Carbohydrate Research, 222 (1991) 99–112
Elsevier Science Publishers B.V., Amsterdam

Synthesis and reactivity toward acetylenic dipolarophiles of imidazo[2,1-*b*]thiazolium-3-olate systems*

Pilar Areces, Martin Avalos, Reyes Babiano, Luis González, Jose L. Jiménez†, Juan C. Palacios, and Maria D. Pilo
Department of Organic Chemistry, University of Extremadura, 06071 Badajoz (Spain)

(Received December 31st, 1990; accepted for publication March 23rd, 1991)

ABSTRACT

The reaction of 1-phenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (**1**) with α-bromophenylacetic acid and cyclisation with acetic anhydride-triethylamine of the thioglycolic acid intermediate led to the mesoionic derivative 2,5-diphenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[1′,2′:4,5]-4a*H*,4b*H*-imidazo[2,1-*b*]thiazolium-3-olate (**5**). Likewise, 7-(4-ethoxyphenyl)-2-phenyl-5-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetriol-1-yl)imidazo[2,1-*b*)]thiazolium-3-olate (**9**) was obtained from 1-(4-ethoxyphenyl)-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)imidazoline-2-thione (**6**). The 1,3-dipolar cycloadditions of **5** and **9** with several acetylenic dipolarophiles gave the corresponding imidazo[1,2-*a*]pyridin-4-ones. With unsymmetrical dipolarophiles, these reactions were highly regioselective and only one regioisomer was isolated.

INTRODUCTION

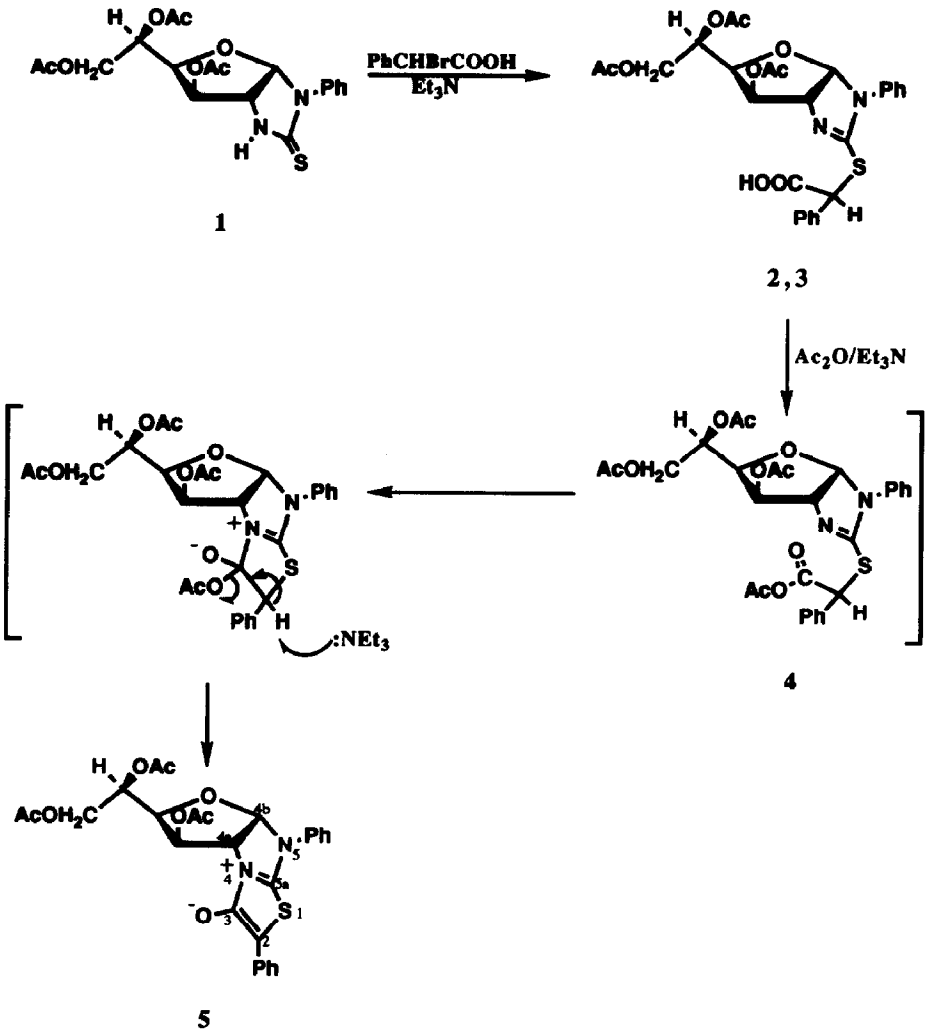
1,3-Dipolar cycloaddition constitutes a valuable approach to the synthesis of a wide variety of heterocyclic systems[1]. Thus, sugar derivatives have been used as 1,3-dipoles[2–5] or dipolarophiles[6–8] to prepare heterocycles joined to carbohydrate frameworks. However, the mesoionic heterocycles have received little attention as "masked" 1,3-dipoles in the carbohydrate field and there appear to be only two reports on the cycloaddition of mesoionic heterocycles to unsaturated sugars[9,10]. Likewise, there are few examples of mesoionic heterocycles fused to carbohydrate moieties[11,12], since some so-called mesoionic derivatives do not accord with the definition proposed by Ollis *et al.*[13]. We now report the synthesis of the first examples of imidazo[2,1-*b*]thiazolium-4-olate systems joined to cyclic and acyclic sugar chains (**5** and **9**). The cycloaddition reactions of these compounds open a versatile route to the synthesis of sugar heterocyclic derivatives and we report also their reactions with acetylenic dipolarophiles.

