Simple and Condensed β-Lactams. Part 30.[1] Attempted Synthesis of a 4-Ureidooxymethyl Analogue of Carumonam

J. Chem. Research (S), 1998, 112–113
J. Chem. Research (M), 1998, 0701–0719

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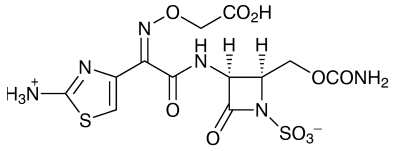
An attempted synthesis of the racemic ureidooxymethyl analogue **3** of carumonam **1** and the synthesis of racemic model compound **2** are described.

In continuation of our studies into the structure–activity relationships in the carumonam **1**[2] series the syntheses of the racemic 4-(ureidooxymethyl) analogue **3** of carumonam and the model compound **2** were attempted.



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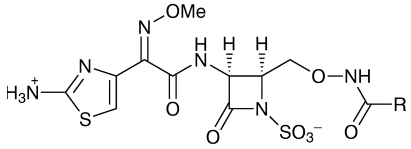
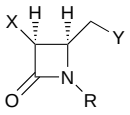


2 R = Me
3 R = NH_2

The known compound **4**[3] served as the starting material for the synthesis of compound **2**·HCl.

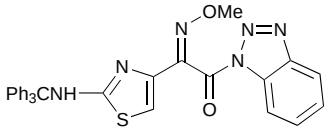


4–14a

PhthN = phthalimido
PMP = 4-methoxphenyl
Z = benzyloxycarbonyl
Ac = acetyl

	X	Y	R
4	PhthN	O_3SMe	PMP
5	H_2N	O_3SMe	PMP
6a	ZNH	O_3SMe	PMP
7a	ZNH	ONPhth	PMP
8a	ZNH	ONPhth	H
9a	ZNH	ONPhth	$SiBu^tMe_2$
10a	ZNH	ONH_2	$SiBu^tMe_2$
11a	ZNH	ONHAc	$SiBu^tMe_2$
12a	ZNH	ONHAc	H
13a	ZNH	ONHAc	$SO_3^-Na^+$
14a	H_3N^+	ONHAc	SO_3^-

Compound **4** was converted by manipulations of the substituents X, Y and R in 10 steps into the zwitterionic compound **14a**. Acylation of the latter with acylating agent **15**[9] followed by detritylation then afforded the desired compound **2**·HCl.



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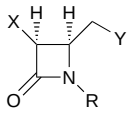
The synthesis of compound **3** was first attempted by an analogous approach. To this end compound **10a** was treated with potassium cyanate and aqueous methanolic hydrochloric acid to afford the expected ureidooxymethyl derivative **19** which was subsequently desilylated by treatment with tetrabutylammonium fluoride to afford compound **20**. Sulfonation of the latter, followed by the usual work-up,[8] however furnished, as shown by FAB-MS, a mixture of the sodium salts of at least one *N*-mono- (M 410) and one *N*,*N*′-disulfonic acid (M 512) which indicates that the reactivites of at least two NH groups of compound **20** towards the sulfonating agent are rather similar. Therefore an attempt was made at blocking some of the NH groups of compound **19**.



10a, **19–29**

Z = benzyloxycarbonyl
BOC = *tert*-butoxycarbonyl

	X	Y	R
10a	ZNH	ONH_2	$SiBu^tMe$
19	ZNH	$ONHCONH_2$	$SiBu^tMe$
20	ZNH	$ONHCONH_2$	H
21	ZNH	ONHZ	$SiBu^tMe$
22	ZNH	ONHZ	H
23a	ZNH	ONHBOC	$SiBu^tMe$
24a	ZNH	ONHBOC	H
25a	ZNH	ONHBOC	$SO_3^-Na^+$
26	H_3N^+	ONHBOC	SO_3^-
27	ZNH	ONH_3^+	SO_3^-
28	ZNH	$ONHCONH_2$	SO_3H
29	H_3N^+	$ONHCONH_2$	SO_3^-

*To receive any correspondence.
†Enantiomer shown. All other structural formulae depicted in the present paper refer to racemic compounds.

Reaction of **19** with benzyloxycarbonyl chloride in the presence of triethylamine led unexpectedly to a mixture of compounds **20** (by desilylation), **21** (by side-chain degradation and benzyloxycarbonylation) and **22** (by desilylation, side-chain degradation and benzyloxycarbonylation).

In our second approach to the synthesis of compound **3**, carbamoylation of the side-chain amino group was postponed and the side-chain amino group of compound **10a** was protected by *tert*-butoxycarbonylation. The resulting **24a** was then converted by straightforward methods into compounds **26** and **29** in two and four steps, respectively. Attempted acylation of **29** by acylating agent **15** to obtain the butyl protected derivative of the desired compound **3**, however, failed in the same way as the attempted acylation of compound **26** by the same acylating agent.

We are grateful to OTKA (Hungarian Scientific Research Fund; grant T-014871) for financial assistance.

Techniques used: IR, ^{1}H and ^{13}C NMR, ms, TLC

References: 9

Schemes: 4

Received, 16th June 1997; Accepted, 19th November 1997
Paper E/7/04165I

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