Pergamon

Tetrahedron: Asymmetry, Vol. 8, No. 10, pp. 1685–1691, 1997

Printed in Great Britain
PII: S0957-4166(97)00167-5
0957-4166/97 $17.00 + 0.00

A convenient preparation of *N*-(2-alkynoyl) derivatives of chiral oxazolidin-2-ones and bornane-10,2-sultam

Sílvia Fonquerna, Albert Moyano*,* Miquel A. Pericàs* and Antoni Riera
Unitat de Recerca en Síntesi Asimètrica, Departament de Química Orgànica, Universitat de Barcelona, c/. Martí i Franquès, 1–11, 08028- Barcelona, Spain

Abstract: Chiral 2-alkynoate derivatives of 4-substituted oxazolidin-2-ones and of Oppolzer's 10,2-camphorsultam have been synthesized in good to excellent yields using a one-pot method involving the nucleophilic attack of the lithium salt or the lithium chloride complex of the chiral auxiliary on a mixed 2-alkynoic-pivalic anhydride. © 1997 Elsevier Science Ltd

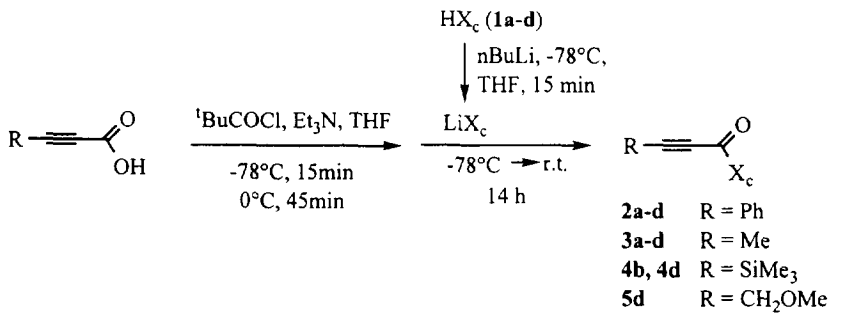
Chiral auxiliaries have played a major role in the development of asymmetric synthesis.[1] Among them, 4-substituted oxazolidin-2-ones and camphor-derived sultams, introduced respectively by the Evans'[2] and Oppolzer's groups,[3] continue to be the object of strong interest.[4] As a continuation of our studies on the chiral-auxiliary stereodirected Pauson–Khand reaction,[5] we wished to explore the use of 2-oxazolidinones and bornane-10,2-sultam as removable, chiral controllers linked to acetylenes by means of amide bonds. However, a bibliographic search showed that while a great number of *N*-alkanoyl and *N*-(2-alkenoyl) derivatives of oxazolidinones and sultams have been prepared for its use in a variety of asymmetric processes, very little is known about the corresponding *N*-(2-alkynoyl) derivatives. In fact, only one brief mention of the use of 2-butynoyl-4-isopropyloxazolidin-2-one in the asymmetric Diels–Alder reaction can be found in the literature.[6] We report in this paper a convenient preparation of several previously unknown oxazolidin-2-one and bornane-10,2-sultam amides derived from 2-alkynoic acids.

Whereas the most commonly employed procedure for the acylation of oxazolidinones or sultams relies on the reaction of the lithium,[7] magnesium[6] or sodium[8] salt of the heterocycle with the corresponding acid chloride, the instability of both propiolyl and tetrolyl chloride seemed to preclude the general applicability of this methodology for our purposes.

We therefore turned our attention to an alternative one-pot method originally developed by Evans,[9] which involves the low temperature attack of the lithium salt of an oxazolidinone or sultam to a mixed alkanoic–pivalic anhydride (which can in turn can be easily generated in situ from a carboxylic acid, pivaloyl chloride and triethylamine). This procedure could be easily adapted to the preparation of 2-alkynoyl derivatives of 4-substituted-2-oxazolidinones **1a–c** and of Oppolzer's camphorsultam **1d**, taking place as a rule in good to excellent yields. (Scheme 1 and Table 1).

