Regioselectivity in the 1,3-Dipolar Cycloaddition of Nitrile Oxides to 1-Substituted 3,3-Methylene-5,5-dimethyl-2-pyrrolidinones

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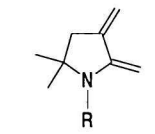
The cycloaddition of aryl- and aroylnitrile oxides to 1-R-substituted 3,3-methylene-5,5-dimethyl-2-pyrrolidinones (where R is H, n-butyl-, 1,1-dimethylethoxycarbonyl-, 1-methylethenyl-, and acetyl-) proceeds regioselectively under the formation of spiroisoxazolines, namely 7-R-substituted 6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]non-2-enes. Semiempirical quantum-mechanical methods AM1 were used to rationalize this exclusive regioselectivity. The regiochemistry of the cycloaddition seems to be controlled by the steric effect of the methyl groups at the ring junction.

The recent observation of the strong herbicidal activity of spirocyclic lactams, coupled with the absence of toxicity to microorganisms [1] and also that some spiroisoxazolines occur naturally, Araplysillins being inhibitors of ATPase [2], stimulated our interest in the synthesis of other spirocyclic derivatives. 2-Isoxazolines (4,5-dihydroisoxazoles) are versatile sources of the functionality present in natural products [3] and there is renewed interest in their synthesis *via* 1,3-dipolar cycloaddition of nitrile oxides to alkenes, particularly in the factors that influence stereo- and regioselectivity [4].

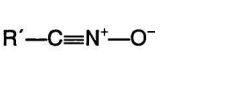
In a continuation of our effort [5—8] to utilize heterocyclic compounds as dipolarophiles in 1,3-dipolar cycloaddition reactions, we have recently shown that arylnitrile oxides react with unsubstituted 3,3-methylene-5,5-dimethyl-2-pyrrolidinone (*Ia*) to produce exclusively spiroisoxazolines of the type *III*. Since the reaction of *I* with 1,3-dipoles could be of some mechanistic interest regarding the peculiarity of the regioselectivity pattern in electron-deficient dipolarophiles in the 1,3-dipolar cycloadditions, we now report on the preparation of 1-substituted derivatives of pyrrolidinone *I* possessing an electron-withdrawing as well as electron-donating substituent on the nitrogen, with the aim to obtain also the second regioisomer *IV* together with quantum-mechanical calculations using the AM1 method.

1-R-Substituted 3,3-methylene-5,5-dimethyl-2-pyrrolidinones *I* (where R is n-butyl-, 1,1-dimethylethoxycarbonyl-, and acetyl-) were prepared from the parent derivative *Ia* by applying an alkylation in the presence of appropriate base (derivatives *Ib, Ic,* and *Ie,* see Experimental). The corresponding 1-(1-methylethenyl) derivative *Id* is formed as a by-product by the preparation of *Ia* involving treatment of 2,2,6,6-tetramethyl-4-piperidone in chloroform with 50 % aqueous NaOH under catalysis of TEBA [9]. Aryl-substituted benzenenitrile oxides *II* (where aryl is phenyl, 4-methyl-, 4-chloro-, 4-bromo-, 4-fluoro-,



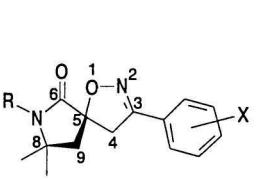
I

a R = H
b R = n-Bu
c R = Boc
d R = CH_2=$(CH_3)C$
e R = $COCH_3$

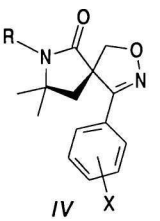


II

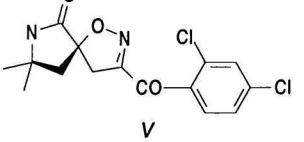
a R′ = C_6H_4—X
b R′ = COC_6H_3-2,4-Cl_2



