115. X-Ray Structure Analyses of Alkyl-Substituted *N*-Acryloyl- and *N*-Crotonoyltoluenesultams[1])

by **Gérald Bernardinelli***, **Christian Chapuis**[2])*, **Arend J. Kingma**[2]), and **Martin Wills**[2])

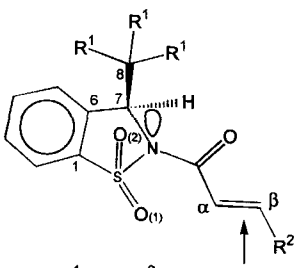
Département de Chimie Organique et Laboratoire de cristallographie Université de Genève, CH-1211 Genève 4

Dedicated to the memory of Professor *Wolfgang Oppolzer*

(14. IV. 97)

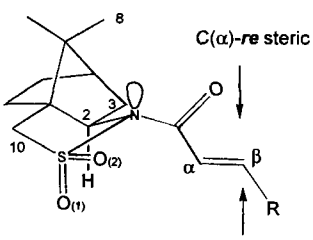
The X-ray crystal-structure analyses of two *N*-enoyl-toluenesultam derivatives **1** are reported. The structural differences with their bornanesultam analogues **2** as well as stereochemical aspects with respect to their [4 + 2] and [3 + 2] cycloadditions are discussed.

The preparation as well as the [4 + 2] and [3 + 2] cycloadditions of *N*-enoyltoluenesultams (–)-**1a,b** have been recently reported [1] [2][3]), simultaneously with the α-alkylation and aldolization of *N*-acyl derivatives [4]. The X-ray structure analyses of the camphor analogues (–)-**2a,b** [5] [6] have been extensively used to rationalize their reactive conformations [7–9]. Both bornane [6] and toluenesultam auxiliaries [10] have been speculatively compared to a disguised C_2-symmetrical 2,5-dimethylpyrrolidine system [8], where the approach on the enoyl side chain is sterically disfavoured either by the C-skeleton in the SO_2/C(O)-*syn*,C(O)/C=C-s-*cis* conformation (*syn*-s-*cis*) or by the O(1) atom in the *anti*-s-*cis* arrangement [6] [8]. We thought it useful to present the crystallographic structure analyses of (–)-**1a** and (+)-**1b**[4]), in view of their very recently outlined structural differences with (–)-**2a,b** [9].



(-)-**1a** R^1= Me, R^2= H
(-)-**1b** R^1= H, R^2= Me

C(α)-*si* steric + electronic



(-)-**2a** R = H
(-)-**2b** R = Me

C(α)-*si* electronic

[1]) Derived from saccharine (= 1,2-benzoisothiazol-3(2*H*)-one, 1,1-dioxide).

[2]) Present addresses: *C.C., Firmenich SA*, Corporate Research Division, P.O.B. 239, CH-1211 Geneva 8; *A. J. K., BASF AG*, Marketing Speciality Chemicals I, ESA/ET-J 550, D-67056 Ludwigshafen; *M. W.*, Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK.

[3]) For recent reviews on asymmetric [4 + 2] and [3 + 2] intermolecular cycloadditions, see [3].

[4]) For convenience, the arbitrary atom labels in **1a,b** are the same; for systematic names, see *Exper. Part.*

In both structures (−)-**1a** and (+)-**1b**, the *N*-enoyl side chain shows a typical *anti*-s-*cis* conformation ((−)-**1a**: S−N−C=O 148.8(4)°, O=C−C=C − 11.5(8)°; (+)-**1b**: S−N−C=O − 161.7(5)°, O=C−C=C − 13(1)°) as already observed for (−)-**2a,b**, although, for an identical absolute configuration, their bornane analogues have an opposite sign of the dihedral angle around the C(O)−C(α) bond ((−)-**2a,b**: O=C−C=C 1.0(9)° [5]; −6.1(8)° [6]). *Oppolzer* had suggested that the twisting of the dienophile around this bond might be important for the stereocontrol [8] [11], although no evidence of this influence could be found by recent PM3 calculations [9].