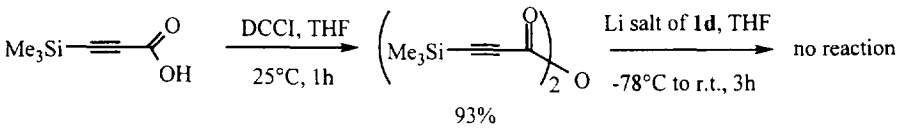
However, this method afforded only low yields of the 2-alkynoyl amide **4d** (entry 10). Together with the formation of the *N*-pivaloyl derivative of bornane-10,2-sultam as major by-product, we also observed the incorporation of a pivaloate moiety due to a Michael type addition to the triple bond in **4d**. Taking into account the origin of the major by-product, we decided to study the use of a symmetrical anhydride derived from 3-trimethylsilyl-2-propynoic acid. This anhydride was prepared in 93% yield by treatment of the acid with *N,N'*-dicyclohexylcarbodiimide,[10] but its subsequent reaction with the lithium salt of **1d** led only to the recovery of the starting products (Scheme 2). In a similar way, several attempts to obtain **4d** starting from 3-trimethylsilyl-2-propinoyl chloride (prepared by reaction of the acid with oxalyl chloride and used without purification) did not improve the yield of Table 1. Even

* Corresponding author.



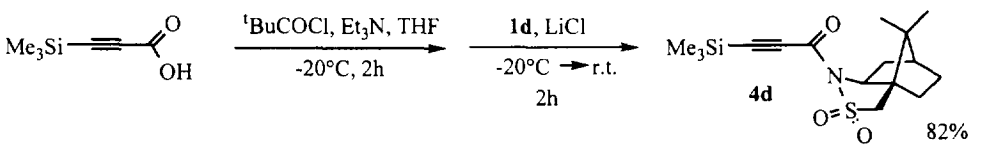
Scheme 1

the methodology developed by Chung *et al.*[11] for the preparation of the *N*-acryloyl derivative of **1d** was not successful in this case.



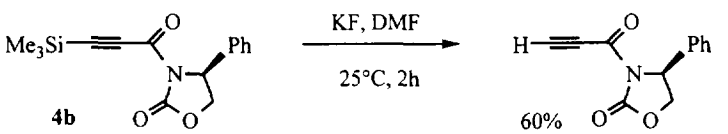
Scheme 2

At the light of these results, we examined a recently published method[12] based on the reaction between a mixed anhydride and the oxazolidinone or sultam in the presence of anhydrous lithium chloride. *Using this procedure, the alkynoyl derivative* **4d** *could be prepared in 82% yield* (Scheme 3).



Scheme 3

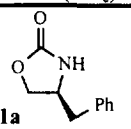
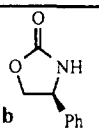
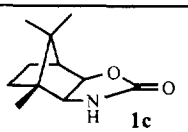
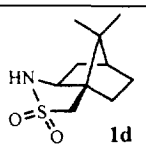
Finally, it is interesting to note that the trimethylsilylpropiolyl derivatives **4b** and **4d** can be regarded as starting products for the preparation of the corresponding unsubstituted propiolyl amides, which were not directly accessible from propiolic acid by means of the above procedures or by the methodology described by Coppola[13] for the synthesis of several 2-propynoyl amides. In fact, in a preliminary experiment, we have found that the fluoride-induced desilylation of **4b** takes place in 60% yield (Scheme 4).