* Carbohydrate-derived Mesoionic Compounds, Part I.
† To whom correspondence should be addressed.

0008-6215/91/$ 03.50

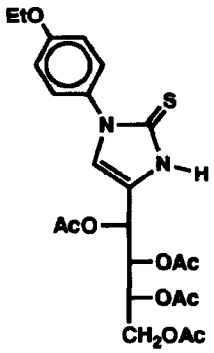
RESULTS AND DISCUSSION

Of the methods described[14–26] for the synthesis of 1,3-thiazolium-4-olate systems, the cyclodehydration reaction of a thioglycolic acid[14–18] is particularly suited to the synthesis of ring-fused systems when a heterocyclic thione is readily available. Thus, treatment of 1-phenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione[27] (**1**) with α-bromophenylacetic acid and triethylamine in benzene gave a crystalline mixture of the diastereomeric thioglycolic acid **2** and **3** that could not be fractionated. Subsequent ring closure with acetic anhydride–triethylamine gave **5**.

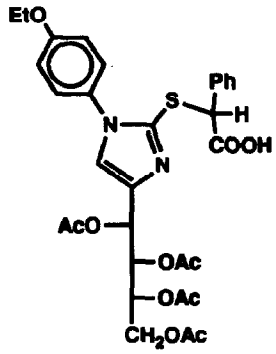


1 **2,3** **4** **5**

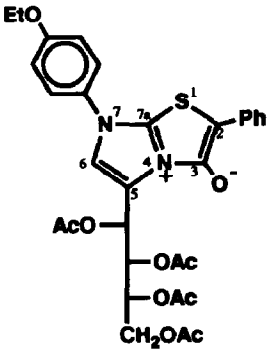
This cyclisation must occur through the mixed anhydride **4**, which undergoes an intramolecular *N*-addition followed by the base-catalysed elimination of acetic acid (**1**→**5**). Similarly, **6**[28] gave the acyclic mesoionic nucleoside **9**. The intermediate mixture of diastereomers **7** and **8** was isolated as a hygroscopic solid that was characterised, as for **2** and **3**, on the basis of spectroscopic data. The ^{1}H-n.m.r. spectrum of **2** and **3** contained only one set of signals for both diastereomers (Tables I and II); in particular, the signals of the protons α to the carboxyl groups appeared at 5.46 p.p.m. (s). For **7** and **8** (Tables III and IV), the analogous protons gave signals at 5.18 (s) and 5.16 p.p.m. (s). However, the presence of two diastereomers was confirmed through two sets of signals in the ^{13}C-n.m.r. spectra (Tables V and VI). The structures assigned to **5** and **9** are also supported by analytical and spectroscopic data. Thus, the i.r. bands at 1640 and 1610 cm^{-1} were analogous to those observed in related mesoionic systems[15], and indicated the low degree of double-bond character of the carbonyl group. Similarly, the u.v. spectra of **5** and **9** showed strong red shifts to 424 and 363 nm, respectively, from 246 nm for **2** and **3**, and 266 nm for **7** and **8**. The ^{13}C-n.m.r. spectrum of **5** contained signals at 83.91, 151.68, and 154.98 p.p.m. that could be assigned to C-2, C-3, and C-5a, respectively. For **9**, the corresponding signals appeared at 84.65, 150.24, and 139.42 p.p.m. The strong shielding of C-7a of **9** compared to C-5a in **5** is due to the presence of the 5,6-double bond in **9**. The resonance of C-6 could be distinguished from those of the aromatic carbons by the large $^1J_{C,H}$ value (~200 Hz). Finally, the ^{1}H δ and *J* values for **5** and **9** are in accord with the respective sugar moieties (Tables I–IV).



6



7,8



9

The mesoionic system **5** underwent rapid cycloaddition reactions with various acetylenic dipolarophiles (dimethyl acetylenedicarboxylate, diethyl acetylenedicarboxylate, methyl propiolate, and ethyl phenylpropiolate) in refluxing benzene or toluene to give the imidazo[1,2-*a*]pyridin-4-one derivatives **10**–**13** through the extrusion of sulphur from the 1:1 cycloadducts **14**–**17** that could not be isolated. In a similar way, the imidazo[1,2-*a*]pyridin-4-ones **18** and **19** were obtained by the reactions of **9** with dimethyl acetylenedicarboxylate and methyl propiolate, respectively. The above cycloaddition reactions were monitored by t.l.c. (the imidazo[1,2-*a*]pyridin-4-ones **10**–**13**, **18**, and **19** fluoresced in u.v. light).