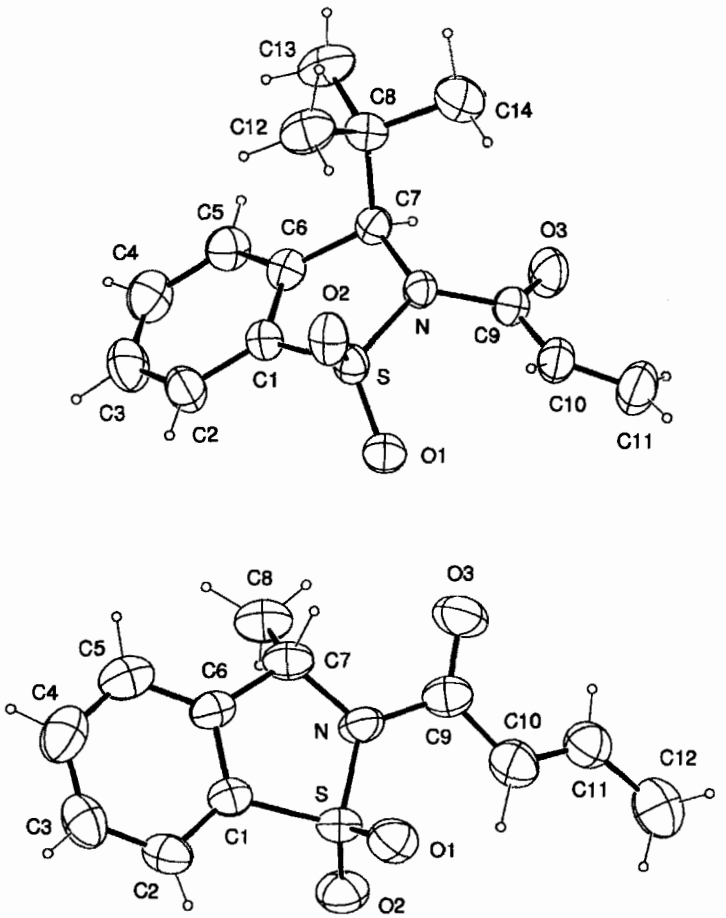


Figure. *ORTEP Diagram of (−)-***1a** (top) *and (+)-***1b** (bottom) *with atom numbering* (arbitrary). Ellipsoids are represented at the 40% probability level.

The *N*-acylbornanesultam derivatives (see **2**) systematically show a pseudoequatorial orientation for the C(2)−C(3) and S=O(2) bonds. For example, for (−)-**2a,b**, the S−N−C(2)−C(3) and O(2)−S−N−C(2) dihedral angles are 144.2(4) and 142.4(4)°, and −131.1(4)° and −125.9(4)°, respectively. This results from the *cis*-fused bicyclic five-

membered rigidified ring system as well as from the steric pressure of the Me(8) group on the O(2) in the bornanesultam skeleton. Indeed, in a pseudoaxial orientation, the O(2) atom would be much closer to Me(8) than the 3.446(9) and 3.230(9) Å observed in (−)-**2a,b**, respectively (for comparison, the distance between O(2) and C(12) in (−)-**1a** is 3.312(6) Å). This characteristic is not always respected in toluenesultams, since the flexible C(8) atom is not integrated in a ring, and because of the S-adjacent C(1) atom which is substituted and part of a benzene moiety. As a consequence, the aromatic ring exerts a *gauche* interaction on both pseudoequatorial alkyl and S=O(2) substituents and, to minimize the steric repulsion, tends to direct them in a pseudoaxial direction. For large alkyl groups, this results in the loss of *Curran*'s postulated C_2 symmetry existing in (−)-**2a,b** [8]. This effect is particularly important for (−)-**1a**, where the *t*-Bu and S=O(2) substituents are frankly pseudoaxial (see *Table 1*), whilst the sterically less demanding Me substituent in (+)-**1b** is oriented in between the pseudoaxial (S−N−C(7)−C(8) *ca.* 100°) and the pseudoequatorial (*ca.* 130°) position. The aromatic ring is practically bisecting the O(1)=S=O(2) angle in the latter case (see *Table 1*).

Table 1. *Selected Bond Lengths* [Å] *and Angles* [°] *for* (−)-**1a** *and* (+)-**1b**

	(−)-**1a**	(+)-**1b**		(−)-**1a**	(+)-**1b**
C(1)–C(6)	1.376(6)	1.377(8)	O(2)–S–N	111.2(2)	111.3(3)
C(6)–C(7)	1.511(6)	1.489(9)	O(1)–S–C(1)	111.7(2)	112.0(3)
C(7)–C(8)	1.557(6)	1.51(1)	O(2)–S–C(1)	111.7(2)	112.1(3)
C(7)–N	1.496(5)	1.470(8)	N–S–C(1)	93.0(2)	93.5(3)
N–S	1.682(3)	1.671(5)	C(7)–N–C(9)	119.0(3)	120.5(5)
S–O(1)	1.432(3)	1.418(5)	C(9)–N–S	122.7(3)	123.2(5)
S–O(2)	1.425(3)	1.417(5)	C(7)–N–S	113.2(2)	114.6(4)
N–C(9)	1.414(6)	1.40(1)	O(3)–C(9)–N	119.2(4)	118.2(6)
C(9)–O(3)	1.201(6)	1.219(9)	O(3)–C(9)–C(10)	124.0(4)	124.0(7)
C(9)–C(10)	1.463(7)	1.45(1)	N–C(9)–C(10)	116.7(4)	117.7(6)
C(10)–C(11)	1.296(7)	1.30(1)	C(9)–C(10)–C(11)	120.7(5)	121.1(7)
C(1)–C(6)–C(7)	114.3(4)	115.5(6)	O(1)–S–N–C(7)	129.9(3)	−112.1(5)
C(6)–C(7)–N	104.6(3)	105.7(5)	O(2)–S–N–C(7)	− 99.2(3)	118.2(5)
S–C(1)–C(6)	111.6(3)	110.6(5)	S–N–C(7)–C(8)	106.2(3)	−125.3(5)
O(1)–S–O(2)	116.6(2)	115.8(3)	C(2)–C(1)–S–O(1)	56.9(5)	−68.4(7)
O(1)–S–N	110.2(2)	110.0(3)	C(2)–C(1)–S–O(2)	−75.7(5)	63.6(7)

