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SYNTHESIS AND STEREOISOMERISM OF DERIVATIVES OF *tert*-BUTYL 7-ALKYLIDENECEPH-3-EM-4-CARBOXYLATE*

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By condensation of tert-butyl 3-methyl-7-oxoceph-3-em-4-carboxylate and its 3-acetoxymethyl analog with acetylmethylenetriphenylphosphorane and 3-trimethylsilylpropyn-2-ylindenetriphenylphosphorane tert-butyl 7Z-acetylmethylene-3-methylceph-3-em-4-carboxylate and also 7Z- and 7E-isomers of tert-butyl 3-acetoxymethyl-7-(3-trimethylsilylpropyn-2-ylidene)ceph-3-em-4-carboxylates were synthesized. Oxidation of these compounds with 1 equivalent of meta-chloroperbenzoic acid gave their 1R- and 1S-sulfoxides, and oxidation with 2 equivalents gave the corresponding sulfones. According to data from ^{1}H NMR spectroscopy, the carbonyl of the β-lactam descreens proton H-9 of the alkylidene group in the 7Z-isomers more strongly than in the 7E-isomers, shifting their signals to weaker field. Analogous shifts of the H-6 signal to weaker field was observed in the 1R-sulfoxides in comparison with that for the 1S-sulfoxide. These results were confirmed by X-ray crystallography of tert-butyl 7Z-acetylmethylene-3-methyl-1S-oxoceph-3-em-4-carboxylate and tert-butyl 7Z-acetylmethylene-3-methyl-1,1-dioxoceph-3-em-4-carboxy-late.

Keywords: *tert*-butyl esters of 7Z-acetylmethylidene-3-methylceph-3-em-4-carboxylic acid and 3-acetoxymethyl-7*Z*-(3-trimethylsylylpropyn-2-ylidene)ceph-3-em-4-carboxylic acid, 1(*S*)-, 1(*R*)-sulfoxides and sulfones of *tert*-butyl esters of 7Z-acetylmethylidene-3-methylceph-3-em-4-carboxylic acid and 3-acetoxymethyl-7*Z*-(3-trimethylsylylpropyn-2-ylidene)ceph-3-em-4-carboxylic acid, X-ray crystallo-graphy, ^{1}H NMR spectroscopy.

We have shown previously that *tert*-butyl esters of 3-acetoxymethylene-7-alkylidene-,1,1-dioxoceph-3-em-4-carboxylic acids, thanks to the presence of the alkylidene groups, are characterized by high cytotoxicity relative to cancer cells *in vitro*, depending not only on the character of the substituent but also on the stereoisomerism of the alkylidene group in position 7 of the ceph-3-em heterocycle [1]. In a continuation of these investigations we have attempted to synthesize derivatives of *tert*-butyl esters of 7-alkylideneceph-3-em-4-carboxylic acid and to investigate their ^{1}H NMR spectra with the objective of establishing the spatial orientation of the substituent in the alkylidene and also of the sulfoxide group, necessary for he study of the interconnection between the structure and biological activity of these substances.

