	111–124
4a + HCl·H-L-Leu-OMe (**25**)	**55/55′a**	A	60	4	1:0[a]	89	46:54	112–115
4b + HCl·H-L-Leu-OMe (**25**)	**55/55′b**	A	20	48	2:1[a]	93	50:50	35–44
4a + HCl· H-L-Gla-di-OEt (**26**)	**56/56′a**	A	20	48	1:0[a]	84	18:82	83–89
4a + HCl·H-L-Cys-OEt (**27**)	**57/57′a**	A	20	48	1:0[a]	90	43:57	73–77
4b + HCl·H-L-Cys-OEt (**27**)	**57/57′b**	A	20	48	2:1[a]	46	52:48	47–53
4c + HCl·H-L-Cys-OEt (**27**)	**57/57′c**	A	80	1	2:1[a]	79	59:41	190–198[b]
4b + HCl·H-L-Phe-OMe (**28**)	**58/58′b**	A	20	48	2:1[a]	96	53:47	39–46
4c + HCl·H-L-Phe-OMe (**28**)	**58/58′c**	A	80	1	3:1[a]	88	60:40	63–66
4b + HCl·H-L-Trp-OMe (**29**)	**59/59′b**	A	20	48	2:1[a]	92	51:49	78–84
4a + HCl·H$_2$NCH$_2$CH$_2$CO$_2$Et (**30**)	**60/60′a**	A	70	6	1:0[a]	95	45:55	128–130
4a + HCl·H$_2$NCH$_2$CN (**31**)	**61/61′a**	B	20	24	–	53	36:64	147–153

Table 1 Experimental and Physical Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′** (continued)

Reactants	Product	Method	Temp (°C)	Time (h)	CC	Yield (%)	*E*:*Z*	Mp (°C)
4b + $\mathrm{HCl\cdot H_2NCH_2CN}$ (**31**)	**61/61′b**	B	20	24	–	87	43:57	140–153
4c + $\mathrm{HCl\cdot H_2NCH_2CN}$ (**31**)	**61/61′c**	B	80	2	–	94	88:12	204–207
4b + $\mathrm{PhCH_2NH_2\cdot HCl}$ (**32**)	**62/62′b**	A	20	48	1:0[a]	84	51:49	41–48
4c + adamantylmethylamine (**33**)	**63/63′c**	B	80	2	–	55	61:39	228–230
4a + $\mathrm{HCl\cdot H_2NOH}$ (**34**)	**64a**	B[d]	20	24	–	62	100:0	159–161
4b + $\mathrm{HCl\cdot H_2NOH}$ (**34**)	**64b**	B	20	48	–	71	100:0	179–182
4c + $\mathrm{HCl\cdot H_2NOH}$ (**34**)	**64/64′c**	B	80	6	–	73	89:11	184–186

[a] EtOAc–hexanes.
[b] With decomposition.
[c] $\mathrm{CHCl_3}$–MeOH.
[d] Precipitation of the product occurred upon addition of water.

Structures of compounds **4**, **35**–**64** were determined by spectroscopic (IR, ^{1}H and ^{13}C NMR, MS, HRMS) methods and by elemental analyses for C, H, and N (Tables 2–5). Compounds **4b**, **40a**, **51b**, **57c**, **59b**, and **62b** were not isolated in analytically pure form. The identities of compounds **4b**, **40a**, **57c**, **59b**, and **62b** were confirmed by ^{13}C NMR and HRMS. The identity of compound **51b** was confirmed by HRMS.

Table 2 Correlation of Chemical Shifts δ of H–C(3′) and H–N–C(3′) Protons and Coupling Constants, $J_{\mathrm{H(3'),NH}}$, with Configuration around the Exocyclic C=C Double Bond in Compounds **35/35′**–**64/64′**

Product	Solvent	δ					
		H–C(3′)		H–N–C(3′)		$J_{\mathrm{H(3'),NH}}$ (Hz)	
		E-Isomer	*Z*-Isomer	*Z*-Isomer	*E*-Isomer	*E*-Isomer	*Z*-Isomer
35/35′a	$\mathrm{CDCl_3}$	7.95	8.13	10.94	11.27	13.6	13.9
35/35′b	$\mathrm{CDCl_3}$	7.97	8.14	10.91	11.32	12.2	13.9
35/35′c[a,b]	DMSO-d_6	8.33	–[c]	11.21	11.55	0	0
36/36′b	$\mathrm{CDCl_3}$	7.93	8.11	10.89	11.32	13.9	14.3
36/36′c	DMSO-d_6	8.29	–[c]	–[d]	11.39	0	–
37/37′a	$\mathrm{CDCl_3}$	7.96	8.12	11.05	11.28	11.3	13.2
37/37′b	$\mathrm{CDCl_3}$	7.99	8.14	11.01	11.33	0	13.6
37/37′c	DMSO-d_6	8.42	–[c]	11.35	11.39	0	0
38/38′c	DMSO-d_6	8.57	8.65	11.28	11.82	13.9	13.9
39/39′c	DMSO-d_6	8.40	–[c]	11.14	11.48	0	0
40/40′a	$\mathrm{CDCl_3}$	7.85	8.03	10.94	11.29	13.7	14.1
40/40′b	$\mathrm{CDCl_3}$	7.87	8.04	10.91	11.36	13.6	13.9
40/40′c	DMSO-d_6	8.23	–[c]	11.23	11.53	0	0
41/41′c	DMSO-d_6	8.63	–[c]	11.30	11.80	12.1	13.6
42/42′c	DMSO-d_6	8.35	–[c]	11.25	11.44	0	0
43/43′b	$\mathrm{CDCl_3}$	7.90	8.07	10.91	11.27	11.7	13.6
43/43′c	DMSO-d_6	8.30	–[c]	–[d]	11.39	0	–[d]
44/44′b	$\mathrm{CDCl_3}$	8.09	8.28	11.12	11.46	11.9	13.6
44/44′c	DMSO-d_6	8.53	8.55	11.81	12.34	12.8	14.3

Table 2 Correlation of Chemical Shifts δ of H–C(3′) and H–N–C(3′) Protons and Coupling Constants, $J_{H(3'),NH}$, with Configuration around the Exocyclic C=C Double Bond in Compounds **35/35′–64/64′** (continued)

Product	Solvent	δ					
		H–C(3′)		H–N–C(3′)		$J_{H(3'),NH}$ (Hz)	
		E-Isomer	*Z*-Isomer	*Z*-Isomer	*E*-Isomer	*E*-Isomer	*Z*-Isomer
45/45′a	$CDCl_3$	8.23	8.46	11.17	11.48	0	13.9
46a	DMSO-d_6	–	8.00	11.48	–	–	0
46b	DMSO-d_6	–	8.02	–[d]	–	–	–[d]
47/47′a	$CDCl_3$	7.81	8.09	10.62	10.89	0	13.6
48/48′c	DMSO-d_6	8.34	–[c]	11.71	11.97	0	0
49/49′a	$CDCl_3$	8.68	8.90	11.00	11.31	12.8	12.8
49/49′c	DMSO-d_6	8.81	8.88	–[d]	11.59	0	–[d]
50/50′a	$CDCl_3$	8.62	8.79	11.09	11.31	11.7	12.8
50/50′b	$CDCl_3$	8.65	8.81	11.06	11.39	11.2	12.8
50c	DMSO-d_6	8.67	–	–	11.75	0	–
51/51′a	$CDCl_3$	8.67	8.84	10.78	11.06	13.2	13.4
51/51′b	$CDCl_3$	8.70	8.87	10.77	11.11	12.8	13.2
52/52′b	$CDCl_3$	8.09	8.28	11.12	11.47	0	13.6
52/52′c	DMSO-d_6	8.45	8.57	11.42	11.76	13.2	14.3
53/53′a	$CDCl_3$	7.36	7.55	9.28	9.65	0	13.9
53/53′c	DMSO-d_6	7.89	8.01	9.66	9.97	0	0
54/54′a	$CDCl_3$	7.42	7.63	9.40	9.85	12.8	14.3
55/55′a[b]	$CDCl_3$	7.36	7.51	9.25	9.67	0	14.2
55/55′b	$CDCl_3$	–[c]	7.53	9.25	9.75	0	14.2
56/56′a	$CDCl_3$	7.37	7.53	9.28	9.71	0	14.3
57/57′a	$CDCl_3$	7.43	7.58	9.38	9.86	0	13.9
57/57′b	$CDCl_3$	–[c]	7.60	9.37	9.90	0	14.0
57/57′c	$CDCl_3$	7.73	7.85	9.57	10.07	0	14.3
58/58′b	$CDCl_3$	–[c]	–[c]	9.38	9.80	0	13.8
58/58′c	$CDCl_3$	–[c]	–[c]	9.43	9.94	0	0
59/59′b	$CDCl_3$	–[c]	–[c]	9.46	9.89	0	13.9
60/60′a[b]	$CDCl_3$	7.43	7.64	9.28	9.74	14.0	14.3
61/61′a	$CDCl_3$	7.60	7.67	9.36	–[d]	–[d]	13.9
61/61′b	$CDCl_3$	7.62	7.66	9.31	–[d]	–[d]	13.2
61/61′c	$CDCl_3$	8.02	–[c]	–[d]	10.00	0	–[d]
62/62′b	$CDCl_3$	–[c]	7.68	9.41	9.87	0	14.3
63/63′c	DMSO-d_6	7.82	7.91	9.54	9.94	14.7	15.1
64a[b]	$CDCl_3$	7.47	–	–	12.27	0	–
64b	$CDCl_3$	–[c]	–	–	12.27	0	–
64/64′c	DMSO-d_6	7.65	7.79	–[d]	11.29	0	–[d]

[a] Structure was determined by X-ray diffraction.

[b] The *Z*/*E*-configuration was determined by HMBC spectroscopy.

[c] Overlapped with other signals.

[d] NH exchanged.

Table 3 Analytical, MS, and IR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a–c,** and **35/35′–64/64′**

Product[a]	EI-MS (*m*/*z*) EI-HRMS (*m*/*z*)	IR (KBr/film) cm^{-1}	$[\alpha]_D^{20}$
2′c	–	3408, 3012, 2939, 1724, 1711, 1679, 1662, 1644, 1566, 1401, 1267, 1022, 812, 742	–
2c	–	3386, 3322, 1718, 1702, 1675, 1528, 1379, 1287, 1262, 1208, 1160, 695	–
3c	290 (M^+) Calcd: 290.090272 Found: 290.091020	3338, 1735, 1718, 1702, 1664, 1632, 1410, 1278, 1181, 970	–
4a	344 (M^+) Calcd: 344.173608 Found: 344.175100	3450, 1767, 1695, 1653, 1616, 1341, 1281, 1255, 1150, 1093, 779, 704	–165[b]
4b	378 (M^+) Calcd: 378.157957 Found: 378.158550	3458, 1767, 1700, 1659, 1616, 1442, 1380, 1302, 1095, 989, 701	–124[b]
4c	345 (M^+) Calcd: 345.132471 Found: 345.133300	3424, 2933, 1726, 1681, 1641, 1497, 1433, 1397, 1073, 908, 754, 697, 662	–
35/35′a	–	3436, 2978, 1769, 1706, 1664, 1628, 1587, 1484, 1298, 1156, 756	–276[b]
35/35′b	426 (M^+) Calcd: 426.157957 Found: 426.159050	3448, 3220, 1774, 1710, 1665, 1628, 1586, 1484, 1447, 1382, 1349, 1291, 1140, 990, 755, 699	–277[b]
35/35′c	–	3312, 1721, 1672, 1645, 1488, 1320, 1262, 1212, 1170, 973, 888, 756	–
36/36′b	–	3428, 1770, 1715, 1667, 1616, 1580, 1485, 1375, 1298, 1218, 998, 698	–286[b]
36/36′c	407 (M^+) Calcd: 407.148121 Found: 407.149250	3329, 1720, 1681, 1653, 1624, 1484, 1307, 1262, 1244, 1218, 1057, 830	–
37/37′a	438 (MH^+, FAB)	3108, 1773, 1668, 1632, 1589, 1509, 1481, 1344, 1292, 1224, 1154, 1110, 750	–350[b]
37/37′b	–	3446, 1774, 1716, 1675, 1659, 1628, 1587, 1511, 1483, 1346, 1291, 1221, 1110, 993, 971, 852, 757, 700	–291[b]
37/37′c	–	3293, 1728, 1709, 1675, 1624, 1589, 1532, 1298, 1257, 855	–
38/38′c	–	3341, 1716, 1690, 1658, 1624, 1589, 1548, 1470, 1385, 1314, 1246, 755	–
39/39′c	–	3314, 1726, 1680, 1589, 1385, 1294, 1249, 1046, 756, 697	–
40/40′a	423 (MH^+, FAB)	3431, 2976, 2932, 1767, 1734, 1705, 1657, 1627, 1588, 1519, 1485, 1348, 1300, 1253, 1156, 1031, 831, 701	–242[b]
40/40′b	–	3470, 2361, 1776, 1713, 1660, 1626, 1588, 1519, 1485, 1377, 1298, 1251, 1179, 835, 698	–284[b]
40/40′c	–	3370, 1715, 1662, 1633, 1481, 1310, 1250, 1163, 1051, 837, 751	–
41/41′c	–	3415, 1734, 1725, 1699, 1662, 1622, 1572, 1456, 1391, 1311, 1223	–

Table 3 Analytical, MS, and IR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a–c,** and **35/35′–64/64′** (continued)