Scheme 4

In summary, we have prepared a series of 2-alkynoyl derivatives of 4-substituted-oxazolidin-2-ones and of Oppolzer's camphorsultam in good to excellent yields using a one-pot method based on the nucleophilic attack on a mixed anhydride. These previously unknown chiral alkynes have already

Table 1. Acylation of the lithium salts of oxazolidin-2-ones and bornane-10,2-sultam by a preformed 2-alkynoic-pivalic mixed anhydride

Entry	Starting oxazolidinone or sultam (HX_c)	R	2-Alkynoate derivative	Yield (%)[a]
1	 **1a**	Ph	**2a**	62
2	"	Me	**3a**	88
3	 **1b**	Ph	**2b**	79
4	"	Me	**3b**	87
5	"	$SiMe_3$	**4b**	69
6	 **1c**	Ph	**2c**	62
7	"	Me	**3c**	79
8	 **1d**	Ph	**2d**	92
9	"	Me	**3d**	56
10[b]	"	$SiMe_3$	**4d**	37[c]
11[b,d]	"	CH_2OMe	**5d**	53

[a]Yields of isolated product after chromatographic purification. [b]After addition of the lithium salt of **1d** to the mixed anhydride at -78°C, the mixture was stirred for 3 h at room temperature. [c]The major isolated product (62% yield) was the *N*-pivaloyl derivative of sultam **1d**. [d]The enantiomer of **1d** was used in this case.

been tested in the intermolecular Pauson–Khand cyclopentenone synthesis with outstanding yields and diastereoselectivities,[14] and can be potentially useful in a variety of asymmetric processes.

Experimental section

Melting points were determined in open ended capillary tubes on a Büchi–Tottoli apparatus or on a Reichert–Thermovar Köfler apparatus and are uncorrected. Infrared spectra were measured with a Perkin–Elmer 681 or Nicolet FT-IR 510 spectrometer using film NaCl or KBr pellet techniques. ^1H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ or CD_3OD, on a Varian Gemini-200 or on a Varian Unity-300 spectrometer with tetramethylsilane or chloroform as an internal standard. Chemical shifts are expressed in δ (ppm) units downfield to TMS. The multiplicity in ^{13}C-NMR spectra was determined by means of DEPT techniques. Mass spectra were recorded at 70 eV ionizing voltage on a Hewlett–Packard HP-5988A apparatus. Ammonia or methane was used for chemical ionization (CI). MS spectra are presented as *m/z* (% rel. int.). Optical rotations were measured at room temperature with a Perkin–Elmer 241 MC automatic polarimeter. Elemental analyses were performed by the "Servei d'Anàlisis Elementals del CSIC de Barcelona". THF used in the reactions was dried by distillation over metallic sodium and benzophenone. All reactions were carried out in oven-dried glassware under an atmosphere of pre-purified nitrogen. LiCl was dried *in vacuo* at 150°C for 5 h before use.

The course of all of the reactions described here could be conveniently monitored by TLC (Merck DC-Alufolien KIESELGEL 60 F_{254}). Silica gel (J. T. Baker, 70–230 mesh) was used for column chromatography. Oxazolidinones **1a–b**, bornane-10,2-sultam **1d**, phenylpropiolic acid and 2-butynoic acid are commercially available (Fluka or Aldrich) and were used as received. Oxazolidinone **1c** can be readily obtained following published procedures.[15] Trimethylsilylpropiolic acid and 4-methoxy-2-butynoic acid were prepared by chromic acid oxidation of the corresponding alcohols.[16]

General procedure for the preparation of 2-alkynoate derivatives of 4-substituted oxazolidin-2-ones and of bornane-10,2-sultam

To a cold (−78°C) solution of the 2-alkynoic acid (0.69 mmol) in 4.5 mL of anhydrous THF, were added 0.09 mL (0.71 mmol) of freshly distilled pivaloyl chloride, followed by 0.1 mL (0.72 mmol) of Et_3N. The mixture was stirred at −78°C for 15 min, at 0°C for 45 min, and then recooled to −78°C. In a separate flask, 0.1 mL (0.72 mmol) of 1.76M *n*-BuLi in hexanes were added to a solution of the chiral oxazolidinone or bornane-10,2-sultam (0.69 mmol) in 2 mL of anhydrous THF at −78°C, stirred for 15 min, and transferred *via* cannula to the flask containing the mixed pivalic-2-alkynoic anhydride at the same temperature. The mixture was allowed to warm up to room temperature and stirred until TLC analysis showed that the reaction was complete. The reaction was quenched with 2M aq. $KHSO_4$ (15 mL) and extracted with AcOEt (3×20 mL). The combined organic phases were washed with brine (20 mL) and dried over $MgSO_4$. After filtration, the solvent was eliminated *in vacuo* and the residue was purified by column chromatography on silica gel, eluting with 10 to 20% hexane/AcOEt mixtures.