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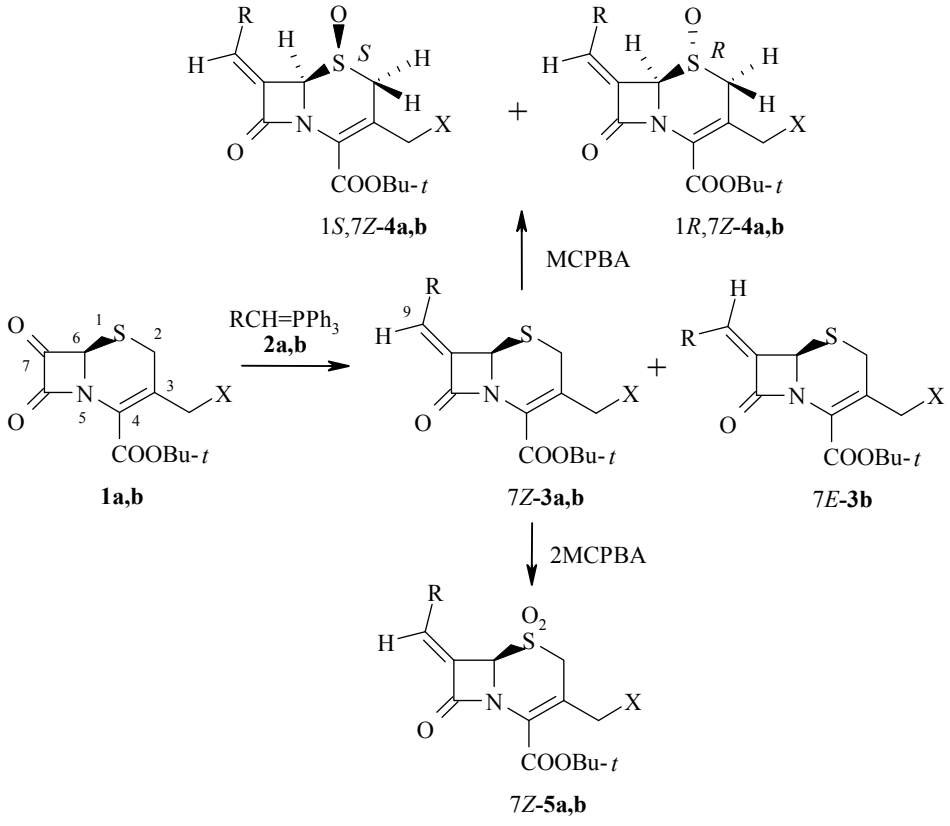
7-Alkylidene-substituted *tert*-butyl esters of ceph-3-em-4-carboxylic acid **3a,b** were synthesized using the Wittig reaction according to the method cited in papers [1,2], by condensation of *tert*-butyl 3-methy-7-oxoceph-3-em-4-carboxylate (**1a**) and its 3-acetoxymethyl analog **1b** with acetylmethylenetriphenylphosphorane (**2a**) and 3-trimethylsilylpropyn-2-ylidenephosphorane (**2b**). As a result *tert*-butyl 7*Z*-acetylmethylidene-3-methylceph-3-em-4-carboxylate (7*Z*-**3a**) was obtained, and also a mixture of 7*Z*- and 7*E*-isomers of *tert*-butyl 3-acetoxymethyl-7-(3-trimethylsilylpropyn-2-ylidene)ceph-3-em-4-carboxylate (7*Z*-**3b**, 7*E*-**3b**) in a ratio of 9:1.

Conversion of the compounds synthesized into the corresponding sulfoxides **4a,b** and sulfones **5a,b** was realized with the help of one or more than two equivalents of *meta*-chloroperbenzoic acid (MCPBA). 1*R*- and 1*S*-Sulfoxides were isolated from the reaction mixture in the pure form by column chromatography.



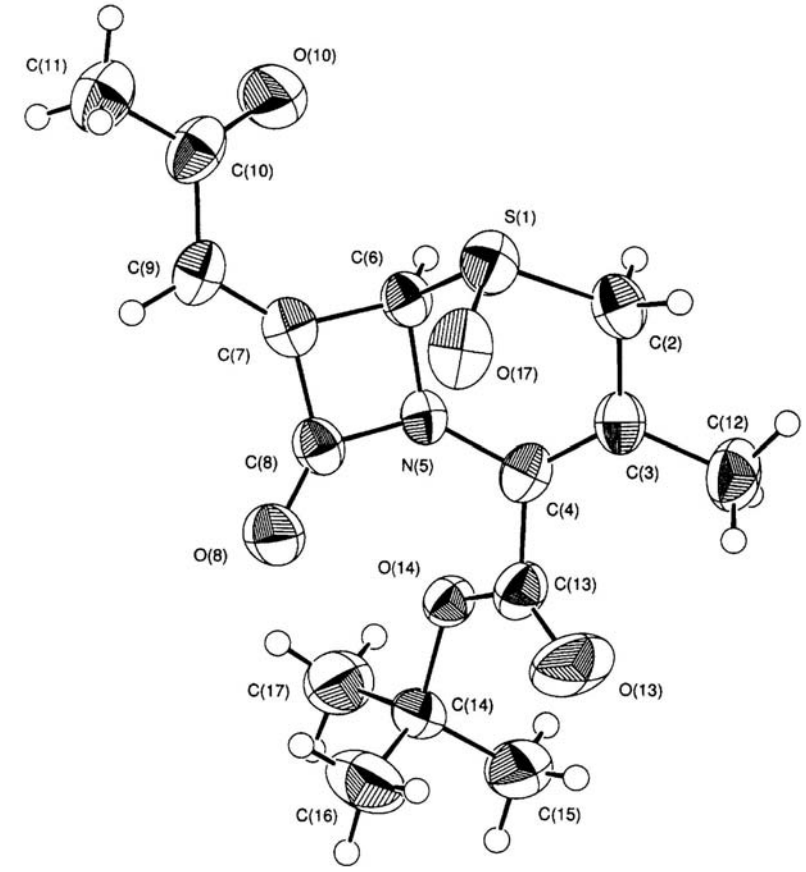
1–5 a X = H, **b** X = OAc; **2–5 a** R = Ac, **b** R = $Me_3SiC{\equiv}C$– ;
MCPBA – *meta*-chloroperbenzoic acid