Product[a]	EI-MS (*m*/*z*) EI-HRMS (*m*/*z*)	IR (KBr/film) cm^{-1}	$[\alpha]_D^{20}$
42/42′c	–	3350, 1728, 1710, 1686, 1662, 1625, 1578, 1385, 1323, 992, 768	–
43/43′b	–	3422, 1764, 1713, 1668, 1652, 1618, 1575, 147,8 1376, 1293, 1216, 1072, 995, 698	–245[b]
43/43′c	–	3294, 1707, 1675, 1614, 1474, 1384, 1256, 1011, 778, 702	–
44/44′b	–	3464, 1771, 1698, 1654, 1639, 1615, 1596, 1493, 1379, 1341, 1300, 1263, 751, 701	–236[b]
44/44′c	–	3310, 1721, 1702, 1687, 1646, 1616, 1596, 1396, 1308, 1256, 770	–
45/45′a	–	3274, 2978, 1765, 1708, 1664, 1624, 1347, 1299, 1254, 1154, 777, 701	–231[b]
46a	384 (M^+) 385 (MH^+, FAB)	3116, 1760, 1698, 1632, 1503, 1286, 1153, 842, 702	–210[c]
46b	–	3447, 3119, 1759, 1697, 1662, 1628, 1586, 1499, 1384, 1272, 1228, 701	–139[c]
47/47′a	398 (MH^+, FAB)	2978, 2932, 1771, 1711, 1676, 1630, 1597, 1467, 1428, 1400, 1368, 1345, 1279, 1156, 787, 701	–206[b]
48/48′c	–	3424, 3191, 1730, 1693, 1661, 1638, 1510, 1401, 1349, 1225, 1003	–
49/49′a	–	2978, 2931, 1769, 1708, 1674, 1625, 1567, 1474, 1425, 1278, 1230, 1150, 1064, 778, 701	–242[b]
49/49′c	–	3322, 1737 (C=O), 1674, 1620, 1567, 1427, 1272, 1245, 1210, 1163, 889, 791	–
50/50′a	–	3470, 1769, 1709, 1677, 1621, 1529, 1397, 1281, 1247, 1144, 702	–269[b]
50/50′b	–	3264, 1770, 1732, 1711, 1684, 1613, 1527, 1387, 1287, 1244, 1145, 1062, 968, 785, 701	–223[b]
50c	–	3322, 1717, 1682, 1615, 1528, 1400, 1246, 1168, 1058, 792	–
51/51′a	–	3419, 2979, 1773, 1713, 1687, 1623, 1553, 1455, 1395, 1276, 1246, 1157, 1068, 789, 702	–226[b]
51/51′b	442 (M^+) Calcd: 442.164105 Found: 442.165080	3446, 1777, 1715, 1686, 1621, 1552, 1455, 1381, 1275, 1245, 994, 700	–163[b]
52/52′b	–	3436, 1765, 1689, 1665, 1627, 1592, 1341, 1268, 1228, 1112, 996, 698	–286[b]
52/52′c	–	3428, 1731, 1717, 1700, 1668, 1629, 1512, 1332, 1230, 761	–
53/53′a	–	3447, 3257, 2976, 1758, 1720, 1697, 1654, 1497, 1344, 1159, 702	–111[b]
53/53′c	–	3304, 1740, 1685, 1649, 1492, 1258, 1214, 1172, 701	–
54/54′a	417 (MH^+) Calcd: 417.202562 Found: 417.203950	3226, 2975, 1766, 1742, 1702, 1659, 1620, 1493, 1349, 1282,1141, 1064, 846, 700	–62.8[b]

Table 3 Analytical, MS, and IR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a–c,** and **35/35′–64/64′** (continued)

Product[a]	EI-MS (m/z) EI-HRMS (m/z)	IR (KBr/film) cm^{-1}	$[\alpha]_D^{20}$
55/55′a	–	3458, 2959, 1747, 1703, 1665, 1620, 1491, 1307, 1152, 752, 698	–120[b]
55/55′b	–	3472, 2957, 1771, 1745, 1709, 1666, 1619, 1493, 1382, 1349, 1297, 1267, 1141, 1001, 745, 700	–90.7[b]
56/56′a	–	3244, 2978, 1762, 1737, 1699, 1655, 1638, 1346, 1281, 1159, 700	–110[b]
57/57′a	–	3464, 2979, 1758, 1701, 1664, 1615, 1494, 1307, 1156, 845, 789, 755, 701	–160[b]
57/57′b	482 (M^+) Calcd: 482.152496 Found: 482.152350	3446, 1769, 1741, 1706, 1666, 1615, 1495, 1382, 1348, 1296, 1263, 1193, 1097, 700	–112[b]
57/57′c	449 (M^+) Calcd: 449.125672 Found: 449.126110	3433, 1727, 1665, 1614, 1493, 1395, 1244, 1169, 698	–22.0[b]
58/58′b	512 (M^+) Calcd: 512.194737 Found: 512.196050	3473, 3030, 1770, 1745, 1708, 1665, 1618, 1495, 1455, 1381, 1349, 1296, 1096, 999, 748, 700	–194[b]
58/58′c	479 (M^+) Calcd: 479.169251 Found: 479.170530	3420, 1726, 1667, 1617, 1493, 1397, 1243, 1172, 701	–149[b]
59/59′b	551 (M^+) Calcd: 551.205636 Found: 551.207050	3328, 1762, 1696, 1661, 1615, 1493, 1349, 1296, 1268, 1096, 743, 700	–234[b]
60/60′a	–	3455, 2977, 1758, 1738, 1697, 1651, 1489, 1347, 1068, 982, 843, 700	–67.5[b]
61/61′a	356 (MH^+, FAB) 711 (M_2H^+, FAB) 1066 (M_3H^+, FAB)	3276, 1278, 1758, 1698, 1653, 1633, 1493, 1349, 1253, 1157, 1097, 700	–80.9[b]
61/61′b	389 (M^+) 390 (MH^+, FAB) 779 (M_2H^+, FAB) Calcd: 389.137556 Found: 389.138650	3436, 3624, 1763, 1697, 1657, 1495, 1381, 1346, 1294, 1267, 1068, 702.	–63.9[b]
61/61′c	356 (M^+) 357 (MH^+, FAB) 713 (M_2H^+, FAB)	3350, 3147, 1724, 1673, 1585, 1495, 1429, 1395, 1251, 1179, 700	–
62/62′b	440 (M^+) Calcd: 440.173608 Found: 440.175250	3251, 1768, 1708, 1660, 162, 1488, 1455, 1382, 1340, 1297, 1209, 1076, 742, 698	–69.8[b]
63/63′c	–	3341, 2902, 1727, 1681, 1661, 1593, 1489, 1397, 1251, 1167, 697	–
64a	–	3420, 3109, 2985, 1756, 1600, 1431, 1351, 1323, 1152, 994, 845, 700	–168[c]
64b	–	3071, 1760, 1607, 1496, 1389, 1356, 1313, 1286,1237, 967, 775, 697	–112[b]
64/64′c	–	3312, 1726, 1660, 1516, 1422, 1400, 1236, 1064, 981, 879, 756, 699	–

[a] Satisfactory microanalyses obtained: C ± 0.43; H ± 0.37; N ± 0.36. Exceptions: **57/57′c**, N –0.57; **59/59′b**, N –0.65; **62/62′b**, N –1.07.

[b] $c = 0.50$, $CHCl_3$.

[c] $c = 0.50$, DMSO.

Table 4 ^{1}H NMR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′**

Product	Solvent	^{1}H NMR, δ
2′c	DMSO-d_6	1.48 (6 H, s, 2 Me), 3.17 (6 H, s, NMe$_2$), 3.64 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 4.14 (2 H, d, *J* = 4.5 Hz, C*H*$_2$NH), 5.06 (2 H, s, PhC*H*$_2$O), 6.93–7.00 (2 H, m, 2 H of pyridine), 7.25–7.40 (5 H, m, Ph), 7.61 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.65 (1 H, t, *J* = 4.5 Hz, CH$_2$N*H*), 8.19–8.24 (2 H, m, 2 H of pyridine), 13.28 (1 H, br s, NH pyridine)
2c	DMSO-d_6	1.64 (6 H, s, 2 Me), 3.67 (2 H, d, *J* = 5.7 Hz, C*H*$_2$NH), 4.47 (2 H, d, *J* = 5.0 Hz, C*H*$_2$NH), 5.05 (2 H, s, PhC*H*$_2$O), 7.27–7.39 (5 H, m, Ph), 7.54 (1 H, t, *J* = 5.7 Hz, CH$_2$N*H*), 8.09 (1 H, t, *J* = 5.0 Hz, CH$_2$N*H*)
3c	DMSO-d_6	4.19 (2 H, s, 5-CH$_2$), 4.24 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 4.99 (1 H, s, 3–H), 5.04 (2 H, s, PhC*H*$_2$O), 7.27–7.39 (5 H, m, Ph), 7.42 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 12.51 (1 H, br s, OH)
4a	CDCl$_3$	1.59 (9 H, s, *t*-Bu), 3.25 (1 H, dd, *J* = 3.0, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.25 (3 H, s, NMe), 3.37 (1 H, dd, *J* = 5.7, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.61 (3 H, s, NMe), 4.34 (1 H, br s, PhCH$_2$C*H*), 7.04–7.11 (2 H, m, 2 H of Ph), 7.14–7.23 (4 H, m, 3 H of Ph, CH=)
4b	CDCl$_3$	3.22 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.26 (3 H, s, NMe), 3.36 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.60 (3 H, s, NMe), 4.41 (1 H, br s, PhCH$_2$C*H*), 5.35 (2 H, s, PhC*H*$_2$O), 6.90–6.98 (2 H, m, 2 H of Ph), 7.08–7.15 (3 H, m, 3 H of Ph), 7.30–7.42 (4 H, m, 3 H of Ph, CH=), 7.45–7.51 (2 H, m, 2 H of Ph)
4c	CDCl$_3$	3.39 (3 H, s, NMe), 3.76 (3 H, s, NMe), 4.02 (2 H, s, 5-CH$_2$), 4.62 (2 H, d, *J* = 5.7 Hz, C*H*$_2$NH), 5.14 (2 H, s, PhC*H*$_2$O), 5.55 (1 H, s, CH$_2$N*H*), 7.29–7.43 (6 H, m, Ph, CH=)
4c	DMSO-d_6	3.41 (3 H, s, NMe), 3.64 (3 H, s, NMe), 3.88 (2 H, s, 5-CH$_2$), 4.33 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 5.05 (2 H, s, PhC*H*$_2$O), 7.27–7.39 (5 H, m, Ph), 7.43 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.55 (1 H, s, CH=)
35/35′a	CDCl$_3$	*Major E-Isomer*: 1.62 (9 H, s, *t*-Bu), 3.33 (1 H, dd, *J* = 3.2, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.41 (1 H, dd, *J* = 6.0, 13.8 Hz, 1 H of PhC*H*$_2$CH), 4.54 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 7.05–7.10 (2 H, m, 2 H of Ph), 7.10–7.30 (6 H, m, 6 H of Ph), 7.35–7.46 (2 H, m, 2 H of Ph), 7.95 (1 H, d, *J* = 13.6 Hz, NHC*H*=), 11.27 (1 H, d, *J* = 13.2 Hz, N*H*CH=) *Minor Z-Isomer*: 1.63 (9 H, s, *t*-Bu), 3.33 (1 H, dd, *J* = 2.9, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.44 (1 H, dd, *J* = 5.8, 13.8 Hz, 1 H of PhC*H*$_2$CH), 4.48 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 8.13 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 10.94 (1 H, d, *J* = 13.6 Hz, N*H*CH=)
35/35′b	CDCl$_3$	*Major E-Isomer:* 3.24–3.35 (1 H, m, 1 H of PhC*H*$_2$CH), 3.40 (1 H, dd, *J* = 5.3, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.58 (1 H, dd, *J* = 2.6, 5.3 Hz, PhCH$_2$C*H*), 5.38 (2 H, s, PhC*H*$_2$O), 6.86–7.00 (2 H, m, 2 H of Ph), 7.05–7.16 (4 H, m, 4 H of Ph), 7.16–7.30 (2 H, m, 2 H of Ph), 7.32–7.46 (5 H, m, 5 H of Ph), 7.46–7.55 (2 H, m, 2 H of Ph), 7.97 (1 H, d, *J* = 12.2 Hz, NHC*H*=), 11.32 (1 H, d, *J* = 12.0 Hz, N*H*CH=) *Minor Z-Isomer*: 4.52 (1 H, dd, *J* = 2.6, 5.3 Hz, PhCH$_2$C*H*), 5.36 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 5.42 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 8.14 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 10.91 (1 H, d, *J* = 13.8 Hz, N*H*CH=)
35/35′c	DMSO-d_6	*Major E-Isomer*: 4.06 (2 H, s, 5-CH$_2$), 4.40 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 5.06 (2 H, s, PhC*H*$_2$O), 7.24–7.40 (6 H, m, 6 H of Ph), 7.40–7.48 (2 H, m, 2 H of Ph), 7.50 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.59–7.65 (2 H, m, 2 H of Ph), 8.33 (1 H, br s, NHC*H*=), 11.55 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 11.21 (1 H, br s, N*H*CH=)
36/36′b	CDCl$_3$	*Major E-Isomer*: 2.36 (3 H, s, Me), 3.29 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.39 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.58 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.38 (2 H, s, PHC*H*$_2$O), 6.89–6.97 (2 H, m, 2 H of Ph), 7.05–7.16 (5 H, m, 5 H of Ph), 7.18–7.24 (2 H, m, 2 H of Ph), 7.31–7.44 (3 H, m, 3 H of Ph), 7.47–7.53 (2 H, m, 2 H of Ph), 7.93 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 11.32 (1 H, d, *J* = 13.6 Hz, N*H*CH=) *Minor Z-Isomer*: 2.34 (3 H, s, Me), 4.52 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.40 (2 H, s, PHC*H*$_2$O), 8.11 (1 H, d, *J* = 14.3 Hz, NHC*H*=), 10.89 (1 H, d, *J* = 14.0 Hz, N*H*CH=)
36/36′c	DMSO-d_6	*Major E-Isomer*: 2.31 (3 H, s, Me), 4.04 (2 H, s, 5-CH$_2$), 4.39 (2 H, d, *J* = 6.4 Hz, C*H*$_2$NH), 5.06 (2 H, s, PhC*H*$_2$O), 7.21–7.27 (2 H, m, 2 H of Ar), 7.28–7.41 (5 H, m, Ph), 7.46–7.53 (3 H, m, 2 H of Ar, CH$_2$N*H*), 8.29 (1 H, s, NHC*H*=), 11.39 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 4.02 (2 H, s, 5-CH$_2$), NH exchanged
37/37′a	CDCl$_3$	*Major E-Isomer*: 1.63 (9 H, s, *t*-Bu), 3.33 (1 H, dd, *J* = 3.0, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.42 (1 H, dd, *J* = 6.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.58 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 7.02–7.08 (2 H, m, 2 H of Ph), 7.14–7.27 (3 H, m, 3 H of Ph), 7.28–7.35 (2 H, m, 2 H of Ar), 7.96 (1 H, br d, *J* = 11.3 Hz, NHC*H*=), 8.25–8.34 (2 H, m, 2 H of Ar), 11.28 (1 H, br d, *J* = 11.3 Hz, N*H*CH=) *Minor Z-Isomer*: 1.64 (9 H, s, *t*-Bu), 4.53 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 8.12 (1 H, d, *J* = 13.2 Hz, NHC*H*=), 11.05 (1 H, d, *J* = 13.2 Hz, N*H*CH=)