(4S)-3-(3-Phenyl-2-propynoyl)-4-benzyloxazolidin-2-one ***2a***

Prepared by the general procedure from **1a** (0.12 g, 0.69 mmol) in 62% yield (0.13 g). White solid. mp 126–128°C; $[\alpha]^{25}_D$=+49.2 (c=1.9, $CHCl_3$); IR (KBr): 3020, 2200, 1795, 1650, 1345, 1320, 1190, 1015, 760, 720, 690 cm^{-1}; ^{1}H-NMR (200 MHz): 2.75–2.92 (dd, J=12.5 Hz, J′=10 Hz, 1H), 3.30–3.45 (dd, J=12.5 Hz, J′=3.5 Hz, 1H), 4.15–4.30 (m, 2H), 4.65–4.80 (m, 1H), 7.23–7.44 (m, 8H), 7.66–7.70 (m, 2H); ^{13}C-NMR (50 MHz): 37.6 (CH_2), 55.1 (CH), 66.0 (CH_2), 81.0 (C), 94.5 (C), 119.7 (C), 127.4 (CH), 128.6 (CH), 129.0 (CH), 129.5 (CH), 131.1 (CH), 133.4 (CH), 134.9 (C), 150.5 (C), 152.0 (C); MS (CI–NH_3): 306 ([M+1]$^+$, 20%), 323 ([M+18]$^+$, 100%); Anal. calcd. for $C_{19}H_{15}NO_3$:C, 74.75%; H, 4.92%; N, 4.59%. Found: C, 74.90%; H, 4.90%; N, 4.67%.

(4S)-3-(3-Phenyl-2-propynoyl)-4-phenyloxazolidin-2-one ***2b***

Prepared by the general procedure from **1b** (0.56 g, 3.43 mmol) in 79% yield (0.78 g). White solid. mp 133–135°C; $[\alpha]^{25}_D$=−59.5 (c=0.97, $CHCl_3$); IR (KBr): 3070, 3000, 2940, 2230, 1800, 1665, 1500, 1395, 1340, 1330, 1240, 1220, 1200, 1170, 1155, 760, 690, 670 cm^{-1}; ^{1}H-NMR (200 MHz): 4.22–4.29 (dd, J=8.8 Hz, J′=3.5 Hz, 1H), 4.64–4.73 (dd, J,J′=8.8 Hz, 1H), 5.43–5.49 (dd, J=8.7 Hz, J′=3.6 Hz, 1H), 7.31–7.65 (m, 10H); ^{13}C-NMR (50 MHz): 57.4 (CH), 69.9 (CH_2), 81.0 (C), 94.3 (C), 119.5 (C), 125.9 (CH), 128.5 (CH), 128.7 (CH), 129.1 (CH), 130.9 (CH), 133.2 (CH), 138.2 (C), 150.2 (C), 152.1 (C); MS (CI–NH_3): 292 ([M+1]$^+$, 10%), 309 ([M+18]$^+$, 100%); Anal. calcd. for $C_{18}H_{13}NO_3$: C, 74.22%; H, 4.50%; N, 4.81%. Found: C, 74.21%; H, 4.62%; N, 4.76%.