TABLE I

^{1}H-N.m.r. chemical shifts (δ) for **2, 3, 5,** and **10–13**[a]

Compound	*H-1′*	*H-2′*	*H-3′*	*H-4′*	*H-5′*	*H-6′a*	*H-6′b*	*SCH*	*H-2*	*CH_3*	*CH_2*	*Ph*	*OAc*
2,3[b]	6.02d	4.59d	5.23d	3.61dd	5.09m	4.33dd	4.03dd	5.46s				7.4–7.2m	2.01s (12 H) 1.95s (6 H)
5[b]	6.56d	5.67d	6.17d	4.17dd	5.32m	4.49dd	4.09dd					7.5–6.7m	2.17s (3 H) 1.98s (3 H) 1.89s (3 H)
10[b]	6.01d	5.04d	6.02d	4.28dd	5.25m	4.51dd	4.37dd			3.54s 2.96s		7.35bs	2.10s (3 H) 2.08s (3 H) 2.02s (3 H)
10[c]	6.20d	4.99d	5.84d	4.41dd	5.09m	4.30dd	4.17dd			3.42s 2.81s		7.5–7.2m	2.10s (3 H) 1.99s (3 H) 1.93s (3 H)
11[b]	6.01d	5.03d	6.02d	4.30dd	5.24m	4.54dd	4.32dd			0.93t 0.90t	4.00q (2 H) 3.75dq (1 H) 3.08dq (1 H)	7.34bs	2.10s (3 H) 2.07s (3 H) 2.01s (3 H)
12[b]	6.01d	5.06d	6.07d	4.23dd	5.26m	4.50dd	4.34dd		7.99s	3.13s		8.0–7.2m	2.11s (3 H) 2.06s (3 H) 2.01s (3 H)
13[b]	6.02d	5.10d	6.14d	4.44dd	5.26m	4.56dd	4.31dd			0.62t	3.21dq (1 H) 2.93dq (1 H)	7.4–6.8m	2.14s (3 H) 2.08s (3 H) 2.02s (3 H)

[a] The primed numbers refer to the sugar moiety. [b] In $CDCl_3$. [c] In $(CD_3)_2SO$.

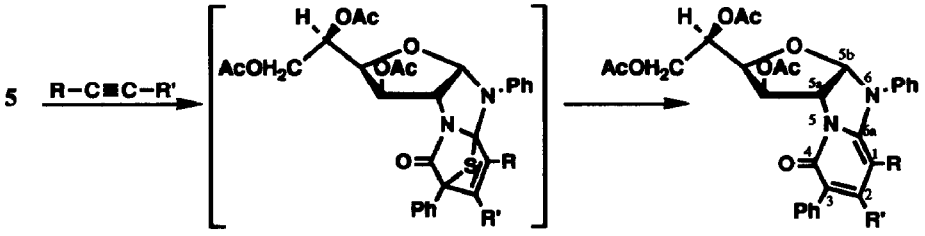
TABLE II

^{1}H-N.m.r. *J* values (Hz) for **2, 3, 5,** and **10–13**

Compound	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$
2,3[a]	5.8	0.0	2.7	9.1	2.2	6.2	12.3
5[a]	6.2	0.0	2.7	9.4	2.3	5.0	12.3
10[a]	6.4	0.0	2.6	9.6	1.8	4.6	12.2
10[b]	6.5	0.0	2.9	9.2	2.3	5.2	12.4
11[a]	6.4	0.0	2.6	9.4	2.1	4.8	12.3
12[a]	6.4	0.0	2.9	9.5	2.1	4.8	12.3
13[a]	6.4	0.0	2.9	9.6	2.1	4.9	12.3

[a] In $CDCl_3$. [b] In $(CD_3)_2SO$.

With the unsymmetrical dipolarophiles, only one regioisomer was detected and isolated. Two orientations are possible in the products of these reactions, but the regioisomers **20–22** were ruled out by the following n.m.r. considerations. The resonances of the protons of the phenyl groups in **10** and **11**, and of the monosubstituted phenyl group of **19**, were singlets which suggested that the corresponding phenyl groups were out of the plane of the pyridone ring, probably due to the steric interactions of the *ortho* protons with the alkoxycarbonyl group. However, for **12** and **19**, these resonances were multiplets. This fact accords with the presence of an unsubstituted C-2 that allows a coplanar disposition of phenyl and pyridone rings. The proximity of the anisotropic C=O group results in the resonances of the phenyl protons appearing as complex multiplets. For **13**, the regiochemistry could be assigned because the chemical shift of *C*(=O)OEt (164.61 p.p.m.) was similar to those of *C*(=O)OMe of **12** (164.24 p.p.m.) and **19** (164.15 p.p.m.). The alkoxycarbonyl groups of **10, 11,** and **18** resonated at 166.84 and 163.66, 166.27 and 163.39, and 167.33 and 163.63 p.p.m., respectively.



14 R=R'=COOMe
15 R=R'=COOEt
16 R=COOMe, R'=H
17 R=COOEt, R'=Ph

10 R=R'=COOMe
11 R=R'=COOEt
12 R=COOMe, R'=H
13 R=COOEt, R'=Ph
20 R=H, R'=COOMe
21 R=Ph, R=COOEt

TABLE III

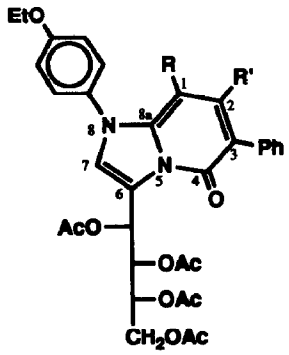
^{1}H-N.m.r. chemical shifts (δ) for **7–9, 18,** and **19** (in $CDCl_3$)