Table 4 ^{1}H NMR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′** (continued)

Product	Solvent	^{1}H NMR, δ
37/37′b	CDCl$_3$	*Major Z-Isomer*: 3.31 (1 H, dd, *J* = 2.7, 13.9 Hz, 1 H of PhCH_2CH), 3.42 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhCH_2CH), 4.58 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.38 (1 H, d, *J* = 12.1 Hz, 1 H of PhCH_2O), 5.43 (1 H, d, *J* = 12.1 Hz, 1 H of PhCH_2O), 6.88–6.95 (2 H, m, 2 H of Ph), 7.10–7.16 (3 H, m, 3 H of Ph), 7.22–7.28 (2 H, m, 2 H of Ar), 7.36–7.46 (3 H, m, 3 H of Ph), 7.48–7.53 (2 H, m, 2 H of Ph), 8.14 (1 H, d, *J* = 13.6 Hz, NHC*H*=), 8.25–8.35 (2 H, m, 2 H of Ar), 11.01 (1 H, d, *J* = 13.9 Hz, N*H*CH=) *Minor E-Isomer*: 3.30 (1 H, dd, *J* = 2.6, 13.9 Hz, 1 H of PhCH_2CH), 3.41 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhCH_2CH), 4.64 (1 H, dd, *J* = 3.0, 5.8 Hz, PhCH$_2$C*H*), 5.40 (2 H, s, PhCH_2O), 7.30–7.36 (2 H, m, 2 H of Ar), 7.99 (1 H, s, NHC*H*=), 11.33 (1 H, br s, N*H*CH=)
37/37′c	DMSO-d_6	*Major E-Isomer*: 4.10 (2 H, s, 5-CH$_2$), 4.41 (2 H, d, *J* = 5.7 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 7.28–7.42 (5 H, m, Ph), 7.53 (1 H, t, *J* = 5.7 Hz, CH$_2$N*H*), 7.85–7.94 (2 H, m, 2 H of Ph), 8.23–8.30 (2 H, m, 2 H of Ph), 8.42 (1 H, br s, NHC*H*=), 11.39 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 11.35 (1 H, br s, N*H*CH=)
38/38′c	DMSO-d_6	*Major E-Isomer*: 3.94 (3 H, s, OMe), 4.10 (2 H, s, 5-CH$_2$), 4.38 (2 H, d, *J* = 6.0 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 6.99–7.09 (1 H, m, 1 H of Ar), 7.19 (1 H, dd, *J* = 1.3, 8.3 Hz, 1 H of Ar), 7.22–7.41 (6 H, m, Ph, 1 H of Ar), 7.49 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.78–7.89 (1 H, m, 1 H of Ar), 8.57 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 11.82 (1 H, d, *J* = 13.9 Hz, N*H*CH=) *Minor Z-Isomer*: 4.03 (2 H, s, 5-CH$_2$), 4.42 (2 H, d, *J* = 6.0 Hz, CH_2NH), 7.53 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 8.65 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 11.28 (1 H, d, *J* = 13.9 Hz, N*H*CH=)
39/39′c	DMSO-d_6	*Major E-isomer*: 3.80 (3 H, s, OMe), 4.06 (2 H, s, 5-CH$_2$), 4.40 (2 H, d, *J* = 6.0 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 6.84 (1 H, dd, *J* = 2.4, 8.1 Hz, 1 H of Ar), 7.17 (1 H, dd, *J* = 1.8, 7.9 Hz, 1 H of Ar), 7.28 (1 H, t, *J* = 2.3 Hz, 1 H of Ar), 7.29–7.40 (6 H, m, Ph, 1 H of Ar), 7.50 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 8.40 (1 H, br s, NHC*H*=), 11.48 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 11.14 (1 H, br s, N*H*CH=)
40/40′a	CDCl$_3$	*Major E-Isomer*: 1.61 (9 H, s, *t*-Bu), 3.32 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhCH_2CH), 3.40 (1 H, dd, *J* = 6.0, 13.6 Hz, 1 H of PhCH_2CH), 3.82 (3 H, s, OMe), 4.52 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 6.87–6.96 (2 H, m, 2 H of Ar), 7.03–7.23 (7 H, m, Ph, 2 H of Ar), 7.85 (1 H, d, *J* = 13.7 Hz, NHC*H*=), 11.29 (1 H, d, *J* = 13.8 Hz, N*H*CH=) *Minor Z-Isomer*: 1.62 (9 H, s, *t*-Bu), 3.33 (1 H, dd, *J* = 2.9, 13.9 Hz, 1 H of PhCH_2CH), 3.43 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhCH_2CH), 3.80 (3 H, s, OMe), 4.46 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 8.03 (1 H, d, *J* = 14.1 Hz, NHC*H*=), 10.94 (1 H, d, *J* = 14.1, N*H*CH=)
40/40′b	CDCl$_3$	*Major E-Isomer*: 3.29 (1 H, dd, *J* = 2.8, 13.8 Hz, 1 H of PhCH_2CH), 3.39 (1 H, dd, *J* = 5.7, 13.7 Hz, 1 H of PhCH_2CH), 3.82 (3 H, s, OMe), 4.57 (1 H, dd, *J* = 3.0, 5.8 Hz, PhCH$_2$C*H*), 5.38 (2 H, s, PhCH_2O), 6.88–6.97 (4 H, m, 4 H of Ph), 7.04–7.16 (5 H, m, 3 H of Ph, 2 H of Ar), 7.31–7.45 (3 H, m, 3 H of Ph), 7.47–7.53 (2 H, m, 2 H of Ar), 7.87 (1 H, d, *J* = 13.6 Hz, NHC*H*=), 11.36 (1 H, d, *J* = 13.6 Hz, N*H*CH=) *Minor Z-Isomer*: 3.30 (1 H, dd, *J* = 2.7, 13.9 Hz, 1 H of PhCH_2CH), 3.41 (1 H, dd, *J* = 5.6, 13.9 Hz, 1 H of PhCH_2CH), 3.81 (3 H, s, OMe), 4.51 (1 H, dd, *J* = 2.9, 5.7 Hz, PhCH$_2$C*H*), 5.35 (1 H, d, *J* = 12.4 Hz, 1 H of PhCH_2O), 5.42 (1 H, d, *J* = 12.4 Hz, 1 H of PhCH_2O), 8.04 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 10.91 (1 H, d, *J* = 14.0 Hz, N*H*CH=)
40/40′c	DMSO-d_6	*Major E-Isomer*: 3.77 (3 H, s, OMe), 4.04 (2 H, s, 5-CH$_2$), 4.39 (2 H, d, *J* = 6.0 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 6.96–7.03 (2 H, m, 2 H of Ar), 7.27–7.40 (5 H, m, Ph), 7.49 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.53–7.60 (2 H, m, 2 H of Ar), 8.23 (1 H, br s, NHC*H*=), 11.53 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 11.23 (1 H, br s, N*H*CH=)
41/41′c	DMSO-d_6	*Major E-Isomer*: 4.15 (2 H, s, 5-CH$_2$), 4.39 (2 H, d, *J* = 6.0 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 7.19–7.27 (1 H, m, 1 H of Ar), 7.28–7.40 (5 H, m, Ph), 7.44–7.58 (2 H, m, CH$_2$N*H*, 1 H of Ar), 7.77 (1 H, dd, *J* = 1.1, 8.0 Hz, 1 H of Ar), 7.92–8.02 (1 H, m, 1 H of Ar), 8.63 (1 H, br, NHC*H*=), 11.80 (1 H, d, *J* = 12.1 Hz, N*H*CH=) *Minor Z-Isomer*: 4.07 (2 H, s, 5-CH$_2$), 4.42 (2 H, d, *J* = 6.0 Hz, CH_2NH), 5.05 (2 H, s, PhCH_2O), 11.30 (1 H, d, *J* = 13.6 Hz, N*H*CH=)
42/42′c	DMSO-d_6	*Major E-Isomer*: 4.07 (2 H, s, 5-CH$_2$), 4.40 (2 H, d, *J* = 6.0 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 7.24–7.42 (6 H, m, Ph, 1 H of Ar), 7.42–7.48 (1 H, m, 1 H of Ar), 7.51 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.59–7.68 (1 H, m, 1 H of Ar), 7.94–7.98 (1 H, m, 1 H of Ar), 8.35 (1 H, br s, NHC*H*=), 11.44 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 11.25 (1 H, br s, N*H*CH=)
43/43′b	CDCl$_3$	*Major E-isomer*: 3.29 (1 H, dd, *J* = 3.0, 13.8 Hz, 1 H of PhCH_2CH), 3.39 (1 H, dd, *J* = 5.9, 13.8 Hz, 1 H of PhCH_2CH), 4.59 (1 H, dd, *J* = 3.0, 5.8 Hz, PhCH$_2$C*H*), 5.38 (2 H, s, PhCH_2O), 6.89–6.95 (2 H, m, 2 H of Ph), 7.05–7.10 (2 H, m, 2 H of Ar), 7.10–7.15 (3 H, m, 3 H of Ph), 7.31–7.45 (3 H, m, 3 H of Ph), 7.47–7.52 (2 H, m, 2 H of Ph), 7.52–7.57 (2 H, m, 2 H of Ar), 7.90 (1 H, d, *J* = 11.7 Hz, NHC*H*=), 11.27 (1 H, d, *J* = 11.7 Hz, N*H*CH=) *Minor Z-Isomer*: 3.30 (1 H, dd, *J* = 2.7, 13.8 Hz, 1 H of PhCH_2CH), 3.41 (1 H, dd, *J* = 4.9, 13.8 Hz, 1 H of PhCH_2CH), 4.53 (1 H, dd, *J* = 2.8, 5.7 Hz, PhCH$_2$C*H*), 5.36 (1 H, d, *J* = 12.1 Hz, 1 H of PhCH_2O), 5.42 (1 H, d, *J* = 12.1 Hz, 1 H of PhCH_2O), 8.07 (1 H, d, *J* = 13.6 Hz, NHC*H*=), 10.91 (1 H, d, *J* = 13.6 Hz, N*H*CH=)

Table 4 ^{1}H NMR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′** (continued)