(1S,2R,6S,7R)-7,10,10-Trimethyl-5-(3-phenyl-2-propynoyl)-3-oxa-5-aza-tricyclo[5.2.1.0^{2,6}]decan-4-one ***2c***

Prepared by the general procedure form **1c** (0.15 g, 0.77 mmol) in 62% yield (0.15 g). White solid. mp 115–117°C; $[\alpha]^{25}_D$=−1.83 (c=1.4, $CHCl_3$); IR (KBr): 3080, 3040, 2970, 2940, 2900, 2240, 1800, 1665, 1495, 1450, 1380, 1330, 1240, 1195, 1060, 1040, 765, 695, 620 cm^{-1}; ^{1}H-NMR (200 MHz): 0.91 (s, 3H), 1.01 (s, 3H), 1.05 (s, 3H), 1.10–1.30 (m, 2H), 1.50–1.70 (td, J=11.5 Hz, J′=4.5 Hz, 1H), 1.75–1.90 (m, 1H), 2.20 (d, J=5 Hz, 1H), 4.40 (d, J=7.5 Hz, 1H), 4.55 (d, J=7.5 Hz, 1H), 7.35–7.42 (m, 3H), 7.64–7.66 (m, 2H); ^{13}C-NMR (50 MHz): 12.0 (CH_3), 19.8 (CH_3), 22.7 (CH_3), 22.8 (CH_2), 33.2 (CH_2), 46.5 (CH), 47.6 (C), 50.4 (C), 66.0 (CH), 81.4 (C), 81.5 (CH), 94.8 (C), 119.9 (C),

128.5 (CH), 130.9 (CH), 133.3 (CH), 151.9 (C), 153.9 (C); MS (CI–CH_4): 324 ($[M+1]^+$, 100%), 352 ($[M+29]^+$, 28%), 364 ($[M+41]^+$, 12%); Anal. calcd. for $C_{20}H_{21}NO_3$: C, 74.28%; H, 6.55%; N, 4.33%. Found: C, 74.03%; H, 6.56%; N, 4.24%.

(1R,5S,7S)-1-(10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo[5.2.1.0^{1,5}]dec-4-yl)-3-phenyl-2-propyn-1-one ***2d***

Prepared by the general procedure from **1d** (0.22 g, 1.00 mmol) in 92% yield (0.32 g). White solid. mp 148–150°C; $[\alpha]^{25}_D$=+47.6 (c=0.8, $CHCl_3$); IR (KBr): 3020, 3000, 29060, 2880, 2230, 1660, 1490, 1450, 1375, 1330, 1300, 1225, 1180, 1140, 770, 730, 695 cm^{-1}; ^{1}H-NMR (200 MHz): 0.99 (s, 3H), 1.21 (s, 3H), 1.30–1.50 (m, 2H), 1.91–2.40 (m, 5H), 3.40–3.60 (m, 2H), 3.90–4.01 (t, J=5.5 Hz, 1H), 7.33–7.45 (m, 3H), 7.63–7.67 (m, 2H); ^{13}C-NMR (50 MHz): 19.8 (CH_3), 20.8 (CH_3), 26.3 (CH_2), 32.7 (CH_2), 38.3 (CH_2), 44.7 (CH), 47.7 (C), 48.4 (C), 52.9 (CH_2), 64.9 (CH), 80.9 (C), 92.2 (C), 119.4 (C), 128.5 (CH), 130.9 (CH), 133.1 (CH), 150.0 (C); MS (CI–NH_3): 344 ($[M+1]^+$, 56%), 361 ($[M+18]^+$, 100%); Anal. calcd. for $C_{19}H_{21}NO_3S$: C, 66.45%; H, 6.16%; N, 4.08%; S, 9.33%. Found: C, 66.15%; H, 6.30%; N, 3.78%; S=8.89%.