Compound	*H-1'*	*H-2'*	*H-3'*	*H-4'a*	*H-4'b*	*SCH*	*H-2*	*H-6*	*H-7*	CH_3	CH_2	*Ph*	*OAc*
7,8	6.15d	5.69t	5.30–5.17m	4.31dd	4.14dd	5.18s		7.10s		1.42t	4.04q	7.3–7.2m	2.14s (3 H)
	6.04d	5.66t	5.30–5.17m	4.29dd	4.14dd	5.16s		7.06s		1.41t	4.03q	6.98dd	2.12s (3 H)
												6.96dd	2.11s (3 H)
													2.09s (3 H)
													2.06s (3 H)
9	7.31d	6.01dd	5.40m	4.37dd	4.25dd			7.29s		1.42t	4.05q	7.7–6.9m	2.17s (3 H)
													2.15s (3 H)
													2.04s (3 H)
													2.02s (3 H)
18	7.34dd	5.91dd	5.34m	4.28dd	4.13dd				6.91d	3.52s	4.02q	7.4–6.9m	2.13s (3 H)
										3.10s			2.06s (3 H)
										1.44t			2.02s (3 H)
													1.94s (3 H)
19	7.27d	5.96dd	5.39m	4.33dd	4.22dd		8.15s		6.89s	3.28s	4.07q	7.8–6.9m	2.15s (3 H)
										1.45t			2.13s (3 H)
													2.04s (3 H)
													1.95s (3 H)

TABLE IV

^{1}H-N.m.r. *J* values (Hz) for **7–9**, **18**, and **19** (in $CDCl_3$)

Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4a}$	$J_{3,4b}$	$J_{4a,4b}$
7,8	4.9	5.2	3.0	6.2	12.3
	5.2	5.1			
9	2.7	8.5	2.7	7.0	12.4
18	2.3	9.3	2.6	5.3	12.3
19	2.0	9.3	2.6	5.3	12.5



18 R=R'=COOMe
19 R=COOMe, R'=H
22 R=H, R'=COOMe

The ^{1}H and ^{13}C chemical shifts of the resonances of the ethyl and methyl groups of C(=O)OR are also significant. The two methyl groups of **10** gave ^{1}H signals at 3.54 and 2.96 p.p.m., and ^{13}C signals at 52.28 and 50.95 p.p.m. The resonances of the analogous more-shielded methyl group in **18** were shifted downfield to 3.10 (^{1}H) and 51.36 p.p.m. (^{13}C). Comparison of these spectra with those of **12** and **19** revealed the remaining signal to be the more shielded (3.13 and 50.80 p.p.m. for **12**; 3.28 and 51.19 p.p.m. for **19**). The same situation applies to **11** and **13**. Only one methylene group (the more shielded) of **11** gave double quartets due to the diastereotopic relationship of its hydrogen atoms, and similar signals were observed for **13**. The proximity of the alkoxycarbonyl group on C-1 and the phenyl group on N-6 restricts the rotation of the latter group in **10–13**, as shown by the broadening of some of the ^{13}C signals due to aromatic carbons. When $(CD_3)_2SO$ was used instead $CDCl_3$ as the solvent for **10**, the chemical shifts of these signals were changed, but not the broadening. At 60°, sharp signals for all ^{13}C resonances were observed.

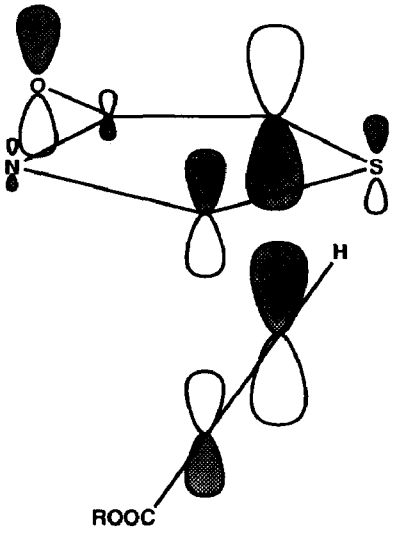


Fig. 1. Frontier orbital interactions in the cycloaddition reactions of 1,3-thiazolium-4-olate systems with propiolates.

The conformational features of **10–13** were well reproduced by theoretical molecular mechanics[29] calculations[30]. The rotation of the *C*-phenyl ring out of the pyridone plane is due to the alkoxycarbonyl group on the neighbouring C-2, and the restrictions to the rotation around the *N*-aryl bond are also due to the alkoxycarbonyl group on C-1. The conformation adopted by this latter group explains the marked differences in chemical shifts of the resonances of the methylene protons (see Table I).

Thus, the above 1,3-dipolar cycloadditions occur with high or total regioselectivity and this can be rationalised by means of frontier molecular orbital (FMO) considerations. The HOMO(dipole)–LUMO(dipolarophile) interaction is the major one for the 1,3-thiazolium-4-olate and acetylenic systems[31]. Thus, the more probable primary interactions of **5** and **9** with the propiolates are represented in Fig. 1. The corresponding transition states lead to the regioisomers **12, 13,** and **19.**

EXPERIMENTAL

General methods. — Solutions were concentrated *in vacuo* at $<50°$. Melting points were determined with a Gallenkamp apparatus and are uncorrected. Optical rotations were measured at $20\pm5°$ with a Perkin–Elmer 141 polarimeter, i.r. spectra (KBr discs) with a Perkin–Elmer 399 spectrophotometer, and u.v. spectra (96% ethanol) with a Pye–Unicam SP8-250 instrument. T.l.c. was conducted on Silica Gel GF_{254} (Merck) with benzene–ether (3:2) and detection with u.v. light or iodine vapour. The ^1H-(200 MHz) and ^{13}C-n.m.r. (50 MHz) spectra (Tables I–VI) were recorded with a Bruker AC 200-E spectrometer. Assignments were confirmed by homo- and hetero-nuclear double-resonance experiments, and DEPT. Elemental microanalyses were obtained