Another important feature of the cyclic sultams is the pyramidalization of the N-atom[5]) and its indubitable correlation observed with respect to the S–N–C=O dihedral angle [9]. The N-lone pair (lp) is believed to be anomerically directed and stabilized, in the absence of major steric interactions, by the *anti*-periplanar S=O bond [9] [14], although, for *N*-acylbornanesultams, neither systematic lengthening of the S–N nor shortening of the S=O(1) bond lengths could be demonstrated [14]. According to this hypothesis, one would expect the N-lone pair to be *anti*-periplanar to the pseudoaxial S=O(2) bond in (−)-**1a**, but this would bring the *N*-enoyl chain close to both pseudoax-

[5]) For planar and pyramidal acyclic sultam X-ray structure analyses, see [12] and [13], respectively.

ial substituents, thus resulting in a strong steric repulsion[6]). For this reason, the N-atom remains pyramidalized in the usual way ((−)-**1a**: ΔhN = 0.198(4) Å; (+)-**1b**: ΔhN = 0.112(7) Å), similarly to the *N*-enoylbornanesultam analogues (−)-**2a,b**.

In conclusion, the structural differences between *N*-enoyltoluene- and *N*-enoylbornanesultams are mainly due to the possible loss of the pseudo-C_2 symmetry. This results in a decrease of the stereoselectivity observed for the uncatalysed [4 + 2] cycloadditions of cyclopentadiene to (−)-**1a,b** at 21° (51% d.e. [1a]; 43% d.e., 75% *endo*, 57% yield) as compared to (−)-**2a,b** (66% d.e. [16]; 52% d.e. [16])[7]). In the case of bornanesultams (−)-**2a,b**, the steric approach is systematically directed onto the C(α)-*re* face for both *syn*- and *anti*-s-*cis* conformers, whilst this should be only the case for the highly reactive *syn*-s-*cis* (−)-**1a** conformer [14][8]). Indeed, intuitively, according to *Curran*'s postulate, a steric C(α)-*si* approach would be expected for (−)-**1a** in the *anti*-s-*cis* conformation[9]). Due to the small size of the Me substituent, resulting in a weaker *gauche* interaction with the aromatic ring and thus in a less pronounced C(8)/O(2) pseudodiaxial conformation, (−)-**1b** represents an intermediate case. Furthermore, as a result of the observed pyramidalization, the weak stereoelectronic preferred interaction[10]) is no longer mismatching the steric effect in the *anti*-s-*cis* (−)-**1a,b** conformers, in contrast to (−)-**2a,b** [9] [14] [19]. Supplementary X-ray structure analyses from cycloadducts derived from (−)-**1a,b**[6]), will be presented in due course.

Experimental Part

*X-Ray Structure Determination of (−)-(3*R*)-3-(*tert*-Butyl)-2,3-dihydro-2-(1-oxoprop-2-enyl)-1,2-benzisothiazole 1,1-Dioxide* ((−)-**1a**) *and (+)-(3*S*)-2,3-Dihydro-3-methyl-2-[(*E*)-1-oxobut-2-enyl]-1,2-benzisothiazole 1,1-Dioxide* ((+)-**1b**). Suitable crystals were grown from hexane/Et_2O and EtOH soln., resp. Cell dimensions and