(4S)-3-(2-Butynoyl)-4-benzyloxazolidin-2-one ***3a***

Prepared by the general procedure from **1a** (0.63 g, 3.57 mmol) in 88% yield (0.76 g). White solid. mp 78–80°C; $[\alpha]^{25}_D$=+60.4 (c=0.84, $CHCl_3$); IR (KBr): 3060, 3020, 2960, 2910, 2220, 2210, 1795, 1650, 1350, 1320, 1210, 1090, 755, 730, 700 cm^{-1}; ^{1}H-NMR (200 MHz): 2.11 (s, 3H), 2.74–2.86 (dd, J=13.5 Hz, J′=9.5 Hz, 1H), 3.25–3.33 (dd, J=13.5 Hz, J′=3.3 Hz, 1H), 4.15–4.19 (m, 2H), 4.60–4.74 (m, 1H), 7.19–7.34 (m, 5H); ^{13}C-NMR (50 MHz): 4.4 (CH_3), 37.4 (CH_2), 54.9 (CH), 65.8 (CH_2), 72.7 (C), 94.7 (C), 127.3 (CH), 129.0 (CH), 129.2 (CH), 134.8 (C), 151.0 (C), 153.0 (C); MS (CI–NH_3): 244 ($[M+1]^+$, 5%), 261 ($[M+18]^+$, 100%); Anal. calcd. for $C_{14}H_{13}NO_3$: C, 69.14%; H, 5.35%; N, 5.76%. Found: C, 69.14%; H, 5.38%; N, 5.75%.

(4S)-3-(2-Butynoyl)-4-phenyloxazolidin-2-one ***3b***

Prepared by the general procedure from **1b** (0.91 g, 2.50 mmol) in 87% yield (0.50 g). Colorless oil. $[\alpha]^{25}_D$=+7.97 (c=4.5, $CHCl_3$); IR (film NaCl): 3060, 3040, 2980, 2930, 2240, 2220, 1795, 1670,1390, 1330, 1200, 1190, 910, 760, 720, 700 cm^{-1}; ^{1}H-NMR (200 MHz): 2.17 (s, 3H), 4.20–4.30 (dd, J=9 Hz, J′=4.5 Hz, 1H), 4.60–4.71 (m, 1H), 5.35–5.45 (dd, J=9 Hz, J′=4.5 Hz, 1H), 7.20–7.40 (m, 5H); ^{13}C-NMR (50 MHz): 4.5 (CH_3), 57.5 (CH), 69.5 (CH_2), 72.8 (C), 94.8 (C), 126.0 (CH), 128.7 (CH), 129.2 (CH), 138.5 (C), 150.0 (C), 152.0 (C); MS (CI–NH_3): 230 ($[M+1]^+$, 6%), 247 ($[M+18]^+$, 100%).

(1S,2R,6S,7R)-7,10,10-Trimethyl-5-(2-butynoyl)-3-oxa-5-azatricyclo[5.2.1.0^{2,6}]decan-4-one ***3c***

Prepared by the general procedure from **1c** (0.20 g, 1.03 mmol) in 79% yield (0.21g). White solid. mp 130–132°C; $[\alpha]^{25}_D$=+27.2 (c=3.2, $CHCl_3$), IR (KBr): 2960, 2920, 2890, 2230, 1785, 1660, 1330, 1105, 1100, 1055, 1045, 990, 950, 800, 765 cm^{-1}; ^{1}H-NMR (200 MHz): 0.96 (s, 3H), 0.98 (s, 3H), 1.01 (s, 3H), 0.90–1.15 (m, 1H), 1.18–1.34 (m, 1H), 1.47–1.65 (td, J=12.3 Hz, J′=4.6 Hz, 1H), 1.74–1.92 (m, 1H), 2.11 (s, 3H), 2.17–2.19 (d, J=4.8 Hz, 1H), 4.34–4.38 (d, J=7.9 Hz, 1H), 4.50–4.54 (d, J=7.8 Hz, 1H); ^{13}C-NMR (50 MHz): 4.6 (CH_3), 11.9 (CH_3), 19.7 (CH_3), 22.7 (CH_3), 22.7 (CH_2), 33.2 (CH_2), 46.5 (C), 47.5 (CH), 50.2 (C), 65.8 (CH), 72.9 (C), 81.4 (CH), 95.0 (C), 151.5 (C), 153.5 (C); MS (CI–CH_4): 262 ($[M+1]^+$, 100%), 290 ($[M+29]^+$, 25%), 302 ($[M+41]^+$, 11%); Anal. calcd. for $C_{15}H_{19}NO_3$: C, 68.95%; H, 7.33%; N, 5.36%. Found: C, 68.85%; H, 7.37%; N, 5.26%.