In accordance with data from [2], the 7*Z*- and 7*E*-isomers of the cephems **3b** were identified by their ^{1}H NMR spectra. The close position of the β-lactam carbonyl descreens the proton of the alkylidene group in the 7*Z*-isomer more strongly than the analogous proton in the 7*E*-isomer. This leads to a weak field shift of the resonance of the signal of H-9 in ceph-3-em 7*Z*-**3b** relative to the same signal in the isomer 7*E*-**3b**.

An analogous descreening effect appeared by the oxygen atom of the 1*R*-sulfoxide group in compounds 7*Z*-**4a,b** relative to protons H-6 and H-2, shifting their signals to weaker field in comparison to the isomeric 1*S*-sulfoxide. This effect is intensified on oxidation of these compounds to the sulfones 7*Z*-**5a,b**. The intensity of the shifts of these signals to weaker fields in the compounds discussed, in dependence on the oxidation state of the sulfur heteroatom, decreases in the following order (Table 1):

7*Z*-**5a,b** (sulfone) > 7*Z*-**4a,b** (1*R*-sulfoxide) > 7*Z*-**4a,b** (1*S*-sulfoxide) > 7*Z*-**3a,b** (sulfide)

a



b

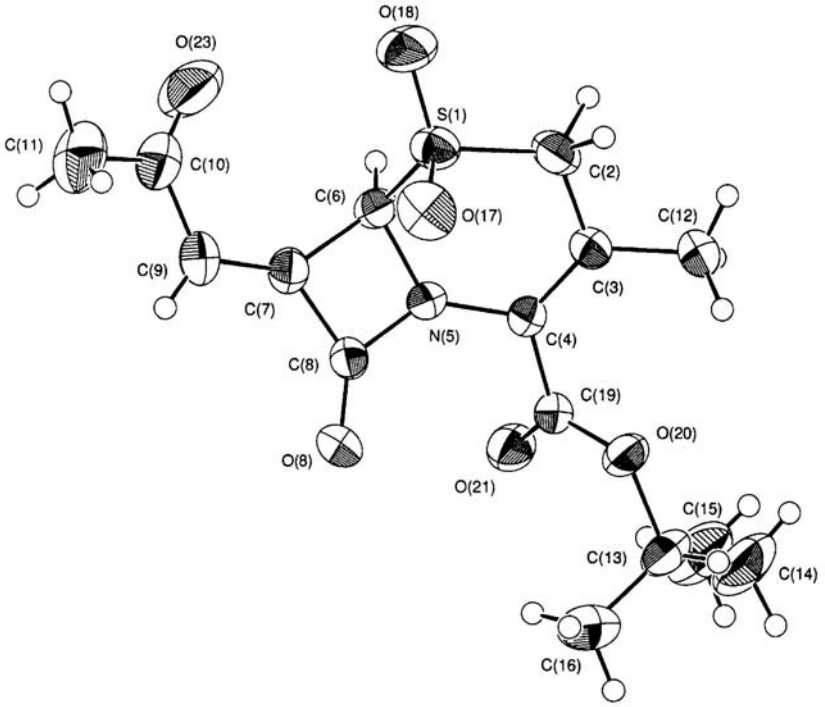


Fig. 1. Spatial models of the molecules of compounds 1*S*,7*Z*-**4a** (*a*) and 7*Z*-**5a** (*b*) with numbering of atoms and their thermal vibration ellipsoids.