Product	Solvent	^{1}H NMR, δ
43/43′c	DMSO-d_6	*Major E-Isomer*: 4.06 (2 H, s, 5-CH$_2$), 4.39 (2 H, d, J = 6.0 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 7.28–7.41 (5 H, m, Ph), 7.50 (1 H, t, J = 6.0 Hz, CH$_2$N*H*), 7.61 (4 H, s, 4 H of Ar), 8.30 (1 H, br s, NHC*H*=), 11.39 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 4.04 (2 H, s, 5-CH$_2$), 5.05 (2 H, s, PhCH_2O), NH exchanged
44/44′b	CDCl$_3$	*Major Z-Isomer*: 3.35 (1 H, dd, J = 3.0, 13.8 Hz, 1 H of PhCH_2CH), 3.46 (1 H, dd, J = 5.7, 13.8 Hz, 1 H of PhCH_2CH), 4.57 (1 H, dd, J = 3.0, 5.6 Hz, PhCH$_2$C*H*), 5.39 (1 H, d, J = 12.1 Hz, 1 H of PhCH_2O), 5.44 (1 H, d, J = 12.2 Hz, 1 H of PhCH_2O), 6.91–7.01 (2 H, m, 2 H of Ph), 7.09–7.16 (3 H, m, 3 H of Ph), 7.32–7.73 (9 H, m, Ph, 4 H of Ar), 7.76–7.84 (1 H, m, 1 H of Ar), 7.85–8.06 (2 H, m, 2 H of Ar), 8.28 (1 H, d, J = 13.6 Hz, NHC*H*=), 11.12 (1 H, d, J = 13.4 Hz, N*H*CH=) *Minor E-Isomer*: 3.33 (1 H, dd, J = 3.0, 13.8 Hz, 1 H of PhCH_2CH), 3.42 (1 H, dd, J = 5.7, 13.8 Hz, 1 H of PhCH_2CH), 4.67 (1 H, dd, J = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.41 (2 H, s, PhCH_2O), 8.09 (1 H, d, J = 11.9 Hz, NHC*H*=), 11.46 (1 H, br, N*H*CH=)
44/44′c	DMSO-d_6	*Major E-Isomer*: 4.17 (2 H, s, 5-CH$_2$), 4.40 (2 H, d, J = 6.0 Hz, CH_2NH), 5.07 (2 H, s, PhCH_2O), 7.26–7.42 (5 H, m, Ph), 7.51 (1 H, t, J = 6.0 Hz, CH$_2$N*H*), 7.54–7.78 (3 H, m, 3 H of Ar), 7.79–8.81 (4 H, m, 4 H of Ar), 8.53 (1 H, d, J = 12.8 Hz, NHC*H*=), 12.34 (1 H, d, J = 12.8 Hz, N*H*CH=) *Minor Z-Isomer*: 4.08 (2 H, s, 5-CH$_2$), 4.48 (2 H, d, J = 6.0 Hz, CH_2NH), 5.08 (1 H, s, PhCH_2O), 8.55 (1 H, d, J = 14.3 Hz, NHC*H*=), 11.81 (1 H, d, J = 14.3 Hz, N*H*CH=)
45/45′a	CDCl$_3$	*Major Z-Isomer*: 1.62 (9 H, s, *t*-Bu), 2.31 (3 H, d, J = 0.7 Hz, Me), 3.30–3.44 (2 H, m, PhCH_2CH), 4.48 (1 H, dd, J = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.81 (1 H, d, J = 0.7 Hz, 1 H of Het), 7.03–7.09 (2 H, m, 2 H of Ph), 7.13–7.22 (3 H, m, 3 H of Ph), 8.46 (1 H, d, J = 13.9 Hz, NHC*H*=), 11.12 (1 H, br s, NH of Het), 11.17 (1 H, d, J = 13.9 Hz, N*H*CH=) *Minor E-Isomer*: 1.61 (9 H, s, *t*-Bu), 2.33 (3 H, d, J = 0.8 Hz, Me), 4.52 (1 H, dd, J = 3.4, 5.7 Hz, PhCH$_2$C*H*), 5.89 (1 H, d, J = 0.8 Hz, 1 H of Het), 8.23 (1 H, br s, NHC*H*=), 11.48 (1 H, br s, N*H*CH=)
46a	DMSO-d_6	1.54 (9 H, s, *t*-Bu), 3.20 (1 H, dd, J = 2.6, 13.9 Hz, 1 H of PhCH_2CH), 3.31 (1 H, dd, J = 6.0, 13.9 Hz, 1 H of PhCH_2CH), 4.56 (1 H, dd, J = 2.6, 6.0 Hz, PhCH$_2$C*H*), 6.92–7.02 (2 H, m, 2 H of Ph), 7.11–7.30 (3 H, m, 3 H of Ph), 8.00 (1 H, br s, NHC*H*=), 11.48 (1 H, br s, N*H*CH=), HN(1′) exchanged
46b	DMSO-d_6	3.20 (1 H, dd, J = 3.0, 13.9 Hz, 1 H of PhCH_2CH), 3.28 (1 H, dd, J = 6.0, 13.9 Hz, 1 H of PhCH_2CH), 4.64 (1 H, dd, J = 3.0, 6.0 Hz, PhCH$_2$C*H*), 5.35 (2 H, s, PhCH_2O), 6.84–6.92 (2 H, m, 2 H of Ph), 7.12–7.18 (3 H, m, 3 H of Ph), 7.34–7.53 (5 H, m, Ph), 8.02 (1 H, br s, NHC*H*=), N*H*CH= and HN(1′) exchanged
47/47′a	CDCl$_3$	*Major Z-Isomer*: 1.62 (9 H, s, *t*-Bu), 2.41 (3 H, d, J = 0.8 Hz, Me), 3.32 (1 H, dd, J = 3.0, 13.9 Hz, 1 H of PhCH_2CH), 3.42 (1 H, dd, J = 6.0, 13.9 Hz, 1 H of PhCH_2CH), 4.50 (1 H, dd, J = 3.0, 6.0 Hz, PhCH$_2$C*H*), 5.88 (1 H, q, J = 0.8 Hz, 1 H of Het), 7.01–7.07 (2 H, m, 2 H of Ph), 7.13–7.24 (3 H, m, 3 H of Ph), 8.09 (1 H, d, J = 13.6 Hz, NHC*H*=), 10.62 (1 H, d, J = 13.2 Hz, N*H*CH=) *Minor E-Isomer*: 1.62 (9 H, s, *t*-Bu), 2.44 (3 H, d, J = 0.8 Hz, Me), 3.40 (1 H, dd, J = 6.0, 13.8 Hz, 1 H of PhCH_2CH), 4.55 (1 H, dd, J = 3.0, 6.0 Hz, PhCH$_2$C*H*), 5.99 (1 H, q, J = 0.8 Hz, 1 H of Het), 7.81 (1 H, s, NHC*H*=), 10.89 (1 H, br s, N*H*CH=)
48/48′c	DMSO-d_6	*Major E-Isomer*: 4.09 (2 H, s, 5-CH$_2$), 4.42 (2 H, d, J = 5.3 Hz, CH_2NH), 5.07 (2 H, s, PhCH_2O), 7.16–7.23 (1 H, m, 1 H of Het), 7.28–7.40 (5 H, m, Ph), 7.40–7.47 (1 H, m, 1 H of Het), 7.48–7.57 (2 H, m, 1 H of Het, CH$_2$N*H*), 7.92–7.98 (1 H, m, 1 H of Het), 8.34 (1 H, br s, NHC*H*=), 11.97 (1 H, br s, N*H*CH=), 13.12 (1 H, s, NH of Het) *Minor Z-Isomer*: 11.71 (1 H, br s, N*H*CH=)
49/49′a	CDCl$_3$	*Major Z-Isomer*: 1.63 (9 H, s, *t*-Bu), 3.34 (1 H, dd, J = 3.0, 13.9 Hz, 1 H of PhCH_2CH), 3.43 (1 H, dd, J = 5.7, 13.9 Hz, 1 H of PhCH_2CH), 4.49 (1 H, dd, J = 3.0, 5.7 Hz, PhCH$_2$C*H*), 6.86 (1 H, ddd, J = 0.8, 0.9, 8.1 Hz, 1 H of Het), 7.04–7.09 (2 H, m, 2 H of Ph), 7.09–7.23 (4 H, m, 3 H of Ph, 1 H of Het), 7.68 (1 H, ddd, J = 1.9, 7.4, 8.1 Hz, 1 H of Het), 8.36–8.40 (1 H, m, 1 H of Het), 8.90 (1 H, d, J = 12.8 Hz, NHC*H*=), 11.00 (1 H, d, J = 13.2 Hz, N*H*CH=) *Minor E-isomer*: 1.62 (9 H, s, *t*-Bu), 3.33 (1 H, dd, J = 3.4, 13.9 Hz, 1 H of PhCH_2CH), 3.41 (1 H, dd, J = 5.9, 13.9 Hz, 1 H of PhCH_2CH), 4.55 (1 H, dd, J = 3.0, 6.0 Hz, PhCH$_2$C*H*), 7.00 (1 H, ddd, J = 0.8, 0.9, 8.1 Hz, 1 H of Het), 7.73 (1 H, ddd, J = 1.9, 7.4, 8.1 Hz, 1 H of Het), 8.68 (1 H, d, J = 12.8 Hz, NHC*H*=), 11.31 (1 H, d, J = 12.8 Hz, N*H*CH=)
49/49′c	DMSO-d_6	*Major E-Isomer*: 4.08 (2 H, s, 5-CH$_2$), 4.41 (2 H, d, J = 5.7 Hz, CH_2NH), 5.06 (2 H, s, PhCH_2O), 7.24–7.42 (6 H, m, Ph, 1 H of Het), 7.52 (1 H, t, J = 5.7 Hz, CH$_2$N*H*), 7.65–7.72 (1 H, m, 1 H of Het), 7.86–7.94 (1 H, m, 1 H of Het), 8.42–8.48 (1 H, m, 1 H of Het), 8.81 (1 H, br s, NHC*H*=), 11.59 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 4.08 (2 H, s, 5-CH$_2$), 4.44 (2 H, d, J = 6.0 Hz, CH_2NH), 7.52 (1 H, t, J = 6.0 Hz, CH$_2$N*H*), 8.88 (1 H, s, NHC*H*=), NH exchanged

Table 4 ^{1}H NMR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′** (continued)