TABLE V

^{13}C-N.m.r. chemical shifts (δ) for **2**, **3**, **5**, and **10–13** (in $CDCl_3$)

	Sugar moiety						*Heterocyclic moiety*										*OAc*	
Compound	*C-1′*	*C-2′*	*C-3′*	*C-4′*	*C-5′*	*C-6′*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5a*	*C-6a*	*SCH*	CH_3	CH_2	*C=O*	CH_3	*C=O*
2,3[a]	96.27	53.37	75.27	75.86	67.28	63.02		161.04					75.05				20.70	170.38, 170.14
	96.08	53.22	75.05	75.53	66.92	63.02		160.56					75.05				20.64	170.06, 169.26
																	20.59	169.26
																	20.51	
5	98.31	66.15	71.23	78.12	66.70	63.01		83.91	151.68		154.98						20.62	170.41, 169.56
																	20.47	168.59
10	95.28	65.37	72.16	75.89	66.56	63.13	89.11	144.80	120.01	158.95		148.84		52.28		166.84	20.64	170.41
														50.95		163.66	20.50	169.71
																	20.37	168.01
10[b]	95.01	65.33	72.25	75.76	66.63	62.87	88.08	144.07	118.07	158.49		149.84		52.04		166.63	20.64	170.11
														50.72		163.63	20.49	169.39
																		168.28
10[c]	94.75	65.04	72.22	75.76	66.59	62.51	87.89	143.86	117.94	158.16		149.43		51.49		166.11	20.15	169.60
														50.30		163.18	20.02	168.90
																		167.77
11	95.42	65.41	72.21	75.92	66.60	63.00	89.77	144.98	120.03	159.00		148.33		13.62	61.51	166.27	20.64	170.44
														13.31	60.74	163.39	20.59	169.74
																	20.38	168.00
12	95.50	65.26	72.43	75.83	66.60	63.19	91.30	140.83	120.74	159.11		149.20		50.80		164.24	20.62	170.33
																	20.43	169.67
																		168.18
13	94.98	65.77	72.61	76.13	66.80	63.30	93.96	146.59	121.04	159.00		151.76		13.20	60.45	164.61	20.75	170.51
																	20.69	169.81
																	20.47	168.10

[a] Signals of COO^- and C=O (acetate) groups are indistinguishable. [b] In $(CD_3)_2SO$. [c] In $(CD_3)_2SO$ at 60°

TABLE VI

^{13}C-N.m.r. chemical shifts (δ) for **7–9**, **18**, and **19** (in $CDCl_3$)

	Sugar moiety				*Heterocyclic moiety*												*OAc*	
Compound	*C-1'*	*C-2'*	*C-3'*	*C-4'*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	*C-7a*	*C-8a*	*SCH*	CH_3	CH_2	*C=O*	CH_3	*C=O*
7,8[a]	66.99	70.92	68.89	61.62		142.65		128.15	121.72					53.83	14.53	63.72		20.40	170.65
	66.50	70.57	68.78	61.51					121.10					53.59					170.46
																			170.40
																			169.76
																			169.71
																			169.66
																			169.63
																			169.50
																			169.37
9	63.91	70.48	68.10	62.10		84.65	150.24		126.97	120.52		139.42			14.34	63.79		20.64	170.40
																		20.43	170.02
																		20.38	168.83
																		20.28	168.81
18	66.70	70.86	68.18	62.43	89.92	143.59	114.58	158.13		124.39	122.73		141.46		14.60	63.98	167.33	20.86	170.68
															51.36[b]		163.63	20.69	170.27
																		20.60	169.14
																		20.38	168.91
19	66.82	71.00	68.24	62.51	91.44	140.16	115.34	158.48		124.60	122.39		142.12		14.65	63.87	164.15	20.90	170.68
															51.19[b]			20.73	170.31
																		20.64	169.25
																		20.43	169.01

[a] Signals of COO^- and C=O (acetate) groups are indistinguishable. [b] OCH_3.

with a Perkin–Elmer 240C analyser. E.i.-mass spectra (35 and 70 eV) were obtained with a Kratos MS-80RFA mass spectrometer.

(R *and* S)-*2-phenyl-2-{(3,5,6-tri*-O-*acetyl-1,2-dideoxy-α-*D-*glucofurano)[2,1-*d*]-2-imidazolin-2-ylthio} acetic acid* (**2** *and* **3**). — To a mixture of **1** (5.2 g, 12.5 mmol) and α-bromophenylacetic acid (2.7 g, 12.5 mmol) in benzene (100 mL) was added triethylamine (1.8 mL, 12.5 mmol) dropwise. The mixture was stirred for 24 h at room temperature, and ethanol (200 mL) was added to give a white solid that was stirred with water. Recrystallisation of the product (6.8 g, 98%) from chloroform–ethanol gave a mixture of **2** and **3**, m.p. 172–173°, $[\alpha]_D$ +83°, $[\alpha]_{578}$ +89°, $[\alpha]_{546}$ +102°, $[\alpha]_{436}$ +193°, $[\alpha]_{365}$ +357° (*c* 0.5, chloroform); λ_{max} 246 nm (ε_{mM} 10.9); ν_{max} 3400 (OH), 1755 (C=O ester), and 1600 cm^{-1} (C=O acid). The ^1H- and ^{13}C-n.m.r. data are given in Tables I, II, and V.