Table 1. Characteristic Signals of Protons in the ^{1}H NMR Spectra of the Ceph-3-ems 7*Z*-**3a,b** to 7*Z*-**5a,b**

Compound	Isomer	Chemical shifts, δ, ppm (*J*, Hz)		
		2-CH_2 (two d, AB system)	H-6 (d)	H-9 (d)
3a	7*Z*	3.15 and 3.57 (^2J = 18)	5.46 (^4J = 1)	6.66 (^4J = 1)
4a	1*S*,7*Z*	3.31 and 3.60 (^2J = 18)	5.15 (^4J = 1)	6.81 (^4J = 1)
4a	1*R*,7*Z*	3.42 and 3.68 (^2J = 18)	5.23 (^4J = 1)	6.78 (^4J = 1)
5a	7*Z*	3.68 and 3.94 (^2J = 18)	5.56 (^4J = 1)	6.88 (^4J = 1)
3b	7*Z*	3.31 and 3.60 (^2J = 16)	5.27 (^4J = 1.5)	6.27 (^4J = 1.5)
3b	7*E*	3.28 and 3.55 (^2J = 18)	5.11 (^4J = 0.8)	5.89 (br. s)
4b	7*Z*,1*S*	3.22 and 3.84 (^2J = 20)	4.89 (^4J = 2)	6.44 (^4J = 2)
4b	7*Z*,1*R*	3.51 and 3.95 (^2J = 18)	4.95 (^4J = 2)	6.44 (^4J = 2)
5b	7*Z*	3.67 and 4.02 (^2J = 18)	5.27 (br. s)	6.47 (^4J = 2)

The correlations discussed above agree completely with the results of X-ray crystallographic studies of the *tert*-butyl esters of 7*Z*-acetylmethylene-3-methyl-1(*S*)-oxoceph-3-em-4-carboxylic acid (1*S*,7*Z*-**4a**) and 7*Z*-acetyl-methylene-3-methyl-1,1-dioxoceph-3-em-4-carboxylic acid (1*S*,7*Z*-**4b**), unequivocally indicating the *Z*-isomeric state of the acetylmethylene group in 7*Z*-**4a** and 7*Z*-**5a**, and also the 1*S*-configuration of the sulfoxide oxygen in 1*S*,7*Z*-**4a** (Fig. 1). In correspondence with literature data [3], the six-membered ring in both molecules has the *envelope* configuration: the sulfur atom diverges considerably from the plane of the atoms C(2), C(3),C(4), B(5), C(6).

The basic geometric characteristics of the cephem systems in the molecules of compounds 7*Z*-**4a** and 7*Z*-**5a** are cited in Table 2. The dihedral angles between this plane and the plane of the atoms C(2), S(1), C(6) are 124.9(8) and 130.7(7)° for the molecules 1*S*,7*Z*-**4a** and 7*Z*-**5a** respectively.

In the crystal structure of compound 1*S*,7*Z*-**4a** one of the parameters of the crystal lattice (parameter *c*) considerably exceeds the other two parameters, consequently this compound crystallizes in the form of thin planes perpendicular to the crystallographic *z* direction. The asymmetric atom C(6), which has the *R* configuration, is surrounded by electron-acceptor atoms; in connection with this atom H(6) participates in the

Table 2. Basic Bond Lengths (*l*) and Valence Angles (ω) in the Molecules of the 1(*S*)-Sulfoxide and the Sulfone of *tert*-Butyl 7*Z*-acetylmethylene-3-methylceph-3-em-4-carboxylate.

Bond	*l*, Å		Angle	ω deg	
	7*Z*-**4a**	7*Z*-**5a**		7*Z*-**4a**	7*Z*-**5a**
S(1)−O(17)	1.497(5)	1.438(4)	C(2)−S(1)−C(6)	92.7(2)	99.2(1)
S(1)−O(18)		1.434(4)	O(17)−S(1)−O(18)		119.8(1)
S(1)−C(2)	1.818(6)	1.773(4)	C(4)−N(5)−C(6)	126.5(4)	127.9(3)
S(1)−C(6)	1.843(5)	1.798(4)	C(4)−N(5)−C(8)	133.6(5)	133.5(3)
C(2)−C(3)	1.512(8)	1.514(7)	C(6)−N(5)−C(8)	93.5(4)	94.8(3)
C(3)−C(4)	1.334(7)	1.352(7)	S(1)−C(6)−C(7)	113.9(4)	117.3(2)
C(4)−N(5)	1.405(7)	1.405(6)	N(5)−C(6)−C(7)	87.7(4)	86.0(3)
N(5)−C(6)	1.469(7)	1.478(7)	C(8)−C(7)−C(9)	134.8(5)	133.5(4)
N(5)−C(8)	1.392(7)	1.384(6)	C(6)−C(7)−C(9)	136.8(5)	137.7(4)
C(6)−C(7)	1.491(7)	1.529(7)	C(6)−C(7)−C(8)	88.3(4)	88.4(3)
C(7)−C(8)	1.501(8)	1.494(7)	N(5)−C(8)−O(8)	132.1(6)	131.7(4)
C(7)−C(9)	1.327(7)	1.321(7)	C(7)−C(8)−O(8)	137.8(5)	137.4(4)
C(8)−O(8)	1.203(7)	1.210(6)	N(5)−C(8)−C(7)	90.2(4)	90.9(3)