Product	Solvent	^{1}H NMR, δ
50/50′a	CDCl$_3$	*Major Z-Isomer*: 1.64 (9 H, s, *t*-Bu), 3.34 (1 H, dd, *J* = 2.6, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.44 (1 H, dd, *J* = 6.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.53 (1 H, dd, *J* = 2.6, 5.7 Hz, PhCH$_2$C*H*), 7.04–7.08 (2 H, m, 2 H of Ph), 7.12–7.24 (3 H, m, 3 H of Ph), 8.30 (1 H, d, *J* = 1.5 Hz, 1 H of Het), 8.33 (1 H, dd, *J* = 1.5, 2.5 Hz, 1 H of Het), 8.40 (1 H, d, *J* = 2.5 Hz, 1 H of Het), 8.79 (1 H, d, *J* = 12.8 Hz, NHC*H*=), 11.09 (1 H, d, *J* = 12.8 Hz, N*H*CH=) *Minor E-Isomer*: 1.62 (9 H, s, *t*-Bu), 3.42 (1 H, dd, *J* = 6.2, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.59 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 8.34 (1 H, dd, *J* = 1.5, 2.6 Hz, 1 H of Het), 8.42–8.44 (2 H, m, 2 H of Het), 8.62 (1 H, d, *J* = 11.7 Hz, NHC*H*=), 11.31 (1 H, d, *J* = 11.9 Hz, N*H*CH=)
50/50′b	CDCl$_3$	*Major Z-Isomer*: 3.32 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.42 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.58 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.38 (1 H, d, *J* = 12.1 Hz, 1 H of PhC*H*$_2$O), 5.43 (1 H, d, *J* = 12.1 Hz, 1 H of PhC*H*$_2$O), 6.87–6.95 (2 H, m, 2 H of Ph), 7.08–7.16 (3 H, m, 3 H of Ph), 7.33–7.46 (3 H, m, 3 H of Ph), 7.48–7.54 (2 H, m, 2 H of Ph), 8.31 (1 H, d, *J* = 1.9 Hz, 1 H of Het), 8.32–8.36 (1 H, m, 1 H of Het), 8.41 (1 H, d, *J* = 2.6 Hz, 1 H of Het), 8.81 (1 H, d, *J* = 12.8 Hz, NHC*H*=), 11.06 (1 H, d, *J* = 12.6 Hz, N*H*CH=) *Minor E-Isomer*: 3.31 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.41 (1 H, dd, *J* = 6.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.64 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.40 (2 H, s, PHC*H*$_2$O), 8.43–8.46 (2 H, m, 2 H of Het), 8.65 (1 H, d, *J* = 11.2 Hz, NHC*H*=), 11.39 (1 H, br d, *J* = 11.3 Hz, N*H*CH=)
50c	DMSO-*d*$_6$	4.11 (2 H, s, 5-CH$_2$), 4.41 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 5.06 (2 H, s, PhC*H*$_2$O), 7.27–7.41 (5 H, m, Ph), 7.53 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 8.50 (1 H, dd, *J* = 1.2, 2.6 Hz, 1 H of Het), 8.52 (1 H, d, *J* = 2.6 Hz, 1 H of Het), 8.67 (1 H, br s, NHC*H*=), 8.99 (1 H, s, 1 H of Het), 11.75 (1 H, br s, N*H*CH=)
51/51′a	CDCl$_3$	*Major Z-Isomer*: 1.63 (9 H, s, *t*-Bu), 2.47 (3 H, d, *J* = 0.4 Hz, Me), 3.34 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.44 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.51 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 6.93 (1 H, dd, *J* = 0.5, 5.0 Hz, 1 H of Het), 7.03–7.08 (2 H, m, 2 H of Ph), 7.10–7.23 (3 H, m, 3 H of Ph), 8.38 (1 H, d, *J* = 5.0 Hz, 1 H of Het), 8.84 (1 H, d, *J* = 13.4 Hz, NHC*H*=), 10.78 (1 H, d, *J* = 13.6 Hz, N*H*CH=) *Minor E-Isomer*: 1.62 (9 H, s, *t*-Bu), 2.49 (3 H, d, *J* = 0.4 Hz, Me), 3.33 (1 H, dd, *J* = 3.1, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.42 (1 H, dd, *J* = 5.4, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.55 (1 H, dd, *J* = 3.1, 5.7 Hz, PhCH$_2$C*H*), 6.96 (1 H, dd, *J* = 0.5, 5.0 Hz, 1 H of Het), 8.42 (1 H, d, *J* = 5.0 Hz, 1 H of Het), 8.67 (1 H, d, *J* = 13.2 Hz, NHC*H*=), 11.06 (1 H, d, *J* = 13.1 Hz, N*H*CH=)
51/51′b	CDCl$_3$	*Major E-Isomer*: 2.50 (3 H, s, Me), 3.31 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.41 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.61 (1 H, dd, *J* = 3.0, 5.8 Hz, PhCH$_2$C*H*), 5.39 (2 H, s, PhC*H*$_2$O), 8.42 (1 H, d, *J* = 5.1 Hz, 1 H of Het), 8.70 (1 H, d, *J* = 12.8 Hz, NHC*H*=), 11.11 (1 H, d, *J* = 12.4 Hz, N*H*CH=) *Minor Z-Isomer*: 2.47 (3 H, s, Me), 3.32 (1 H, dd, *J* = 2.6, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.42 (1 H, dd, *J* = 5.7, 13.8 Hz, 1 H of PhC*H*$_2$CH), 4.56 (1 H, dd, *J* = 2.9, 5.7 Hz, PhCH$_2$C*H*), 5.37 (1 H, d, *J* = 12.1 Hz, 1 H of PhC*H*$_2$O), 5.42 (1 H, d, *J* = 12.1 Hz, 1 H of PhC*H*$_2$O), 6.88–7.00 (3 H, m, 2 H of Ph, 1 H of Het), 7.08–7.15 (3 H, m, 3 H of Ph), 7.31–7.46 (3 H, m, 3 H of Ph), 7.48–7.54 (2 H, m, 2 H of Ph), 8.39 (1 H, d, *J* = 5.1 Hz, 1 H of Het), 8.87 (1 H, d, *J* = 13.2 Hz, NHC*H*=), 10.77 (1 H, d, *J* = 13.2 Hz, N*H*CH=)
52/52′b	CDCl$_3$	*Major Z-Isomer*: 3.35 (1 H, dd, *J* = 3.0, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.46 (1 H, dd, *J* = 5.7, 13.8 Hz, 1 H of PhC*H*$_2$CH), 4.57 (1 H, dd, *J* = 3.0, 5.6 Hz, PhCH$_2$C*H*), 5.39 (1 H, d, *J* = 12.1 Hz, 1 H of PhC*H*$_2$O), 5.44 (1 H, d, *J* = 12.2 Hz, 1 H of PhC*H*$_2$O), 6.91–7.01 (2 H, m, 2 H of Ph), 7.09–7.16 (3 H, m, 3 H of Ph), 7.32–7.73 (9 H, m, Ph, 4 H of Ar), 7.76–7.84 (1 H, m, 1 H of Ar), 7.85–8.06 (2 H, m, 2 H of Ar), 8.28 (1 H, d, *J* = 13.6 Hz, NHC*H*=), 11.12 (1 H, d, *J* = 13.4 Hz, N*H*CH=) *Minor E-Isomer*: 3.33 (1 H, dd, *J* = 3.0, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.42 (1 H, dd, *J* = 5.7, 13.8 Hz, 1 H of PhC*H*$_2$CH), 4.67 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.41 (2 H, s, PhC*H*$_2$O), 8.09 (1 H, s, NHC*H*=), 11.47 (1 H, br s, N*H*CH=)
52/52′c	DMSO-*d*$_6$	*Major E-Isomer*: 4.12 (2 H, s, 5-CH$_2$), 4.40 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 5.07 (2 H, s, PhC*H*$_2$O), 7.27–7.42 (5 H, m, Ph), 7.51 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.61–7.70 (1 H, m, 1 H of Het), 7.71–7.80 (1 H, m, 1 H of Het), 7.95–8.06 (2 H, m, 2 H of Het), 8.45 (1 H, d, *J* = 13.2 Hz, NHC*H*=), 8.64 (1 H, s, 1 H of Het), 9.17 (1 H, t, *J* = 2.6 Hz, 1 H of Het), 11.76 (1 H, d, *J* = 13.6 Hz, N*H*CH=) *Minor Z-Isomer*: 4.08 (2 H, s, 5-CH$_2$), 4.45 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 7.54 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 8.57 (1 H, d, *J* = 14.3 Hz, NHC*H*=), 11.42 (1 H, d, *J* = 14.3 Hz, N*H*CH=)
53/53′a	CDCl$_3$	*Major E-Isomer*: 1.59 (9 H, s, *t*-Bu), 3.28 (1 H, dd, *J* = 3.0, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.37 (1 H, dd, *J* = 6.0, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.81 (3 H, s, OMe), 4.11 (2 H, s, C*H*$_2$NH), 4.46 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 7.01–7.09 (2 H, m, 2 H of Ph), 7.12–7.23 (3 H, m, 3 H of Ph), 7.36 (1 H, br s, NHC*H*=), 9.65 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 3.38 (1 H, dd, *J* = 6.0, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.77 (3 H, s, OMe), 4.04–4.08 (2 H, m, C*H*$_2$NH), 4.41 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 7.55 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 9.28 (1 H, br, N*H*CH=)
53/53′c	DMSO-*d*$_6$	*Major E-Isomer*: 3.69 (3 H, s, OMe), 3.98 (2 H, s, 5-CH$_2$), 4.34 (2 H, d, *J* = 6.0 Hz, C*H*$_2$NH), 4.36 (2 H, d, *J* = 4.9 Hz, C*H*$_2$CO$_2$Me), 5.05 (2 H, s, PhC*H*$_2$O), 7.25–7.40 (5 H, m, Ph), 7.44 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.89 (1 H, br s, NHC*H*=), 9.97 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 3.95 (2 H, s, 5-CH$_2$), 7.47 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 8.01 (1 H, br s, NHC*H*=), 9.66 (1 H, br s, N*H*CH=)

Table 4 ^{1}H NMR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′** (continued)

Product	Solvent	^{1}H NMR, δ
54/54′a	CDCl$_3$	*Major Z-Isomer*: 1.29 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.52 (3 H, d, *J* = 7.2 Hz, CHC*H*$_3$), 1.62 (9 H, s, *t*-Bu), 3.30 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.41 (1 H, dd, *J* = 6.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.01–4.15 (1 H, m, NHC*H*COO), 4.21 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.42 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 7.03–7.12 (2 H, m, 2 H of Ph), 7.13–7.25 (3 H, m, 3 H of Ph), 7.63 (1 H, d, *J* = 14.3 Hz, NHC*H*=), 9.40 (1 H, br dd, *J* = 7.9, 14.3 Hz, N*H*CH=) *Minor E-Isomer*: 1.33 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.58 (3 H, d, *J* = 7.2 Hz, CHC*H*$_3$), 1.61 (9 H, s, *t*-Bu), 4.26 (2 H, d, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.45 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 7.42 (1 H, br d, *J* = 12.8 Hz, NHC*H*=), 9.85 (1 H, br, N*H*CH=)
55/55′a	CDCl$_3$	*Major Z-Isomer*: 0.87 (3 H, d, *J* = 7.2 Hz, CHC*H*$_3$), 1.61 (9 H, s, *t*-Bu), 3.26 (1 H, dd, *J* = 3.6, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.39 (1 H, dd, *J* = 5.7, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.74 (3 H, s, OMe), 3.89–3.98 (1 H, m, NHC*H*COO), 4.41 (1 H, dd, *J* = 3.4, 5.7 Hz, PhCH$_2$C*H*), 7.51 (1 H, d, *J* = 14.2 Hz, NHC*H*=), 9.25 (1 H, br, N*H*CH=) *Minor E-Isomer*: 0.92 (3 H, d, *J* = 6.8 Hz, CHC*H*$_3$), 0.94 (3 H, d, *J* = 6.8 Hz, CHC*H*$_3$), 1.59 (9 H, s, *t*-Bu), 1.56–1.63 [1 H, m, C*H*(CH$_3$)$_2$], 1.66–1.83 (2 H, m, CHC*H*$_2$CH), 3.28 (1 H, dd, *J* = 3.0, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.37 (1 H, dd, *J* = 6.0, 13.6 Hz, 1 H of PhC*H*$_2$CH), 3.79 (3 H, s, OMe), 3.96–4.06 (1 H, m, NHC*H*COO), 4.45 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 7.01–7.09 (2 H, m, 2 H of Ph), 7.11–7.22 (3 H, m, 3 H of Ph), 7.36 (1 H, br s, NHC*H*=), 9.67 (1 H, br s, N*H*CH=)
55/55′b	CDCl$_3$	*Z-Isomer*: 0.85–0.96 [6 H, m, CH(C*H*$_3$)$_2$], 1.37–1.50 [1 H, m, C*H*(CH$_3$)$_2$], 1.60–1.79 (2 H, m, CHC*H*$_2$CH), 3.25 (1 H, dd, *J* = 3.7, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.37 (1 H, dd, *J* = 5.6, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.75 (3 H, s, OMe), 3.95 (1 H, ddd, *J* = 4.9, 9.0, 9.0 Hz, NHC*H*COO), 4.47 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.33 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 5.38 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 6.88–6.96 (2 H, m, 2 H of Ph), 7.06–7.14 (3 H, m, 3 H of Ph), 7.30–7.44 (3 H, m, 3 H of Ph), 7.45–7.51 (2 H, m, 2 H of Ph), 7.53 (1 H, d, *J* = 14.2 Hz, NHC*H*=), 9.25 (1 H, br dd, *J* = 9.0, 14.2 Hz, N*H*CH=) *E-Isomer*: 3.24 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.36 (1 H, dd, *J* = 6.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.98–4.07 (1 H, m, NHC*H*COO), 4.51 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 5.36 (2 H, s, PhC*H*$_2$O), 9.75 (1 H, br s, N*H*CH=)
56/56′a	CDCl$_3$	*Major Z-Isomer*: 1.27 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.29 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.60 (9 H, s, *t*-Bu), 1.91–2.06 (1 H, m, 1 H of C*H*$_2$CH$_2$CO$_2$Et), 2.15–2.40 (3 H, m, CH$_2$C*H*$_2$CO$_2$Et, 1 H of C*H*$_2$CH$_2$CO$_2$Et), 3.27 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.39 (1 H, dd, *J* = 5.7, 13.6 Hz, 1 H of PhC*H*$_2$CH), 4.03–4.19 (1 H, m, NHC*H*COO), 4.15 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.21 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.42 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 7.02–7.09 (2 H, m, 2 H of Ph), 7.11–7.23 (3 H, m, 3 H of Ph), 7.53 (1 H, d, *J* = 14.3 Hz, NHC*H*=), 9.28 (1 H, br dd, *J* = 9.4, 14.2 Hz, N*H*CH=) *Minor E-Isomer*: 1.59 (9 H, s, *t*-Bu), 4.45 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 7.37 (1 H, br s, NHC*H*=), 9.71 (1 H, br s, N*H*CH=)
57/57′a	CDCl$_3$	*Major Z-Isomer*: 1.29 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.50 (1 H, t, *J* = 9.1 Hz, SH), 1.61 (9 H, s, *t*-Bu), 2.81–3.04 (2 H, m, C*H*$_2$SH), 3.27 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.40 (1 H, dd, *J* = 5.7, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.97–4.05 (1 H, m, NHC*H*COO), 4.24 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.43 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 7.02–7.09 (2 H, m, 2 H of Ph), 7.11–7.22 (3 H, m, 3 H of Ph), 7.58 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 9.38 (1 H, br dd, *J* = 9.4, 13.5 Hz, N*H*CH=) *Minor E-Isomer*: 1.33 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.60 (9 H, s, *t*-Bu), 3.29 (1 H, dd, *J* = 3.0, 13.8 Hz, 1 H of PhC*H*$_2$CH), 3.39 (1 H, dd, *J* = 5.7, 13.8 Hz, 1 H of PhC*H*$_2$CH), 4.09–4.15 (1 H, m, NHC*H*COO), 4.26–4.34 (2 H, m, OC*H*$_2$CH$_3$), 4.47 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 7.43 (1 H, br s, NHC*H*=), 9.86 (1 H, br s, N*H*CH=)
57/57′b	CDCl$_3$	*Major E-Isomer*: 1.34 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 3.27 (1 H, dd, *J* = 2.9, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.08–4.16 (1 H, m, NHC*H*COO), 4.27–4.35 (2 H, m, OC*H*$_2$CH$_3$), 4.53 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 5.34 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 5.40 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 9.90 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 1.29 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.51 (1 H, t, *J* = 9.1 Hz, SH), 2.87–3.09 (2 H, m, C*H*$_2$SH), 3.25 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.38 (1 H, dd, *J* = 5.6, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.98–4.06 (1 H, m, NHC*H*COO), 4.25 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.49 (1 H, dd, *J* = 2.9, 5.6 Hz, PhCH$_2$C*H*), 5.34 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 5.40 (1 H, d, *J* = 12.4 Hz, 1 H of PhC*H*$_2$O), 6.86–6.95 (2 H, m, 2 H of Ph), 7.05–7.14 (3 H, m, 3 H of Ph), 7.30–7.44 (3 H, m, 3 H of Ph), 7.44–7.52 (2 H, m, 2 H of Ph), 7.60 (1 H, d, *J* = 14.0 Hz, NHC*H*=), 9.37 (1 H, br dd, *J* = 8.7, 14.0 Hz, N*H*CH=)
57/57′c	CDCl$_3$	*Major E-Isomer*: 1.34 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.56 (1 H, t, *J* = 9.0 Hz, CH$_2$S*H*), 3.03–3.11 (2 H, m, C*H*$_2$SH), 4.14 (2 H, s, 5-CH$_2$), 4.17–4.26 (1 H, m, NHC*H*CH$_2$), 4.32 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.60–4.67 (2 H, m, C*H*$_2$NH), 5.14 (2 H, s, PhC*H*$_2$O), 5.52 (1 H, br s, CH$_2$N*H*), 7.30–7.40 (5 H, m, Ph), 7.73 (1 H, br s, NHC*H*=), 10.07 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 1.34 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 4.10 (2 H, s, 5-CH$_2$), 4.28–4.37 (2 H, m, OC*H*$_2$CH$_3$), 7.85 (1 H, d, *J* = 14.3 Hz, NHC*H*=), 9.57 (1 H, br, N*H*CH=)