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[6]) For two X-ray structure analyses of cycloadducts with inverted N-pyramidalization, see [1b] for (3*R*)-*N*-[(1,2-dimethylcyclohex-3-en-1-yl)carbonyl]-3-methyltoluenesultam (= (3*R*)-2-[(1,2-dimethylcyclohex-3-en-1-yl)-carbonyl]-2,3-dihydro-3-methyl-1,2-benzisothiazol 1,1-dioxide; ΔhN = − 0.06(2) Å, O(2)−S−N-lp 177.6(9)°) and [15] for (3*R*) *N*-[(1,2-dimethylcyclohex-4-en-1-yl)carbonyl]-3-methyltoluenesultam (= (3*R*)-2-[(1,2-dimethylcyclohex-4-en-1-yl)carbonyl]-2,3-dihydro-3-methyl-1,2-benzisothiazol 1,1-dioxide; ΔhN = − 0.088(5) and 0.036(5) Å, O(1)−S−N−C(7) 136.0(3) and 139.0(3)°, O(2)−S−N−C(7) −91.6(3) and −89.0(3)°, S−N−C(7)−C(8) 96.6(4) and 99.3(4)°, and O(2)−S−N-lp 173.7(3) and 2.9(3)° for the two molecules of the asymmetric unit, resp.). In the latter case, the N-atom is practically planar with a lone pair almost symmetrically distributed on both π faces.

[7]) For a rationalization of the high diastereoselectivity observed in the presence of hypothetically unchelated dicoordinated (−)-**1a** during its [4 + 2] cycloaddition to cyclopentadiene, see [9].

[8]) For PM3 calculations showing the higher reactivity of the *syn*-s-*cis* conformer during the [3 + 2] cycloaddition of (−)-**1a**, see footnote 41 in [9]. This hypothesis better explains the observed stereoselectivity by competition with an *anti*-s-*cis* C(α)-*re* approach on the sterically more hindered face, shielded by the pseudoaxial *t*-Bu and O(2) substituents [17]. This is well highlighted by the [3 + 2] cycloadditions of acetonitrile and 2,2-dimethyl propiononitrile oxides to (−)-**1a** (92% d.e.; 96% d.e., [2]) and (−)-**2a** (80% d.e.; 90% d.e., [5]), respectively.

[9]) For more precise PM3 calculations of [4 + 2] transition states of (−)-**1a**, see [9].

[10]) We believe that the stereoelectronic interaction is weaker than the steric interaction on the basis of the calculated transition-state energy for the cyclopentadiene cycloaddition to *N,N'*-fumaroylbis[(2*R*)-bornanesultam] [9] [18]. Indeed, comparison of the contra-steric bis(*syn*-s-*cis*) and bis(*anti*-s-*cis*) C(α)-*si* approaches, shows that, in contrast to (−)-**2a,b**, attack on the stereoelectronically favoured face, *anti* to the N-lone pair, is not always the origin of the minor diastereoisomer. Furthermore, the stereoelectronically non-additive *syn*-s-*cis*-s-*cis*-*anti* conformer has a lower activation energy than the bis(*syn*-s-*cis*) conformer for C(α)-*re* face attack.

Table 2. *Summary of Crystal Data Intensity Measurement, and Structure Refinement for (−)-***1a** *and (+)-***1b**

	(−)-**1a**	(+)-**1b**
Formula	$C_{14}H_{17}NO_3S$	$C_{12}H_{13}NO_3S$
Mol. wt.	279.4	251.3
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a [Å]	10.5994(7)	7.274(2)
b [Å]	11.0282(10)	12.101(2)
c [Å]	12.2262(9)	13.943(4)
V [Å^3]	1429.2(2)	1227.3(5)
Z 4	4	4
$F(000)$	592	528
D_c [gr · cm^{-3}]	1.30	1.36
$\mu(MoK_\alpha)$ [mm^{-1}]	0.219	0.247
$((\sin\theta)/\lambda)_{max}$ [Å^{-1}]	0.64	0.58
No. measured reflections	1824	1147
No. observed reflections	1630	916
Criterion for observed	$\|F_o\| > 2\sigma(F_o)$	$\|F_o\| > 2\sigma(F_o)$
Refinement (on F)	full-matrix	full-matrix
No. parameters	172	154
Weighting scheme	$\omega = 1/(\sigma^2(F_o) + 0.0005(F_o^2))$	$\omega = 1/(\sigma^2(F_o) + 0.0006(F_o^2))$
Max. and min. $\Delta\rho$ [e · Å^{-3}]	0.27, −0.30	0.34, −0.38
S	1.34	1.23
R, ωR	0.054, 0.060	0.063, 0.054

intensities were measured at r.t. on *Philips-PW-1100* and *Nonius-CAD4* diffractometers with graphite-monochromated MoK_α radiation ($\lambda = 0.71069$ Å). Data were corrected for *Lorentz* and polarization effects but not for absorption. The structures were solved by direct methods using MULTAN 87 [20], all other calculations used XTAL [21] system and ORTEP [22] programs. All H-atoms were observed and contributed to F_c calculations but were not refined. *Table 2* shows details of the data collections and refinements. Crystallographic data have been deposited with the *Cambridge Crystallographic Data Center*, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, England, as supplementary publication No. CCDC-10/54.

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