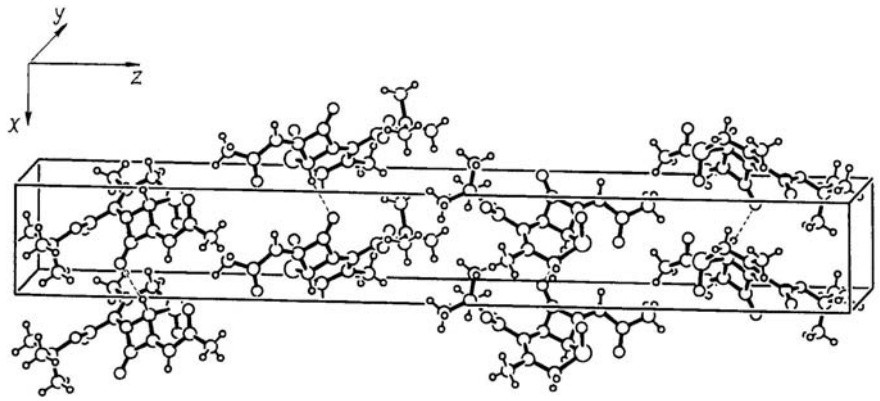


Fig. 2. Fragment of the packing of the molecule of *tert*-butyl 7*Z*-acetylmethylene-3-methyl-1(*R*)-oxoceph-3-em-4-carboxylate (1*S*,7*Z*-**4a**) in the crystal showing the intermolecular CH···O bonds.

formation of intermolecular hydrogen bonds C(6)–H(6)···O(8) of length 3.092(6) Å (C–H 0.97 Å, H···O 2.18 Å, C-H···O 157°). In consequence of these bonds, the molecules in the crystal form a ribbon along the *x* direction. In Fig. 2 the packing of the molecule 1*S*,7*Z*-**4a** in the unit cell of the lattice, indicating the CH···O bond, is shown. It should be noted that no such bond occurs in the structure of compound 7*Z*-**5a.**

Investigation allowed to us synthesize new derivatives of *tert*-butyl 7-alkylideneceph-3-em-4-carboxylates, and also deciphere compounds differing by the spatial disposition of substituents in the alkylidene and sulfoxide groups using ^{1}H NMR spectroscopy and X-ray crystallography.

Table 3. Crystallographic Data and Parameters for the Refining of the Crystal Structures of the 1(*S*)-sulfoxide and Sulfone of *tert*-Butyl 7*Z*-Acetylmethylene-3-methylceph-3-em-4-carboxylate.

Characteristics	1*S*,7*Z*-**4a**	7*Z*-**5a**
Empirical formula	$C_{15}H_{19}NO_5S$	$C_{15}H_{19}NO_6S$
M_r	325.38	341.38
Color of crystals	Yellowish	Yellowish
Form of crystal	Plate	Prizm
Size, mm	0.03 × 0.21 × 0.37	0.19 × 0.25 × 0.28
Crystal system	Rhombic	Rhombic
Parameters of the unit cell		
a, Å	5.6544(1)	7.7811(2)
b, Å	6.8559(1)	13.6880(5)
c, Å	42.9741(9)	15.8792(5)
V, Å^3	1665.93(5)	1691.32(6)
Space group	$P\,2_12_12_1$	$P\,2_12_12_1$
Z	4	4
F(000)	688	720
Density, g/cm^3	1.297	1.341
μ, mm^{-1}	0.22	0.29
$2\theta_{max}$	55.0	60.0
Number of reflexions		
observed	3494	5518
independent	2361	4806
used	1295 ($I > 3\sigma(I)$)	3559 ($I > 2\sigma(I)$)
Number of parameters refined	199	208
R-factor	0.067	0.063
*wR*2	0.194	0.184