Table 4 ^{1}H NMR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a**–**c**, and **35/35′**–**64/64′** (continued)

Product	Solvent	^{1}H NMR, δ
58/58′b	CDCl$_3$	*Major E-Isomer*: 3.04 (1 H, dd, *J* = 8.7, 13.9 Hz, 1 H of PhCH_2CHNH), 3.15–3.31 (2 H, m, 1 H of PhCH_2CH, 1 H of PhCH_2CHNH), 3.33 (1 H, dd, *J* = 5.9, 13.9 Hz, 1 H of PhCH_2CH), 3.82 (3 H, s, OMe), 4.13–4.23 (1 H, m, NH-C*H*COO), 4.49 (1 H, dd, *J* = 3.0, 6.0 Hz, PhCH$_2$C*H*), 5.33 (2 H, s, PhCH_2O), 6.85–6.92 (2 H, m, 2 H of Ph), 6.94–7.01 (1 H, m, 1 H of Ph), 7.03–7.21 (5 H, m, 5 H of Ph), 7.23–7.52 (8 H, m, 7 H of Ph, NHC*H*=), 9.80 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 2.94 (1 H, dd, *J* = 8.8, 13.9 Hz, 1 H of PhCH_2CHNH), 3.34 (1 H, dd, *J* = 5.9, 13.9 Hz, 1 H of PhCH_2CH), 3.76 (3 H, s, OMe), 4.06–4.16 (1 H, m, NHC*H*COO), 4.41 (1 H, dd, *J* = 2.9, 5.7 Hz, PhCH$_2$C*H*), 5.33 (1 H, d, *J* = 12.4 Hz, 1 H of PhCH_2O), 5.38 (1 H, d, *J* = 12.1 Hz, 1 H of PhCH_2O), 9.38 (1 H, dd, *J* = 9.4, 13.8 Hz, N*H*CH=)
58/58′c	CDCl$_3$	*Major E-Isomer*: 3.07 (1 H, dd, *J* = 9.1, 13.7 Hz, 1 H of PhCH_2CH), 3.34 (1 H, dd, *J* = 4.2, 13.9 Hz, 1 H of PhCH_2CH), 3.83 (3 H, s, OMe), 4.08 (2 H, s, 5–CH$_2$), 4.27 (1 H, m, PhCH$_2$C*H*), 4.58 (2 H, d, *J* = 5.6 Hz, CH_2NH), 5.13 (2 H, s, PhCH_2O), 5.50 (1 H, br s, CH$_2$N*H*), 7.10–7.17 (2 H, m, 2 H of Ph), 7.28–7.44 (9 H, m, 8 H of Ph, NHC*H*=), 9.94 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 4.03 (2 H, s, 5-CH$_2$), 4.63 (2 H, d, *J* = 6.0 Hz, CH_2NH), 5.15 (2 H, s, PhCH_2O), 9.43 (1 H, br s, N*H*CH=)
59/59′b	CDCl$_3$	*Z-Isomer*: 3.06–3.25 (2 H, m, CH$_2$), 3.28–3.50 (2 H, m, CH$_2$), 3.74 (3 H, s, OMe), 4.15 (1 H, deg dt, *J* = 3.8, 8.7 Hz, C*H*CO$_2$Me), 4.42 (1 H, dd, *J* = 3.0, 5.6 Hz, PhCH$_2$C*H*), 5.27–5.41 (2 H, m, PhCH_2O), 6.61 (1 H, d, *J* = 2.3 Hz, 1 H of Het), 6.84–6.89 (1 H, m, 1H of Ar), 6.92–6.99 (2 H, m, 2 H of Ph), 7.03–7.23 (5 H, m, 3 H of Ph, 2 H of Het), 7.31–7.41 (4 H, m, 3 H of Ph, 1 H of Het), 7.42–7.51 (3 H, m, 2 H of Ph, NHC*H*=), 8.02 (1 H, s, NH of indole), 9.46 (1 H, dd, *J* = 9.4, 13.9 Hz, N*H*CH=) *E-Isomer*: 3.82 (3 H, s, OMe), 4.20–4.28 (1 H, m, C*H*CO$_2$Me), 4.44 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 9.89 (1 H, br s, N*H*CH=)
60/60′a	CDCl$_3$	*Major Z-Isomer*: 1.26 (3 H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 1.59 (9 H, s, *t*-Bu), 2.57 (2 H, t, *J* = 6.0 Hz, CH$_2$COO), 3.27 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhCH_2CH), 3.38 (1 H, dd, *J* = 5.3, 13.9 Hz, 1 H of PhCH_2CH), 3.55–3.67 (2 H, m, NHCH_2), 4.16 (2 H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 4.38 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 7.01–7.09 (2 H, m, 2 H of Ph), 7.13–7.22 (3 H, m, 3 H of Ph), 7.64 (1 H, d, *J* = 14.3 Hz, NHC*H*=), 9.28 (1 H, br, N*H*CH=) *Minor E-Isomer*: 1.28 (3 H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 2.62 (2 H, t, *J* = 6.0 Hz, CH$_2$COO), 3.26 (1 H, dd, *J* = 3.0, 13.6 Hz, 1 H of PhCH_2CH), 3.36 (1 H, dd, *J* = 5.3, 13.6 Hz, 1 H of PhCH_2CH), 4.20 (2 H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 4.42 (1 H, dd, *J* = 3.0, 5.7 Hz, PhCH$_2$C*H*), 7.43 (1 H, d, *J* = 14.0 Hz, NHC*H*=), 9.74 (1 H, br, N*H*CH=)
61/61′a	CDCl$_3$	*Major Z-Isomer*: 1.59 (9 H, s, *t*-Bu), 3.27–3.32 (2 H, m, PhCH_2CH), 4.27–4.37 (1 H, m, PhCH$_2$C*H*), 4.38–4.44 (2 H, m, CH$_2$CN), 7.01–7.07 (2 H, m, 2 H of Ph), 7.14–7.25 (3 H, m, 3 H of Ph), 7.67 (1 H, d, *J* = 13.9 Hz, NHC*H*=), 9.36 (1 H, br, N*H*CH=) *Minor E-Isomer*: 1.60 (9 H, s, *t*-Bu), 4.46–4.50 (2 H, m, CH$_2$CN), 7.60 (1 H, s, NHC*H*=)
61/61′b	CDCl$_3$	*Major Z-Isomer*: 3.21–3.37 (2 H, m, PhCH_2CH), 4.23–4.29 (2 H, m, CH_2CN), 4.48 (1 H, dd, *J* = 3.4, 5.4 Hz, PhCH$_2$C*H*), 5.30 (2 H, s, PhCH_2O), 6.84–6.94 (2 H, m, 2 H of Ph), 7.08–7.18 (3 H, m, 3 H of Ph), 7.32–7.50 (5 H, m, Ph), 7.66 (1 H, d, *J* = 13.2 Hz, NHC*H*=), 9.31 (1 H, br, N*H*CH=) *Minor E-Isomer*: 4.30 (2 H, d, *J* = 1.6 Hz, CH_2CN), 4.54 (1 H, dd, *J* = 3.3, 5.8 Hz, PhCH$_2$C*H*), 5.35 (2 H, s, PhCH_2O), 7.62 (1 H, s, NHC*H*=)
61/61′c	CDCl$_3$	*Major E-Isomer*: 3.97 (2 H, s, 5-CH$_2$), 4.35 (2 H, d, *J* = 6.0 Hz, CH_2NH), 4.61 (2 H, s, CH_2CN), 5.05 (2 H, s, PhCH_2O), 7.27–7.39 (5 H, m, Ph), 7.47 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 8.02 (1 H, s, NHC*H*=), 10.00 (1 H, br s, N*H*CH=) *Minor Z-Isomer*: 3.95 (2 H, s, 5-CH$_2$)
62/62′b	CDCl$_3$	*Z-Isomer*: 3.25 (1 H, dd, *J* = 3.0, 13.8 Hz, 1 H of PhCH_2CH), 3.37 (1 H, dd, *J* = 5.6, 13.8 Hz, 1 H of PhCH_2CH), 4.43–4.55 (3 H, m, PhCH$_2$C*H*, PhCH_2NH), 5.30 (1 H, d, *J* = 12.1 Hz, 1 H of PhCH_2O), 5.37 (1 H, d, *J* = 12.1 Hz, 1 H of PhCH_2O), 6.87–6.95 (2 H, m, 2 H of Ph), 7.06–7.20 (5 H, m, 5 H of Ph), 7.30–7.42 (6 H, m, 6 H of Ph), 7.43–7.51 (2 H, m, 2 H of Ph), 7.68 (1 H, d, *J* = 14.3 Hz, NHC*H*=), 9.41 (1 H, br, N*H*CH=) *E-Isomer*: 3.23 (1 H, dd, *J* = 3.0, 13.6 Hz, 1 H of PhCH_2CH), 3.36 (1 H, dd, *J* = 5.7, 13.7 Hz, 1 H of PhCH_2CH), 5.36 (2 H, s, PhCH_2O), 9.87 (1 H, br s, N*H*CH=)
63/63′c	DMSO-d_6	*Major E-Isomer*: 1.44 (6 H, br s, 6 H of adamantyl), 1.60 (3 H, br d, *J* = 12.1 Hz, 3 H of adamantyl), 1.67 (3 H, br d, *J* = 12.1 Hz, 3 H of adamantyl), 1.96 (3 H, br s, 3 H of adamantyl), 3.16–3.24 (2 H, m, CH_2NHCH=), 3.98 (2 H, s, 5-CH$_2$), 4.33 (2 H, d, *J* = 6.0 Hz, CH_2NHCO$_2$Bn), 5.05 (2 H, s, PhCH_2O), 7.26–7.40 (5 H, m, Ph), 7.43 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.82 (1 H, d, *J* = 14.7 Hz, NHC*H*=), 9.94 (1 H, dt, *J* = 6.9, 14.7 Hz, N*H*CH=) *Minor Z-Isomer*: 3.92 (2 H, s, 5-CH$_2$), 4.36 (2 H, d, *J* = 6.0 Hz, CH_2NH), 7.46 (1 H, t, *J* = 6.0 Hz, CH$_2$N*H*), 7.91 (1 H, d, *J* = 15.1 Hz, NHC*H*=), 9.54 (1 H, br, N*H*CH=)
64a	CDCl$_3$	1.63 (9 H, s, *t*-Bu), 3.26 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhCH_2CH), 3.32 (1 H, dd, *J* = 5.3, 13.9 Hz, 1 H of PhCH_2CH), 4.41 (1 H, dd, *J* = 3.0, 4.9 Hz, PhCH$_2$C*H*), 7.01–7.09 (2 H, m, 2 H of Ph), 7.13–7.24 (3 H, m, 3 H of Ph), 7.47 (1 H, s, NHC*H*=), 12.27 (1 H, br s, N*H*CH=), 14.33 (1 H, br s, OH)

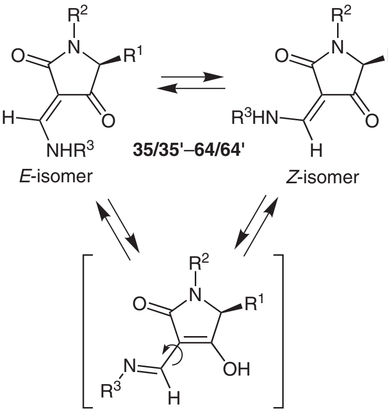
Table 4 ^{1}H NMR Data for Compounds **2′c** and **2c** and Tetramic Acid Derivatives **3c**, **4a–c**, and **35/35′–64/64′** (continued)

Product	Solvent	^{1}H NMR, δ
64b	CDCl$_3$	3.21 (1 H, dd, *J* = 3.0, 13.9 Hz, 1 H of PhC*H*$_2$CH), 3.28 (1 H, dd, *J* = 5.3, 13.9 Hz, 1 H of PhC*H*$_2$CH), 4.51 (1 H, dd, *J* = 3.0, 5.3 Hz, PhCH$_2$C*H*), 5.33 (1 H, d, *J* = 11.9 Hz, 1 H of PhC*H*$_2$O), 5.39 (1 H, d, *J* = 11.9 Hz, 1 H of PhC*H*$_2$O), 6.84–6.91 (2 H, m, 2 H of Ph), 7.11–7.17 (3 H, m, 3 H of Ph), 7.36–7.49 (6 H, m, Ph, NHC*H*=), 12.27 (1 H, br s, N*H*CH=), 14.47 (1 H, br s, OH)
64/64′c	DMSO-*d*$_6$	*Major E-Isomer*: 4.10 (2 H, s, 5-CH$_2$), 4.31 (2 H, d, *J* = 6.4 Hz, C*H*$_2$NH), 5.05 (2 H, s, PhC*H*$_2$O), 7.25–7.41 (5 H, m, Ph), 7.46 (1 H, t, *J* = 6.4 Hz, CH$_2$N*H*), 7.65 (1 H, s, NHC*H*=), 11.29 (1 H, br s, N*H*CH=), 14.01 (1 H, br s, OH) *Minor Z-Isomer*: 7.79 (1 H, s, NHC*H*=)