Anal. Calc. for $C_{27}H_{28}N_2O_9S$: C, 58.26; H, 5.07; N, 5.03. Found: C, 58.25; H, 5.05; N, 4.99.

*2,5-Diphenyl-(3,5,6-tri-*O-*acetyl-1,2-dideoxy-α-*D-*glucofurano)[1′,2′:4,5]-4a*H,*4b*H-*imidazo[2,1-*b*]thiazolium-3-olate* (**5**). — To a solution of the mixture (6.0 g, 10.8 mmol) of **2** and **3** in acetic anhydride (40 mL) was added triethylamine (15 mL, 107.1 mmol). The mixture turned yellow and a yellow solid (4.4 g, 76%) crystallised. Recrystallisation from chloroform–ether gave **5**, m.p. 189–191°, $[\alpha]_D$ +23°, $[\alpha]_{578}$ +25°, $[\alpha]_{546}$ +32° (*c* 0.5, chloroform); λ_{max} 424, 293, and 256 nm (ε_{mM} 10.2, 11.4, and 11.9); ν_{max} 1750 (C=O ester) and 1610 cm^{-1} (C–O⁻heterocyclic). The ^1H- and ^{13}C-n.m.r. data are given in Tables I, II, and V.

Anal. Calc. for $C_{27}H_{26}N_2O_8S$: C, 60.21; H, 4.86; N, 5.20. Found: C, 59.80; H, 4.81; N, 5.07.

(R *and* S)-*2-[1-(4-ethoxyphenyl)-4-(1,2,3,4-tetra-*O-*acetyl-*D-arabino-*tetritol-1-yl)-2-imidazolylthio]-2-phenylacetic acid* (**7** *and* **8**).—To a mixture of **6** (37.6 g, 74 mmol) and α-bromophenylacetic acid (15.8 g, 74 mmol) in benzene (600 mL) was added triethylamine (10.3 mL, 74 mmol) dropwise. The mixture was stirred for 24 h at room temperature, then filtered, and concentrated. A solution of the residue in methanol (100 mL) was poured slowly into ice–water, and the resulting white solid (47.8 g, 98%), which was collected and washed with cold water, had m.p. 80–81°, $[\alpha]_D$ −28°, $[\alpha]_{578}$ −28°, $[\alpha]_{546}$ −33°(*c* 0.5, chloroform); λ_{max} 266 and 229 nm (ε_{mM} 9.0 and 21.0); ν_{max} 3400 (OH), 1750 (C=O ester), and 1600 cm^{-1} (C=O acid). The ^1H- and ^{13}C-n.m.r. data are given in Tables III, IV, and VI.

*7-(4-Ethoxyphenyl)-2-phenyl-5-(1,2,3,4-tetra-*O-*acetyl-*D-arabino-*tetritol-1-yl)-imidazo[2,1-*b*]thiazolium-3-olate* (**9**). — To a solution of the mixture (45.2 g, 70.4 mmol) of **7** and **8** in acetic anhydride (100 mL) was added triethylamine (33 mL, 236.7 mmol). After 30 min, ether was added and the resulting solid (32.8 g, 75%), which was recrystallised from chloroform–ether–light petroleum, decomposed without melting at 144° and had $[\alpha]_D$ −4°, $[\alpha]_{578}$ −6.5°, $[\alpha]_{546}$ −8.5°(*c* 0.4, chloroform); λ_{max} 363, 310, and 235 nm (ε_{mM} 8.9, 9.4, and 19.5); ν_{max} 1750 (C=O ester) and 1648 cm^{-1}(C–O⁻ heterocyclic). The ^1H- and ^{13}C-n.m.r. data are given in Tables III, IV, and VI.

Anal. Calc. for $C_{31}H_{32}N_2O_{10}S$: C, 59.61; H, 5.16; N, 4.48. Found: C, 59.72; H, 5.19; N, 4.34.

*1,2-Dimethoxycarbonyl-3,6-diphenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-*D*-glucofurano)[1',2':4,5]-5a*H*,5b*H*-imidazo[1,2-*a*]pyridin-4-one* (**10**). — On mixing **5** (0.5 g, 0.9 mmol), toluene (6 mL), and dimethyl acetylenedicarboxylate (0.15 g, 1.0 mmol), an exothermic reaction occurred. The mixture was boiled under reflux for 4 h, the solvent was then evaporated, and the residue was crystallised from ethanol to give **10** (0.4 g, 64%), m.p. 240–241°, $[\alpha]_D$ −161°, $[\alpha]_{578}$ −169°, $[\alpha]_{546}$ −200°, $[\alpha]_{436}$ −425° (*c* 0.4, chloroform); λ_{max} 344, 289, and 242 nm (ε_{mM} 10.2, 11.4, and 12.0); ν_{max} 1740 and 1720 (C=O ester) and 1660 cm^{-1} (C=O heterocycle). The ^{1}H- and ^{13}C-n.m.r. data are given in Tables I, II, and V.

Anal. Calc. for $C_{33}H_{32}N_2O_{12}$: C, 61.10; H, 4.97; N, 4.32. Found: C, 60.74; H, 4.94; N, 4.30.