EXPERIMENTAL

^{1}H NMR spectra of $CDCl_3$ solutions with TMS as internal standard were recorded with a Bruker WH90/DS instrument (90 MHz). Elemental analyses were determined with a Carlo Erba 1108 analyzer. HPLC data were obtained with a Du-Pont Model 8800 instrument equipped with a UV detector (λ = 254 nm) and column (4.6×250 mm) filled with μ Porsil in a 20:80 ethyl acetate–hexane system, Altima C18 with 50:50 acetonitrile-0.1M phosphate buffer (pH 2.5), Zorbax RxC_{18} with 60:40 acetonitrile–water. Monitoring of the course of reactions was carried out by TLC on Merck Kieselgel plates with UV light as developer. Merck Kieselgel (silica gel 0.063-0.230 mm) was used for column chromatography. Reagents and materials from Acros, Aldrich, and Sigma were used in experiments.

***tert*-Butyl 7*Z*-acetylmethylene-3-methylceph-3-em-4-carboxylate (7*Z*-3a).** Acetylmethylene-triphenylphosphorane (248 mg, 0.78 mmol) dissolved was added with stirring at 0° to a solution of *tert*-butyl 3-methyl-7-oxoceph-3-em-4-carboxylate (200 mg, 0.74 mmol), prepared according to [4], in dichloromethane (20 ml). The mixture was stirred for 30 min at 18°C. The solvent was evaporated at low pressure. The residue was fractionated on a silica gel column with 1:3 ethyl acetate–petroleum ether as eluent. The fractions with R_f were collected and evaporated . Yield 158 mg (69%) of an amorphous substance containing 95% of the basic substance according to HPLC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.55 (9H, s, C_4H_9); 2.11 (3H, s, 3-CH_3); 2.40 (3H, s, CH_3COC=); 3.15 and 3.57 (2H, two d, AB system, ^2J = 18, SCH_2); 5.46 (1H, d, ^4J = 1, H-6); 6.66 (1H, d, ^4J = 1, COCH=).

***tert*-Butyl 7*Z*-Acetylmethylene-3-methyl-1*S*-oxoceph-3-em-4-carboxylate (1*S*,7*Z*-4a) and *tert*-butyl 7*Z*-acetylmethylene-3-methyl-1*R*-oxoceph-3-em-4-carboxylate (1*R*,7*Z*-4a).** 75% 3-Chloroperbenzoic acid (117 mg, 0.51 mmol) was added to a solution of *tert*-butyl 7*Z*-acetylmethylene-3-methylceph-3-em-4-carboxylate (158 mg, 0.51 mmol) in dichloromethane (20 ml) at 0°C. The mixture was stirred for 4 h at room temperature, washed with 5% Na_2SO_3 solution (50 ml), 5% Na_2CO_3 solution (2×50 ml), and dried over anhydrous Na_2SO_4. The solvent was evaporated at low pressure and the residue was fractionated on a silica gel column with 1:3 ethyl acetate–petroleum ether as eluent.

The fraction with R_f 0.14 was collected, and evaporated to give compound 1*S*,7*Z*-**4a** (101 mg, 61%); mp 153-155°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.53 (9H, s, C_4H_9); 2.09 (3H, s, CH_3); 2.38 (3H, s, CH_3COC=); 3.31 and 3.60 (2H, two d, AB system, ^3J =18, $SOCH_2$); 5.15 (1H, d, ^4J = 1, H-6); 6.81 (1H, d, ^4J = 1, COCH=). Found, %: C 55.45;, H 5.95; N 4.28. $C_{15}H_{19}NO_5S$. Calculated, %: C 55.37; H 5.89; N 4.30.

Fractions with R_f 0.08 were collected and evaporated to give compound 1*R*,7*Z*-**4a** (50 mg, 30%); mp 177°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.53 (9H, s, C_4H_9); 2.25 (3H, s, CH_3); 2.46 (3H, s, CH_3COC=); 3.42 and 3.68 (2H, two d, AB system, ^2J =18, $SOCH_2$); 5.23 (1H, d, ^4J = 1, H-6); 6.78 (1H, d, ^4J =1, COCH=). Found, %: C 55.41; H 5.97; N 4.35. $C_{15}H_{19}NO_5S$. Calculated, %: C 55.37; H 5.89; N 4.30.