(1R,5S,7S)-1-(10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo[5.2.1.0^{1,5}]dec-4-yl)-2-butyn-1-one ***3d***

Prepared by the general procedure from **1d** (0.22 g, 1.00 mmol) in 56% yield (0.16 g). White solid. mp 170–172°C; $[\alpha]^{25}_D$=+108.4 (c=2, $CHCl_3$); IR (KBr): 2990, 2960, 2930, 2240, 1650, 1410, 1340, 1320, 1310, 1285, 1250, 1170, 1140, 1050, 1000, 730 cm^{-1}; ^{1}H-NMR (200 MHz): 0.98 (s, 3H), 1.18

(s, 3H), 1.23–1.60 (m, 4H), 1.88–2.19 (m, 3H), 2.08 (s, 3H), 3.37–3.44 (d, J=14 Hz, 1H), 3.46–3.52 (d, J=13.8 Hz, 1H), 3.82–3.88 (dd, J=7.9 Hz, J'=4.8 Hz, 1H); ^{13}C-NMR (50 MHz): 4.2 (CH_3), 19.8 (CH_3), 20.8 (CH_3), 26.3 (CH_2), 32.7 (CH_2), 38.2 (CH_2), 44.7 (CH), 47.7 (C), 48.3 (C), 52.9 (CH_2), 64.8 (CH), 72.7 (C), 92.3 (C), 150.0 (C); MS (CI–NH_3): 299 ([M+18]$^+$, 100%); Anal. calcd. for $C_{14}H_{19}NO_3S$: C, 59.76%; H, 6.81%; N, 4.98%; S, 11.40%. Found: C, 59.06%; H, 6.83%; N, 4.73%; S=10.92%.

(4S)-3-(3-Trimethylsilyl-2-propynoyl)-4-phenyloxazolidin-2-one ***4b***

Prepared by the general procedure from **1b** (0.30 g, 1.90 mmol) in 69% yield (0.36 g). White solid. mp 104–106°C; $[\alpha]^{25}_D$=+1.6 (c=1.8, $CHCl_3$); IR (KBr): 3060, 3030, 2960, 2180, 1800, 1670, 1385, 1330, 1295, 1210, 1160, 1150, 870, 850, 760, 710 cm^{-1}; ^{1}H-NMR (200 MHz): 0.23 (s, 9H), 4.25–4.29 (dd, J=9 Hz, J'=3.9 Hz, 1H), 4.65–4.70 (dd, J=J'=8.7 Hz, 1H), 5.39–5.44 (dd, J=8.4 Hz, J'=3.3 Hz, 1H), 7.33–7.42 (m, 5H); ^{13}C-NMR (50 MHz): 0.0 (CH_3), 57.5 (CH), 69.9 (CH_2), 94.3 (C), 103.4 (C), 126.0 (CH), 128.9 (CH), 129.2 (CH), 138.1 (C), 149.6 (C), 152.0 (C); MS (CI–CH_4): 288 ([M+1]$^+$, 100%), 316 ([M+29]$^+$, 44%), 328 ([M+41]$^+$, 20%); Anal. calcd. for $C_{15}H_{17}NO_3Si$: C, 62.69%; H, 5.96%; N, 4.87%. Found: C, 62.76%; H, 5.97%; N, 4.89%.

(1R,5S,7S)-1-(10,10-Dimethyl-3,3-dioxo-3-thia-4-aza-tricyclo[5.2.1.0^{1,5}]dec-4-yl)-3-trimethylsilyl-2-propyn-1-one ***4d***

