Simple and Condensed β-Lactams. Part 28.[1] The Synthesis of *C*-Methylcarumonams and of a Related Bis(carbamate)

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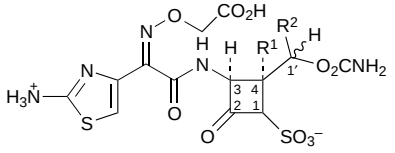
Racemic carumonam analogues **2a–d** are synthesised and found to be devoid of any bacterial activity; $NaBH_4$ reduction of **18** affords both epimers of **8c** with the (3*RS*,4*RS*)-4-[(1*RS*)] epimer as the main product, and cyclocondensation of phthalimidoacetyl chloride with racemic imine **14** gives rise to the formation of (3*RS*,4*RS*)-4-[(1*RS*)]-**15** as a single epimer.

In the course of our studies into structure–activity relationships in the carumonam **1**[2] series we have synthesised racemic *C*-substituted derivatives **2a–d** of carumonam *via* key intermediates **8a–c** and **25**, respectively, as outlined in the Scheme.

The two epimers of compound **8c** were obtained by sodium tetrahydroborate reduction of acetyl derivative **18**[5] (resulting from imine **17**[5] on acid hydrolysis), followed by *N*-deacylation. As shown by X-ray molecular structure determination,[13] the (3*RS*,4*RS*)-4-[(1*RS*)] epimer of compound **8c** was formed as the main product. This is in agreement with the Felkin–Anh model[14,15] of nucleophilic additions to the carbonyl group. On the other hand, cyclocondensation of phthalimidoacetyl chloride with racemic imine **14** afforded, in agreement with our expectation, the (3*RS*,4*RS*)-4-[(1*RS*)] compound **15** as the only epimer.

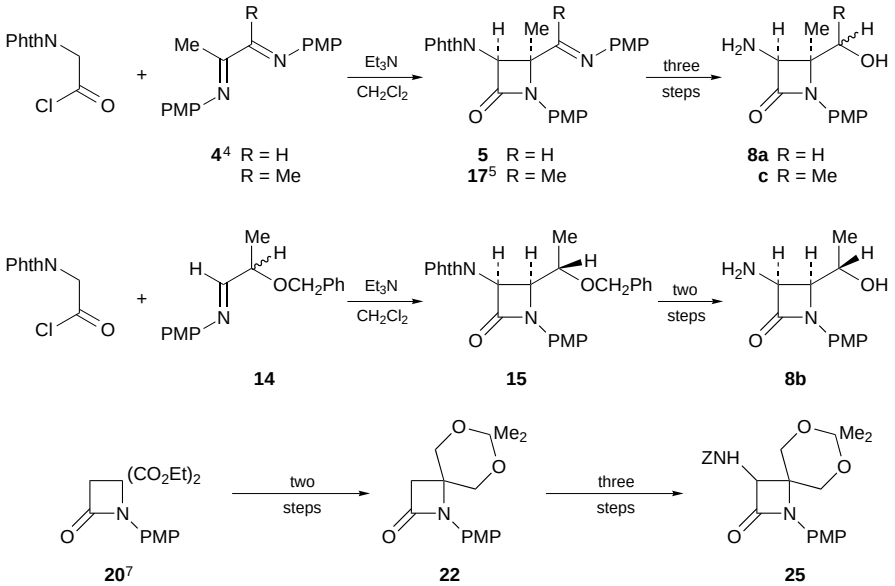
Compounds **8a–c** were subsequently converted by benzyloxycarbonylation into compounds **26a–c**, while treatment of compound **25** with cation exchange resin Varion KS/H^+ afforded compound **26d**. Compounds **26a–d** were converted in five steps (successive treatment with chlorosulfonyl isocyanate and aqueous $NaSO_3$; demethoxyphenylation with CAN;[8] *N*-sulfonation with pyridiniosulfonate, ion pair extraction[9] and treatment with cation exchange resin Varion KS/Na^+; debenzyloxycarbonylation by catalytic hydrogenolysis; acylation with acylating agent **33**[10] and de-*tert*-butylation) into the corresponding compounds **2a–d**, none of which exhibited antibacterial activities.

Techniques used: column chromatography, TLC, IR, ^1H and ^{13}C NMR, NOE, elemental analysis



Carumonan **1**, **2a–d**†

1 $R^1 = R^2 = H$
2a $R^1 = Me$, $R^2 = H$
b $R^1 = H$, $R^2 = Me$
c $R^1 = R^2 = Me$
d $R^1 = CH_2O_2CNH_2$, $R^2 = H$

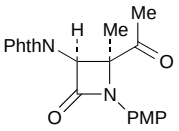


Scheme Synthesis of key intermediates **8a–c** and **25**. PhthN = phthalimido, PMP = 4-methoxyphenyl, Z = benzyloxycarbonyl. Compounds **5**, **8a–c**, **14**, **15** and **17** are racemic; only one enantiomer is shown. Both epimers of compound **8c** have been isolated.

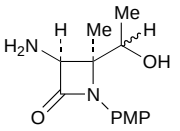
*To receive any correspondence.
†Compounds **2a–d** are racemic, only one enantiomer shown; **2b,c** have 2 epimers each.

References: 15

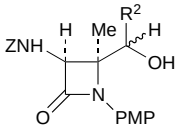
Schemes: 7



18[a]



(3*RS*,4*RS*)-4-[(1*RS*)]-**8c**[a]



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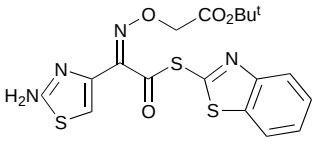

33[10]

	R^1	R^2
a	Me	H
b	H	Me[b]
c	Me	Me[c]
d	CH_2OH	H

[a] Racemic compounds, only one enantiomer shown.
[b] (3*RS*,4*RS*)-4-[(1*RS*)] epimer. [c] Both epimers.

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