***tert*-Butyl 7*Z*-Acetylmethylene-3-methyl-1,1-dioxoceph-3-em-4-carboxylate (7*Z*-5a).** 75% 3-Chloro-perbenzoic acid (669 mg, 2.91 mmol) was added to a solution of *tert*-butyl 7*Z*-acetylmethylene-3-methylceph-3-em-4-carboxylate (300 mg, 0.97 mmol) in dichloromethane (40 ml) at 0°C with stirring. The mixture was stirred at room temperature for 4 h, diluted with dichloromethane (40 ml), washed with 5% Na_2SO_3 solution (2×50 ml) and 5% Na_2CO_3 solution (2×50 ml), and dried over anhydrous Na_2SO_4. The solvent was removed under low pressure and the residue was fractionated on a silica gel column (1:3 ethyl acetate–petroleum ether as eluent). The fractions with R_f 0.28 were collected and evaporated to give compound 7*Z*-**5a** (258 mg, 78%); mp 187-188°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.53 (9H, s, C_4H_9). 2.12 (3H, s, CH_3); 2.42 (3H, s, CH_3COC=); 3.68 and 3.94 (2H, two d, AB system, ^2J = 18, SO_2CH_2); 5.56 (1H, d, ^4J = 1, H-6); 6.88 (1H, d, ^4J = 1, COCH=). Found, %: C 52.83; H 5.65; N 3.94. $C_{15}H_{19}NO_6S$. Calculated, %, C 52.77; H 5.61; N 4.10.

***tert*-Butyl 3-Acetoxymethyl-7*Z*-(3-trimethylsilylpropyn-2-ylidene)ceph-3-em-4-carboxylate (7*Z*-3b) and *tert*-Butyl 3-Acetoxymethyl-7*E*-(3-trimethylsilylpropyn-2-ylidene)ceph-3-em-4-carboxylate (7*E*-3b).** A solution of 1.6 M butyl lithium in hexane (0.7 ml) was added to a suspension of (3-trimethylsilyl-

2-propynyl)triphenylphosphonium bromide (367 mg, 0.81 mmol) in absolute THF (10 ml) at 10°C with stirring until a clear solution was obtained. Stirring was continued for 30 min at 10°C, the mixture was cooled to -78°C, and a solution of *tert*-butyl 3-acetoxymethyl-7-oxoceph-3-em-4-carboxylate (265 mg, 0.81 mmol), prepared according to [4], in absolute THF (5 ml) was added and stirred for 30 min at -78°C and poured into a saturated solution of NH_4Cl (100 ml) with ice. The mixture was stirred until ice dissolved and extracted with dichloromethane (2×20 ml). The organic phase was washed with cooled NH_4Cl solution and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was fractionated on a silica gel column with 1:3 ethyl acetate–petroleum ether eluent. The fractions with R_f = 0.25 were collected and evaporated to give compound 7*Z*-**3b** (147 mg, 43%). The product contained 97% of the basic material according the HPLC. ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 0.24 (9H, s, $(CH_3)_3Si$); 1.33 (9H, s, C_4H_9); 2.06 (3H, s, CH_3OCO); 3.31 and 3.60 (2H, two d, AB system, ^2J = 16, SCH_2); 4.78 and 5.06 (2H, two d, AB system, ^2J = 14, 3-CH_2OCO); 5.27 (1H, d, ^4J = 1.5, H-6); 6.27 (1H, d, ^4J = 1.5, C≡C–CH=). The fractions with R_f = 0.08 were collected and evaporated to give compound 7*E*-**3b** (15 mg, 4%). ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 0.22 (9H, s, $(CH_3)_3Si$); 1.33 (9H, s, C_4H_9); 2.06 (3H, s, CH_3OCO); 3.28 and 3.55 (2H, two d, AB system, ^2J = 18, SCH_2); 4.73 and 5.04 (2H, two d, AB system, ^2J = 12, 3-CH_2OCO); 5.11 (1H, d, ^4J = 0.8, H-6); 5.90 (1H, br. s, C≡C–CH=).