*1,2-Diethoxycarbonyl-3,6-diphenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-*D*-glucofurano)[1',2':4,5]-5a*H*,5b*H*-imidazo[1,2-*a*]pyridin-4-one* (**11**). — A solution of **5** (1.0 g, 1.9 mmol) in benzene (20 mL) was treated with diethyl acetylenedicarboxylate (0.35 g, 2.1 mmol), as described for **10**. After evaporation of the solvent, the residue was chromatographed on silica gel, using benzene–acetonitrile (3:1), and crystallised from ethanol to give **11** (0.5 g, 38%), m.p. 217–218°, $[\alpha]_D$ −150°, $[\alpha]_{578}$ −157°, $[\alpha]_{546}$ −187°, $[\alpha]_{436}$ −390°(*c* 1, chloroform); λ_{max} 345, 301, and 236 nm (ε_{mM} 17.2, 7.8, and 17.4); ν_{max} 1750, 1725, and 1690 (C=O ester) and 1650 cm^{-1} (C=O heterocycle). The ^{1}H- and ^{13}C-n.m.r. data are given in Tables I, II, and V.

Anal. Calc. for $C_{35}H_{36}N_2O_{12}$: C, 62.12; H, 5.36; N, 4.14. Found: C, 61.85; H, 5.32; N, 4.08.

*1-Methoxycarbonyl-3,6-diphenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-*D*-glucofurano)[1',2':4,5]-5a*H*,5b*H*-imidazo[1,2-*a*]pyridin-4-one* (**12**). — A solution of **5** (0.5 g, 0.9 mmol) in benzene (20 mL) was treated with methyl propiolate (0.2 g, 2.2 mmol), as described for **10**, to give **12** (1.0 g, 91%), m.p. 213–214° (from ethanol), $[\alpha]_D$ −203°, $[\alpha]_{578}$ −215°, $[\alpha]_{546}$ −258°, $[\alpha]_{436}$ −619°(*c* 0.5, chloroform); λ_{max} 347, 307, and 242 nm (ε_{mM} 20.1, 11.5, and 20.0); ν_{max} 1760 and 1710 (C=O ester) and 1665 cm^{-1} (C=O heterocycle). The ^{1}H- and ^{13}C-n.m.r. data are given in Tables I, II, and V.

Anal. Calc. for $C_{31}H_{30}N_2O_{10}$: C, 63.04; H, 5.12; N, 4.74. Found: C, 63.34; H, 5.12; N, 4.55.

*1-Ethoxycarbonyl-2,3,6-triphenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-*D*-glucofurano)[1',2':4,5]-5a*H*,5b*H*-imidazo[1,2-*a*]pyridin-4-one* (**13**). — A solution of **5** (1.0 g, 1.9 mmol) in toluene (15 mL) was treated with ethyl phenylpropiolate (0.4 g, 2.1 mmol), as described for **10**. After evaporation of the solvent, the residue was chromatographed on silica gel with benzene–acetonitrile (3:1), then crystallised from ethanol to give **13** (0.2 g, 17%), m.p. 250–251°, $[\alpha]_D$ +1.5°, $[\alpha]_{578}$ +1°, $[\alpha]_{546}$ −2°, $[\alpha]_{436}$ −38.5° (*c* 1, chloroform); λ_{max} 345 and 236 nm (ε_{mM} 17.1 and 16.3); ν_{max} 1755, 1740, and 1710 (C=O ester), and 1650 cm^{-1} (C=O heterocycle). The ^{1}H- and ^{13}C-n.m.r. data are given in Tables I, II and V.

Anal. Calc. for $C_{38}H_{36}N_2O_{10}$: C, 67.05; H, 5.33; N, 4.12. Found: C, 67.35; H, 5.33; N, 4.15.

*8-(4-Ethoxyphenyl)-1,2-dimethoxycarbonyl-3-phenyl-6-(1,2,3,4-tetra-*O*-acetyl-*

D-arabino-*tetritol-1-yl)imidazo[1,2-a]pyridin-4-one* (**18**). — A suspension of **9** (2.0 g, 3.2 mmol) in toluene (50 mL) was boiled under reflux with dimethyl acetylenedicarboxylate (0.5 g, 3.2 mmol) for 4 h and the solvent was then evaporated. Column chromatography (benzene–acetonitrile, 10:1) of the residue on silica gel followed by t.l.c. (ether–light petroleum, 10:1) gave **18** (0.2 g, 9%), m.p. 110–111°, $[\alpha]_D$ −36°, $[\alpha]_{578}$ −40°, $[\alpha]_{546}$ −50°, $[\alpha]_{436}$ −188° (*c* 0.5, chloroform); λ_{max} 362, 307, and 231 nm (ε_{mM} 24.0, 12.0, and 29.0); ν_{max} 1740 (C=O ester) and 1650 cm^{-1} (C=O heterocycle). The ^{1}H- and ^{13}C-n.m.r. data are given in Tables III, IV, and VI.

Anal. Calc. for $C_{37}H_{38}N_2O_{14}$: C, 60.49; H, 5.21; N, 3.81. Found: C, 60.28; H, 5.20; N, 3.72.