Table 5 ^{13}C NMR Data for Compounds **2′c**, **2c**, **3c**, **4a–c**, **35/35′**, **40/40′a**, **46/46′b**, **57/57′c**, **58/58′b**, **59/59′b**, **60/60′a**, **61/61′b**, **62/62′b**, and **64a**

Product	Solvent	δ
2′c	DMSO-*d*$_6$	26.9, 44.8, 49.6, 66.4, 87.4, 100.3, 107.8, 128.4, 128.6, 129.2, 137.9, 140.2, 157.4, 157.8, 164.8, 169.4, 188.6
2c	DMSO-*d*$_6$	27.0, 44.3, 44.7, 66.4, 90.7, 104.9, 128.56, 128.64, 129.2, 137.9, 157.3, 165.3, 170.4, 192.4
3c	DMSO-*d*$_6$	46.0, 49.1, 66.3, 94.7, 128.5, 128.6, 129.2, 137.9, 157.4, 169.2, 171.8, 177.5
4a	CDCl$_3$	28.6 [(*C*H$_3$)$_3$COOC], 36.6 (Ph*C*H$_2$), 44.3 (NMe), 48.6 (NMe), 64.0 (5–C), 82.7 [(CH$_3$)$_3$*C*OOC], 97.3 (3-C), 127.0 (1 C of Ph), 128.5 (2 C of Ph), 130.3 (2 C of Ph), 135.8 (1 C of Ph), 150.2 [(CH$_3$)$_3$COO*C*], 155.7 (3’–C), 157.3 (2-C), 190.6 (4-C)
4b	CDCl$_3$	36.3, 44.4, 48.7, 64.0, 68.1, 97.2, 127.0, 128.5, 128.7, 129.0, 130.3, 135.6, 136.2, 151.7, 156.0, 169.9, 190.3
4c	DMSO-*d*$_6$	44.7, 46.5, 48.8, 52.5, 66.3, 96.4, 128.5, 128.6, 129.2, 137.9, 156.6, 157.4, 169.7, 190.3
35/35′c	DMSO-*d*$_6$ + D$_2$O	*Mixture of Isomers*: 46.4, 52.7, 53.2, 66.4, 100.8, 119.6, 119.7, 127.6, 128.5, 128.7, 129.3, 130.6, 137.7, 138.9, 148.5, 148.7, 157.5, 169.0, 169.9, 170.1, 170.3, 191.2, 193.1
40/40′a	CDCl$_3$	*Mixture of Isomers*: 28.61, 28.62, 36.1, 36.4, 55.99, 56.01, 64.1, 65.1, 83.1, 83.4, 99.7, 100.8, 115.6, 119.5, 119.7, 127.3, 128.7, 130.1, 130.3, 131.2, 131.3, 135.3, 135.4, 146.3, 147.1, 150.1, 150.3, 158.9, 159.0, 167.4, 170.7, 193.2, 196.3
46/46′b	DMSO-*d*$_6$	35.2, 35.8, 64.8, 68.2, 103.2, 127.7, 128.9, 129.0, 129.1, 130.3, 135.7, 136.6, 146.8, 151.6, 156.7
57/57′c	CDCl$_3$	*Mixture of Isomers*: 14.5, 27.1, 28.1, 34.6, 36.7, 46.9, 52.3, 53.1, 63.4, 63.5, 63.9, 64.2, 67.3, 67.4, 99.5, 100.1, 128.4, 128.5, 128.9, 136.8, 154.9, 155.3, 156.9, 168.0, 168.1, 168.3, 169.4, 169.7, 170.7, 190.5, 193.6
58/58′b	CDCl$_3$	*Mixture of Isomers*: 35.9, 36.1, 39.9, 40.1, 53.5, 63.9, 64.0, 64.2, 65.0, 68.2, 68.4, 99.0, 99.9, 127.11, 127.14, 128.2, 128.4, 128.5, 128.6, 128.7, 128.9, 128.99, 129.05, 129.5, 129.6, 130.1, 130.2, 134.5, 135.2, 151.8, 153.2, 154.0, 166.7, 169.3, 169.6, 169.9, 192.7, 196.0
59/59′b	CDCl$_3$	*Mixture of Isomers*: 30.3, 36.0, 36.1, 53.5, 53.6, 62.6, 62.8, 64.0, 64.9, 68.2, 68.5, 98.6, 99.5, 107.9, 108.2, 112.2, 112.3, 118.3, 120.3, 122.9, 124.4, 124.6, 126.8, 126.9, 127.06, 127.15, 128.5, 128.6, 128.8, 128.97, 129.00, 129.1, 130.1, 130.5, 135.2, 135.6, 135.9, 136.0, 136.7, 136.8, 151.4, 151.7, 153.4, 154.0, 167.0, 169.9, 170.1, 170.2, 192.5, 195.8
60/60′a	CDCl$_3$	*Mixture of Isomers*: 14.50, 14.55, 28.59, 28.61, 34.8, 35.1, 36.1, 36.3, 46.2, 46.3, 61.7, 61.8, 63.9, 64.9, 82.8, 83.1, 98.5, 99.5, 127.07, 127.12, 128.50, 128.55, 130.1, 130.3, 135.55, 135.56, 150.1, 150.4, 154.6, 155.2, 167.5, 170.5, 170.7, 170.8, 192.8, 195.9
61/61′b	CDCl$_3$	*Mixture of Isomers*: 35.3, 36.3, 36.5, 37.3, 64.3, 65.3, 68.7, 100.0, 100.9, 114.7, 127.4, 128.7, 128.8, 129.07, 129.12, 129.17, 129.23, 129.3, 130.06, 130.11, 135.0, 135.1, 135.3, 135.6, 150.8, 151.6, 154.2, 155.8, 166.8, 169.9, 192.7, 196.3
62/62′b	CDCl$_3$	*Mixture of Isomers*: 36.1, 54.1, 54.2, 64.0, 64.9, 68.2, 68.3, 98.4, 99.3, 127.1, 127.2, 127.9, 128.0, 128.5, 128.6, 128.7, 128.76, 128.85, 128.9, 129.0, 129.1, 129.5, 129.6, 130.2, 130.3, 135.29, 135.34, 135.4, 135.5, 136.0, 136.1, 151.5, 151.9, 154.5, 155.4, 167.3, 170.3, 192.7, 195.7
64a	CDCl$_3$	28.8, 36.3, 63.2, 84.1, 95.2, 127.5, 128.8, 130.1, 134.5, 140.0, 150.4, 169.7, 192.5

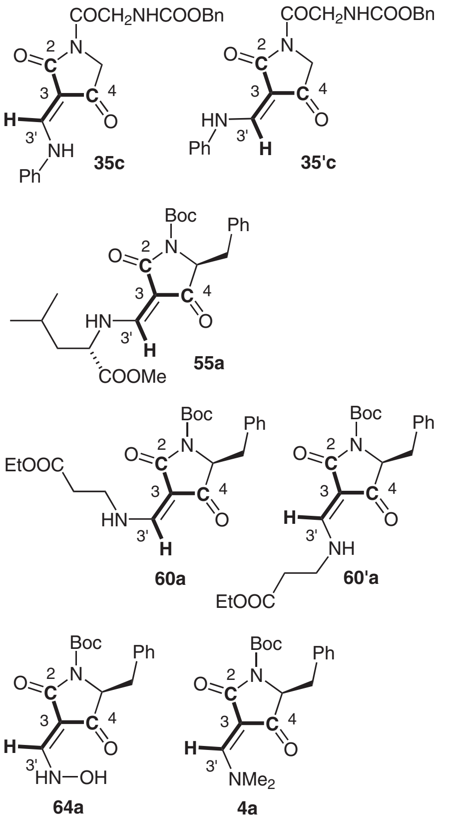
Compounds **4a–c**, **46a**,**b**, **50c**, and **64a**,**b** were isolated in isomerically pure form, while the other coupling products **35–45**, **47–49**, and **51–63** were isolated as the *E*/*Z*-mixtures of the major isomers **35–45**, **47–49**, and **51–63** and the minor isomers **35′–45′**, **47′–49′**, and **51′–63′**. Attempted chromatographic separations of isomeric compounds **35/35′–64/64′** failed, most probably due to fast isomerisation around the exocyclic C(3)=C(3′) double bond in solution. Equilibration between the isomers **35/35′–64/64′** in solution can be explained by involvement of tautomeric structures **35″–64″**, with a C(3)–C(3′) single bond. In related (+)-camphor derived enaminone series, a free energy between the isomers, $\Delta G^0_{296} = 4.9$ kJ mol^{-1}, was recently measured (Scheme 3).[8d] As in related enaminones,[6b,f,8d,e] the ratio between the two isomers is solvent dependent also in the case of compounds **35/35′–64/64′**. For example, (*S*)-5-benzyl-1-benzyloxycarbonyl-3-{[(4-nitrophenyl)amino]methylidene}pyrrolidin-2,4-dione (**37b**) precipitated from ethanol as a mixture of isomers in a ratio of *E*:*Z* = 62:38 as determined by ^{1}H NMR taken in CDCl$_3$. When this CDCl$_3$ solution of **37b** was allowed to stand at r.t. for 24 h, the ratio between the isomers changed to *E*:*Z* = 44:56 (Scheme 3).



Scheme 3

Configurations around the exocyclic C=C double bond in compounds **4a**, **35c**, **35′c**, **55a**, **60a**, **60′a**, and **64a** were determined by HMBC spectroscopy on the basis of long-range coupling constants ($^3J_{C,H}$) between the methylidene proton [H–C(3′)] and the carbonyl carbon atoms [O=C(2) and O=C(4)], measured from the antiphase splitting of cross peaks in the HMBC spectrum. Generally, the magnitude of coupling constant, $^3J_{C,H}$, for nuclei with *cis*-configuration around the C=C double bond are smaller (2–6 Hz) than that for *trans*-oriented nuclei (8–12 Hz).[6–8,10,11] In compounds **4a**, **35c**, **60′a**, and **64a**, the magnitudes of coupling constants, $^3J_{C(2),H(3')} = 2$–3 Hz (*cis*) and $^3J_{C(4),H(3')} = 6$–7 Hz (*trans*) showed the *E*-configuration around the exocyclic C=C double bond. In the same manner, the *Z*-configuration in compounds **35′c**, **55a** and **60a** was determined on the basis of coupling constants, $^3J_{C\text{-}(2),H(3')} = 9$ Hz (*trans*) and $^3J_{C\text{-}(4),H(3')} = 3$ Hz (*cis*) (Figure 2).

Structures of compounds **4a** and **35c** were determined by X-Ray diffraction (Figures 3 and 4). The C(3)–C(4) (ca. 1.39 Å) and C(3)–C(3′) (ca. 1.42 Å) bond lengths in compounds **4a** and **35a** indicate a partial bond character, which support tautomeric equilibrium in solution according to structural investigations of 3-acyltetramic acids reported by Steyn and co-workers (Figures 3, 4).[12]



Compound	$^3J_{C,H}$ [Hz]		(*E*) or (*Z*)
	C(2)-H(3′)	C(4)-H(3′)	
4a	2 (*cis*)	7 (*trans*)	(*E*)
35c (major isomer)	3 (*cis*)	7 (*trans*)	(*E*)
35′c (minor isomer)	9 (*trans*)	3 (*cis*)	(*Z*)
55a (major isomer)	9 (*trans*)	3 (*cis*)	(*Z*)
60a (major isomer)	9 (*trans*)	3 (*cis*)	(*Z*)
60′a (minor isomer)	3 (*cis*)	7 (*trans*)	(*E*)
64a	3 (*cis*)	7 (*trans*)	(*E*)

Figure 2 Determination of configuration around the exocyclic C(3)=C(3′) double bond by HMBC spectroscopy

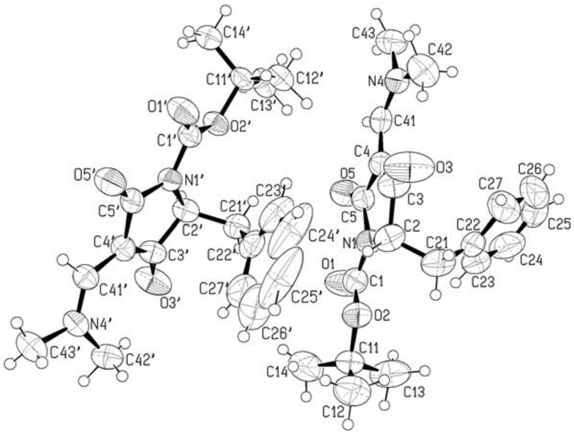


Figure 3 ORTEP view of compound **4a**

The configurations around the exocyclic C=C double bond in compounds **35–64** were correlated with chemical shifts δ for H–C(3′) and H–N–C(3′) and with magnitudes of the vicinal coupling constants $^3J_{H(3'),NH}$. Within each set

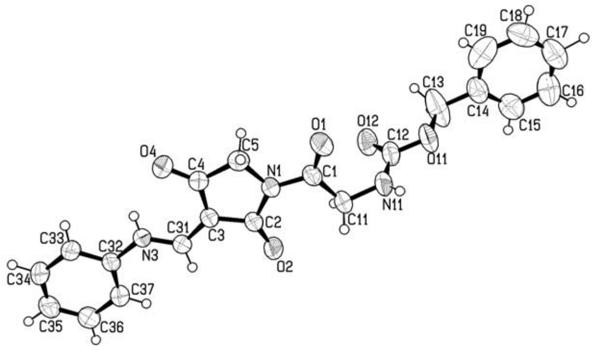


Figure 4 ORTEP view of compound **35c**

of isomeric compounds **35/35′–64/64′**, the signal for H–C(3′) of the *Z*-isomer appeared at lower field (7.51–8.90 ppm) than the signal for H–C(3′) of the *E*-isomer (7.36–8.81 ppm) with typical chemical shift difference, $\Delta\delta = 0.1–0.2$ ppm. On the other hand, within each set of isomers **35/35′–64/64′**, the signal for H–N–C(3′) of the *E*-isomer appeared at lower field (9.65–12.34 ppm) than the signal for H–N–C(3′) of the *Z*-isomer (9.29–11.81 ppm) with a typical chemical shift difference, $\Delta\delta = 0.1–0.4$ ppm. In addition to this, the magnitude of the vicinal coupling constant, $^3J_{H(3'),NH}$, was larger in the case of the *Z*-isomers ($^3J_{H(3'),NH} = 12.8–15.1$ Hz) than in the case of the *E*-isomers ($^3J_{H(3'),NH} = 10.2–14.7$ Hz). In the ^{1}H NMR spectra of isomeric mixtures **35/35′–37/37′c**, **39/39′c**, **40/40′c**, **42/42′c**, **46a**, **48/48′c**, **53/53′c**, and **64/64′c**, a very small coupling constant, $^3J_{H(3'),NH} = \sim 0$ Hz was observed for both isomers (Table 2). Typical example of differentiation between the *E*-isomer **40a** and the *Z*-isomer **40′a** on the basis of chemical shifts for protons H–C(3′) and H–N–C(3′) and coupling constants, $^3J_{H(3'),NH}$, is depicted in Figure 5.