***tert*-Butyl 3-Acetoxymethyl-1*R*-oxo-7*Z*-(3-trimethylsilylpropyn-2-ylidene)ceph-3-em-4-carboxylate (1*R*,7*Z*-4b) and *tert*-Butyl 3-Acetoxymethyl-1*S*-oxo-7*Z*-(3-trimethylsilylpropyn-2-ylidene)ceph-3-em-4-carboxylate (1*S*,7*Z*-4b).** 75% 3-Chloroperbenzoic acid (46 mg, 0.20 mmol) was added with stirring to a solution of compound 7*Z*-**3b** (80 mg, 0.19 mmol) in dichloromethane (20 ml) at 0°C. The mixture was stirred for 4 h at room temperature, diluted with dichloromethane (20 ml), washed with 5% Na_2SO_3 solution (50 ml) and 5% Na_2CO_3 solution (2 x 50 ml), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was fractionated on a silica gel column with 1:3 ethyl acetate–petroleum ether eluent. The fractions with R_f 0.25 were collected and evaporated to give compound 1*R*,7*Z*-**4b** (10 mg, 12%). The product contained 95% of the basic material according to HPLC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.24 (9H, s, $(CH_3)_3Si$); 1.55 (9H, s, C_4H_9); 2.09 (3H, s, CH_3OCO); 3.51 and 3.95 (2H, two d, AB system, ^2J = 18, $SOCH_2$); 4.78 and 5.04 (2H, two d, AB system, ^2J = 14, 3-CH_2OCO); 4.95 (1H, d, ^4J = 2, H-6); 6.44 (1H, d, ^4J =2, C≡C–CH=). The fractions with *Rf* 0.18 were collected and evaporated to give compound 1*S*, 7*Z*-**4b** (30 mg, 36%); mp 30°C. The product contained 95% of the basic material according to HPLC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.24 (9H, s, $(CH_3)_3Si$); 1.58 (9H, s, C_4H_9); 2.09 (3H, s, CH_3OCO); 3.22 and 3.84 (2H, two d, AB system. ^2J = 20, $SOCH_2$); 4.69 and 5.31 (2H, two d, AB system, ^2J = 14, 3-CH_2OCO); 4.89 (1H, d, ^4J = 2, H-6); 6.44 (1H, d, ^4J =2, C≡C–CH=). Found, %: C 56.50; H 6.65; N 2.68. $C_{20}H_{27}NO_6Si{\cdot}0.25C_6H_{14}$. Calculated, %: C 56.24; H 6.69; N 3.05.

***tert*-Butyl 3-Methyl-1,1-dioxo-7*Z*-(3-trimethylsilylpropyn-2-ylidene)ceph-3-em-4-carboxylate (7*Z*-5b).** 75% 3-Chloroperbenzoic acid (138 mg, 0.60 mmol) was added with stirring at 0°C to a solution of compound 7*Z*-**3b** (100 mg, 0.24 mmol) in dichloromethane (20 ml). The mixture was stirred for 4 h at room temperature, washed with 5% Na_2SO_3 solution (50 ml) and 5% Na_2CO_3 solution (2×50 ml), dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was fractionated on a silica gel column with 1:3 ethyl acetate–petroleum ether eluent. The fraction with R_f 0.35 were collected and evaporated to give compound 7*Z*-**5b** (25 mg, 23%); mp 40-41°C. The product contained 97% of the basic material according to HPLC. ^{1}H NMR spectrum, δ ppm (*J*, Hz): 0.23 (9H, s, $(CH_3)_3Si$); 1.56 (9H, s, C_4H_9); 2.08 (3H, s, CH_3OCO); 3.67 and 4.02 (2H, two d, AB system, ^2J = 18, SO_2CH_2); 4.69 and 5.08 (2H, two d, AB system, ^2J = 14, 3-CH_2OCO); 5.27 (1H, br. s, H-6), 6.47 (1H, d, ^4J = 2, C≡C-CH-).

X-ray crystallographic analysis was carried out with a Nonius KappaCCD automatic diffractometer (operating at room temperature, molybdenum irradiation with λ =0.71073 Å, graphite monochromator, φ- and ω-scanning). The structure was solved by direct methods [5] and refined by full matrix least squares analysis with the help of maxus [6] (for 1*S*,7*Z*-**4a**) and SHELXL [7] (for 7*Z*-**5a).** The absolute configuration of the chiral

crystal structures was determined from the anomalous diffraction of the sulfur atom. The basic crystal characteristics for compounds 1*S, 7Z*-**4a** (1:3 ethyl acetate–petroleum ether) and 7*Z*-**5a** (1:3 ethyl acetate–petroleum ether) and also the conditions for recording and the parameters of the refinement are cited in Table 3. Crystallographic information has been deposited in the Cambridge Structural Data Bank (deposit No: CCDC 681162 (7*Z*-**4a**) 681163 (7*Z*-**5a**).

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