To a cold (−20°C) solution of 3-trimethylsilyl-2-propynoic acid (0.10 g, 0.70 mmol) in anhydrous THF (1.7 mL) were added 0.19 mL (1.36 mmol) of Et_3N followed by 0.08 mL (0.65 mmol) of freshly distilled pivaloyl chloride. The mixture was stirred at −20°C for 2 hours. Subsequently, 0.025 g (0.596 mmol) of anhydrous LiCl and a solution of 0.12 g (0.54 mmol) of bornane-10,2-sultam (**1d**) in anhydrous THF (1 mL) were added at −20°C. The mixture was warmed slowly to room temperature until TLC analysis showed the reaction was complete. The reaction was quenched with 0.2M HCl (15 mL) and extracted with AcOEt (3×20 mL). The combined organic phases were washed with brine (20 mL), 1M $NaHCO_3$ (20 mL) and brine (20 mL). After drying over $MgSO_4$ and filtration, the solvent was eliminated *in vacuo*. The residue was purified by column chromatography on silica gel eluting with 20% hexane/AcOEt mixture, affording 0.15 g (82% yield) of **4d** as a colorless oil. $[\alpha]^{25}_D$=+88.3 (c=3.1, $CHCl_3$); IR (film NaCl): 2960, 2180, 1765, 1660, 1345, 1290, 1250, 1170, 1140, 990, 845, 765, 625, 610 cm^{-1}; ^{1}H-NMR (200 MHz): 0.26 (s, 9H), 0.98 (s, 3H), 1.18 (s, 3H), 1.10–1.25 (m, 2H), 1.90–2.25 (m, 5H), 3.37–3.44 (d, J=14 Hz, 1H), 3.46–3.53 (d, J=14 Hz, 1H), 3.84–3.91 (dd, J=8 Hz, J'=4.8 Hz, 1H); ^{13}C-NMR (50 MHz): −1.12 (CH_3), 19.8 (CH_3), 20.9 (CH_3), 26.4 (CH_2), 32.8 (CH_2), 38.4 (CH_2), 44.8 (CH), 47.7 (C), 48.6 (C), 52.9 (CH_2), 64.8 (CH), 100.9 (C), 104.9 (C), 150.9 (C); MS (CI–NH_3): 357 ([M+18]$^+$, 30%); Anal. calcd. for $C_{16}H_{25}NO_3SSi$: C, 56.60%; H, 7.42%; N, 4.13%; S, 9.44%. Found: C, 56.56%; H, 7.58%; N, 4.04%; S, 9.21%.

(1S,5R,7R)-1-(10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo[5.2.1.0^{1,5}]dec-4-yl)-4-methoxy-2-butyn-1-one ***5d***

Prepared by the general procedure from **1d** (0.22 g, 1.00 mmol) in 53% yield (0.17 g). White solid. mp 88–90°C; $[\alpha]^{25}_D$=−89.3 (c=1.8, $CHCl_3$); IR (KBr): 2980, 2890, 2830, 2240, 1655, 1340, 1310, 1290, 1250, 1170, 1140, 1100, 1055, 1000, 905, 765, 730 cm^{-1}; ^{1}H-NMR (200 MHz): 1.02 (s, 3H), 1.21 (s, 3H), 1.30–1.50 (m, 2H), 1.85–2.30 (m, 5H), 3.55–3.30 (m, 5H), 3.80–3.90 (dd, J=8.6 Hz, J'=5 Hz, 1H), 4.25–4.40 (m, 2H); ^{13}C-NMR (75 MHz): 19.8 (CH_3), 20.8 (CH_3), 26.4 (CH_2), 32.7 (CH_2), 37.0 (CH_2), 44.7 (CH), 47.5 (C), 53.0 (CH_2), 58.5 (C), 59.5 (CH_2), 59.5 (CH_3), 64.9 (CH), 70.7 (C), 89.7 (C), 149.0 (C); MS (CI–NH_3): 311 ([M+18]$^+$, 100%); Anal. calcd. for $C_{15}H_{21}NO_4S$: C, 57.86%; H, 6.80%; N, 4.50%; S, 10.30%. Found: C, 57.68%; H, 7.01%; N, 4.58%; S=10.17%.

Acknowledgements

We thank the DGICYT (PB95-0265) for financial support, and Dr Claudio Palomo (Universidad del País Vasco) for a generous gift of oxazolidinone **1c**. A fellowship award from Ministerio de Educación y Ciencia to Sílvia Fonquerna is also gratefully acknowledged.

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(Received in UK 2 April 1997)