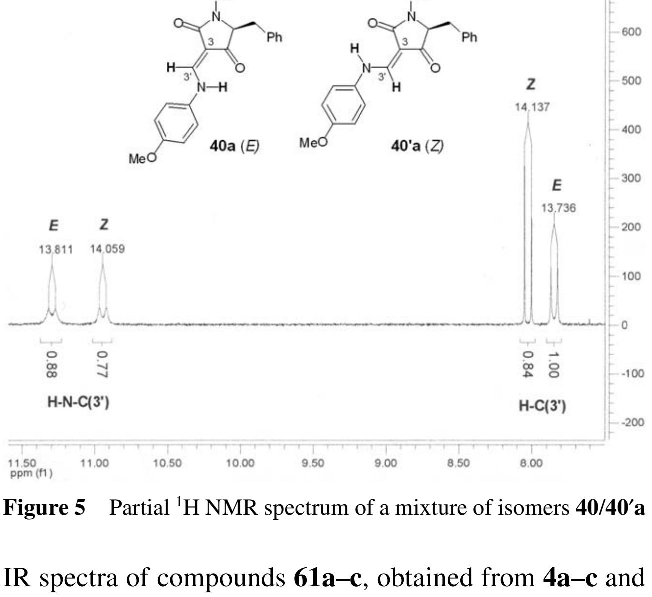


Figure 5 Partial ^{1}H NMR spectrum of a mixture of isomers **40/40′a**

IR spectra of compounds **61a–c**, obtained from **4a–c** and aminoacetonitrile (**31**), exhibit no typical C≡N vibration (~2230 cm^{-1}), although these compounds gave correct CHN-analyses. This could be explained by trimerisation of cyano compounds **61a–c** into the corresponding 1,3,5-triazine derivatives.[13] Appearance of fragments, corresponding to MH$^+$, M$_2$H$^+$, and M$_3$H$^+$, in the FAB mass spectrum of compound **61a**, could be in agreement with the trimeric structure. However, the absence of a typical 1,3,5-triazine carbon signal at ca. 170 ppm[13] and the presence of typical C≡N peak at 114.7 ppm in ^{13}C NMR spectrum of **61a** support the proposed monomeric structures of **61a–c**.

Melting points were determined on a Kofler micro hot stage. The ^{1}H NMR spectra were obtained on a Bruker Avance DPX 300 at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C nucleus, using DMSO-d_6 and CDCl$_3$ with TMS as the internal standard, as solvents. Mass spectra were recorded on an AutoSpecQ spectrometer, IR spectra on a Perkin-Elmer Spectrum BX FTIR spectrophotometer. Microanalyses were performed on a Perkin-Elmer CHN Analyser 2400. Column chromatography (CC) was performed on silica gel (Fluka, silica gel 60, 0.04–0.06 mm) and on aluminium oxide (Fluka, type 507 C neutral, 0.05–0.15 mm, pH 7.0 ± 0.5). The *Z*/*E*-ratios of isomers were determined by ^{1}H NMR spectroscopy.

Boc-L-phenylalanine (**1a**), Z-L-phenylalanine (**1b**), *N*-(glycyl)glycine, Meldrum's acid, 4-dimethylaminopyridine (DMAP), *N*,*N*'-dicyclohexylcarbodiimide (DCC), *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA), and amines **5–34** are commercially available (Sigma-Aldrich). *N*-[*N*-(Benzyloxycarbonyl)glycyl]glycine (**1c**) was prepared from *N*-(glycyl)glycine according to the general procedure for the preparation of *N*-benzyloxycarbonyl protected amino acids.[14] (*S*)-5-Benzyl-1-*tert*-butoxycarbonyl-4-hydroxy-2,5-dihydropyrrol-2-one (**3a**)[9a] and (*S*)-5-benzyl-1-benzyloxycarbonyl-4-hydroxy-2,5-dihydropyrrol-2-one (**3b**)[9b] were prepared according to the literature procedures.

1-[*N*-(Benzyloxycarbonyl)glycyl]-4-hydroxy-2,5-dihydropyrrol-2-one (3c)

A solution of DCC (2.65 g, 12.9 mmol) in anhyd CH$_2$Cl$_2$ (15 mL) was slowly added to a stirred cold (0 °C) solution of **1c** (3 g, 11.3 mmol), Meldrum's acid (1.79 g, 12.4 mmol), and DMAP (2.07 g, 16.9 mmol) in anhyd CH$_2$Cl$_2$. Upon addition of DCC, the mixture was stirred at r.t. for 24 h, filtered, and the precipitate was washed with CH$_2$Cl$_2$ (2 × 10 mL). The filtrate was poured into cold (0 °C) EtOAc (100 mL), scratched with a glass stick, and the precipitate was collected by filtration to give 4-(dimethylamino)pyridinium 2-{[*N*-(benzyloxycarbonyl)glycyl]amino}-1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethanolate (**2′c**) in 93% yield. The salt **2′c** was then dissolved in CH$_2$Cl$_2$ (100 mL), the solution was washed with 1 M aq NaHSO$_4$ (100 mL) and brine (100 mL), dried (Na$_2$SO$_4$), filtered, and the filtrate was evaporated in vacuo to give **2c** in quantitative yield. Compound **2c** (3.31 g, 8.4 mmol) was dissolved in EtOAc (100 mL), the solution was refluxed for 30 min, cooled, and evaporated in vacuo to give **3c**. Experimental, analytical, and spectral data for compounds **2′c**, **2c**, and **3c** are given in Tables 2–5.

(3*E*,5*S*)-5-Benzyl-1-(*tert*-butoxycarbonyl)-3-[(dimethylamino)methylidene]pyrrolidine-2,4-dione (4a)

A mixture of **3a** (1.45 g, 5 mmol), anhyd toluene (15 mL), and DMFDMA (0.8 mL, 5.5 mmol) was stirred at 80–90 °C for 45 min, cooled, and evaporated in vacuo. The residue was purified by CC (Al$_2$O$_3$, EtOAc). Fractions containing product were combined and evaporated in vacuo to give **4a**. Experimental, analytical, and spectral data for compound **4a** are given in Tables 2–5.

(3*E*,5*S*)-5-Benzyl-1-(benzyloxycarbonyl)-3-[(dimethylamino)methylidene]pyrrolidine-2,4-dione (4b)

A mixture of **3b** (3.25 g, 10.1 mmol), anh CH_2Cl_2 (50 mL), and DMFDMA (2.4 mL, 16 mmol) was stirred under reflux for 3 h, cooled, and evaporated in vacuo. The residue was purified by CC (silica gel, $CHCl_3$–MeOH, 40:1). Fractions containing product were combined and evaporated in vacuo to give **4b**. Experimental, analytical, and spectral data for compound **4b** are given in Tables 2–5.

(3*E*)-1-[*N*-(Benzyloxycarbonyl)glycyl]-3-[(dimethylamino)methylidene]pyrrolidine-2,4-dione (4c)

A mixture of **3c** (2.75 g, 9.5 mmol), anhyd CH_2Cl_2 (50 mL) and DMFDMA (1.6 mL, 11 mmol) was stirred under reflux for 30 min, cooled, and evaporated in vacuo. The residue was dissolved in CH_2Cl_2 (100 mL), silica gel (5 g) was added, the mixture was stirred at r.t. for 2 h, filtered, and the filtrate was evaporated in vacuo to give **4c**. Experimental, analytical, and spectral data for compound **4c** are given in Tables 2–5.

Coupling of Enaminones 4a–c with Primary Amines 5–34; N(3′)-Substituted 3-Aminomethylidenetetramic Acid Derivatives 35–64; General Procedure

Method A: Amine hydrochloride **5**–**34** (0.5 mmol) or amine **5**–**34** (0.5 mmol) and 37% aq HCl (2 drops) were added to a solution of **4** (0.5 mmol) in EtOH (3 mL) and the mixture was stirred at 20–60 °C for 1–48 h. Volatile components were evaporated in vacuo and the residue was purified by CC (silica gel, EtOAc–hexanes). Fractions containing the product were combined and evaporated in vacuo to give **35**–**64**. Experimental, analytical, and spectral data for compounds **35**–**64** are given in Tables 2–5.

Method B: Amine hydrochloride **5**–**34** (0.5 mmol) or amine **5**–**34** (0.5 mmol) and 37% aq HCl (2 drops) were added to a solution of **4** (0.5 mmol) in EtOH (3 mL) and the mixture was stirred at r.t. for 1–48 h. The precipitate was collected by filtration and washed with cold EtOH and Et_2O to give **35**–**64**. Experimental, analytical, and spectral data for compounds **35**–**64** are given in Tables 2–5.

X-ray Structure Analysis

Single crystal data were collected at r.t. on an Enraf-Nonius CAD4 (for **4a**) and on a Nonius Kappa CCD (for **35c**) diffractometer using graphite monochromatic Mo-K_α radiation. Structures were solved by direct methods using SIR92.[15] We employed full-matrix least-squares refinements on F magnitudes with anisotropic displacement factors for all non-hydrogen atoms. All hydrogen atoms of both compounds were located from difference Fourier maps. The parameters of hydrogen atoms were not refined. In the final cycle of the refinement we used 2013 and 2610 reflections (included were those less-than reflections for which FC was greater than FO) and 453 and 319 parameters for **4a** and **35c**, respectively. The final R and R_w were 0.037 and 0.045 for **4a** and 0.051 and 0.055 for **35c**, respectively. The Xtal3.4[16] system of crystallographic programs was used for the structure refinement and interpretation. ORTEPII[17] was used to produce molecular graphics. The asymmetric units with atom-numbering scheme are shown in Figures 3 and 4 for **4a** and **35c**, respectively. Crystal data for **4a** and **35c** are given in Table 6.[18]

Table 6 Crystal Data for Compounds **4a** and **35c**

Compound	4a	35c
Formula	$C_{19}H_{24}N_2O_4$	$C_{21}H_{19}N_3O_5$
M_r	344.411	393.399
System	orthorhombic	monoclinic
Sp. Group	$P2_12_12_1$	$P2_1/c$
a (Å)	9.758(1)	21.1556(4)
b (Å)	17.364(2)	11.3544(2)
c (Å)	22.031(3)	7.9603(1)
β (°)		91.2968(8)
Vol. (Å^3)	3732.9(8)	1911.65(6)
Z^a	8	4
D_x (mg/m^3)	1.226	1.367
μ (mm^{-1})	0.0863	0.0993
Appearance	prismatic yellow crystal	pale green plate
Dimensions (mm)	0.44 × 0.34 × 0.33	0.30 × 0.25 × 0.025

[a] *Z*: Multiplicity of the space group.

Acknowledgment

The financial support from the Ministry of Education, Science, and Sport (project numbers: PS-0502-0103, P1-0179, and J1-6689), Slovenia, is gratefully acknowledged. We acknowledge with thanks the financial support from pharmaceutical companies Krka d.d. (Novo mesto, Slovenia) and Lek d. d., a new Sandoz company (Ljubljana, Slovenia). The authors wish to express their gratitude to the Alexander von Humboldt Foundation, Germany, for the donation of a Büchi medium pressure liquid chromatograph. Crystallographic data were collected on the Kappa CCD Nonius diffractometer in the Laboratory of Inorganic Chemistry, Faculty of Chemistry and chemical Technology, University of Ljubljana, Slovenia. We acknowledge with thanks the financial contribution of the Ministry of Science and technology, Republic of Slovenia through grant Packet X-2000 and PS-511-102, which thus made the purchase of the apparatus possible.

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