*8-(4-Ethoxyphenyl)-1-methoxycarbonyl-3-phenyl-6-(1,2,3,4-tetra-*O*-acetyl-*D*-arabino-tetritol-1-yl)imidazo[1,2-a]pyridin-4-one* (**19**). — A suspension of **9** (2.0 g, 3.2 mmol) in toluene (34 mL) was treated with methyl propiolate (0.3 g, 3.8 mmol), as described for **18**, to give **19** (0.8 g, 38%), m.p. 96–97° (from ether–light petroleum), $[\alpha]_D$ −46°, $[\alpha]_{578}$ −48°, $[\alpha]_{546}$ −59°, $[\alpha]_{436}$ −159° (*c* 1.8, chloroform); ν_{max} 1740 and 1700 (C=O ester) and 1650 cm^{-1} (C=O heterocycle). The ^{1}H- and ^{13}C-n.m.r. data are given in Tables III, IV, and VI. Mass spectrum: *m/z* 676 (M^+).

Anal. Calc. for $C_{35}H_{36}N_2O_{12}$: C, 62.12; H, 5.36; N, 4.14. Found: C, 62.10; H, 5.23; N, 4.07.

ACKNOWLEDGMENT

This work was supported by Dirección General de Investigación Científica y Técnica (Grant No. PB86-0255).

REFERENCES

1 K. T. Potts, in A. Padwa (Ed), *1,3-Dipolar Cycloaddition Chemistry*, Vol. 2, Wiley, New York, 1984.
2 E. M. Acton, K. J. Ryan, and L. Goodman, *J. Chem. Soc., Chem. Commun.*, (1970) 313–314.
3 W. Schoerkhuber and E. Zbiral, *Chem. Ber.*, 114 (1981) 3165–3169.
4 P. DeShong and J. M. Leginus, *Tetrahedron Lett.*, 25 (1984) 5355–5358.
5 A. P. Kozikowski and S. Goldstein, *J. Org. Chem.*, 48 (1983) 1139–1141.
6 F. G. de las Heras, S. Y-K. Tan, R. S. Klein, and J. J. Fox, *J. Org. Chem.*, 41 (1976) 84–90.
7 J. G. Buchanan, A. R. Edgar, and M. J. Power, *J. Chem. Soc., Perkin Trans. 1*, (1974) 1943–1949.
8 M. Mancera, E. Rodríguez, I. Roffé, and J. A. Galbis, *J. Org. Chem.*, 53 (1988) 5648–5651.
9 Z. Zaheer, Ph.D. Thesis, Rensselaer Polytechnic Institute, New York, 1980.
10 M. Avalos, R. Babiano, I. Bautista, J. I. Fernández, J. L. Jiménez, J. C. Palacios, J. Plumet, and F. Rebolledo, *Carbohydr. Res.*, 186 (1989) c7–c8.
11 H. Ogura and H. Takahashi, *J. Org. Chem.*, 39 (1974) 1374–1379.
12 M. Hayashi, T. Hirano, M. Yaso, K. Mizuno, and T. Ueda, *Chem. Pharm. Bull.*, 23 (1975) 245–246.
13 W. D. Ollis, S. P. Stanforth, and C. A. Ramsden, *Tetrahedron*, 41 (1985) 2239–2329.
14 M. Ohta and S. Sato, *J. Chem. Soc. Jpn.*, 89 (1968) 199–202.
15 K. T. Potts, E. Houghton, and U. P. Singh, *J. Org. Chem.*, 39 (1974) 3627–3631.
16 K. T. Potts and D. R. Choudhury, *J. Org. Chem.*, 43 (1978) 2697–2700.
17 K. V. Fedotov, N. N. Romanov, and A. I. Tolmachev, *Khim. Geterotsikl. Soedin.*, (1984) 969–973; *Chem. Abstr.*, 101 (1984) 191 838r.
18 P. B. Talukdar, S. K. Sengupta, and A. K. Datta, *Indian J. Chem., Sect. B*, 23 (1984) 316–320.
19 D. H. R. Barton, E. Buschmann, J. Haüsler, C. W. Holzapfel, T. Sheradsky, and D. A. Taylor, *J. Chem. Soc., Perkin Trans. 1*, (1977) 1107–1114.

20 K. T. Potts, S. J. Chen, J. Kane, and J. L. Marshall, *J. Org. Chem.*, 42 (1977) 1633–1638.
21 K. T. Potts and D. R. Choudhury, *J. Org. Chem.*, 43 (1978) 2700–2703.
22 K. T. Potts and S. Kanemasa, *J. Org. Chem.*, 44 (1979) 3803–3808, 3808–3811.
23 H. K. Singh and C. S. Gandhi, *Indian J. Chem.*, Sect. B, 16 (1978) 331–332.
24 H. K. Singh, A. S. Ahuja, and C. S. Gandhi, *J. Chem. Res. (S)*, (1979) 264.
25 M. Baudy, A. Robert, and A. Foucaud, *J. Org. Chem.*, 43 (1978) 3732–3736.
26 M. Baudy and A. Robert, *Tetrahedron Lett.*, 21 (1980) 2517–2520.
27 M. Avalos, J. L. Jiménez, J. C. Palacios, M. D. Ramos, and J. A. Galbis, *Carbohydr. Res.*, 161 (1987) 49–64.
28 J. Fernández-Bolaños, F. García González, J. Gasch Gómez, and M. Menéndez Gallego, *Tetrahedron*, 19 (1963) 1883–1892.
29 N. L. Allinger, *J. Am. Chem. Soc.*, 99 (1977) 8127–8134.
30 P. Areces, M. Avalos, R. Babiano, L. González, J. L. Jiménez, and J. C. Palacios, unpublished results.
31 M. Baudy, A. Robert, and C. Guimon, *Tetrahedron*, 38 (1982) 2129–2137.