III



IV



V

Formulae 1

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4-cyano-, 4-nitro-, 3-nitro-, 4-methoxy-, 3-methoxy-, 2,4-dichloro-, and 2,6-dichlorophenyl) were generated from the corresponding benzohydroximoyl chlorides and triethylamine in the presence of methylenepyrrolidinones *I*. The formation of the cycloadducts 7-R-substituted 6-oxo-8,8-dimethyl-1-oxa-2,7-diazaspiro[4,4]non-2-enes *III* was accompanied by very small amounts (< 10 %) of 3,4-diarylfuroxan — the nitrile oxide dimer [10] — as by-product (Formulae 1). Cycloaddition of *I* with 2,4-dichlorobenzoylnitrile oxide, which was generated from 2,4-dichlorophenylglyoxylhydroximoyl chloride (see Ref. [11]) and triethylamine, proceeded analogously to give a cycloadduct *III*. The corresponding regioisomer *IV* has not been detected in the crude reaction mixture by NMR spectroscopy (Formulae 1, Table 1).

The assignment of the regiochemistry in isoxazolines *IIIa—IIIv* was unequivocally made on the basis of diagnostic ^1H and ^{13}C NMR data of the isoxazoline ring moiety and by comparison with the cycloadducts of *Ia* [5]. Their C-5 resonances lie at lower fields (δ = 86.03—90.18) and are roughly by 40 ppm higher than those of the other possible regioisomers *IV*. On the other hand, C-4 resonances (δ = 40.02—46.66) attest the shielding effect of a spiro-fused pyrrolidin-

Table 1. Physicochemical Characteristics of Compounds *IIIc—IIIv*, *Va*, *Vb*

Compound	R	X	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	N	Yield %	M.p. °C
IIIc	n-Bu	H	$C_{18}H_{24}N_2O_3$ 300.38	–	–	–	75	Oil
IIId	n-Bu	4-NO_2	$C_{18}H_{23}N_3O_4$ 345.39	62.59 62.63	6.71 6.56	12.16 12.10	52	117—118
IIIe	Boc	4-CH_3	$C_{20}H_{26}N_2O_4$ 358.40	67.02 66.98	7.21 7.35	7.82 7.77	65	169—170
IIIf	Boc	4-CN	$C_{20}H_{23}N_3O_4$ 369.40	65.02 65.10	6.27 6.13	7.58 7.59	75	179—180
IIIg	Boc	2,4,6-$(CH_3)_3$	$C_{22}H_{30}N_2O_4$ 386.47	68.37 68.23	7.82 7.76	7.25 7.14	45	112—113
IIIh	CH_2=(CH_3)C	H	$C_{17}H_{20}N_2O_2$ 284.36	71.81 71.90	7.09 7.01	9.85 9.79	80	78—79
IIIi	CH_2=(CH_3)C	4-NO_2	$C_{17}H_{19}N_3O_4$ 329.36	62.00 61.98	5.81 5.90	12.76 12.81	35	119—120
IIIj	CH_2=(CH_3)C	3-NO_2	$C_{17}H_{19}N_3O_4$ 329.36	62.00 62.03	5.81 5.78	12.76 12.79	72	127—128
IIIk	CH_2=(CH_3)C	4-CH_3	$C_{18}H_{22}N_2O_2$ 298.39	72.46 72.52	7.43 7.39	9.39 9.38	45	140—142
IIIℓ	CH_2=(CH_3)C	4-Cl	$C_{17}H_{19}N_2O_2$ 318.81	64.05 63.99	6.01 6.05	8.79 8.84	31	112—115
IIIm	CH_2=(CH_3)C	2,4-Cl_2	$C_{17}H_{18}Cl_2N_2O_2$ 352.26	57.80 57.77	5.14 5.15	7.93 7.93	55	80—82
IIIn	CH_2=(CH_3)C	2,6-Cl_2	$C_{17}H_{18}Cl_2N_2O_2$ 352.26	57.80 57.81	5.14 5.11	7.93 7.89	45	149—150
IIIo	CH_2=(CH_3)C	4-Br	$C_{17}H_{19}BrN_2O_2$ 363.27	56.21 56.19	5.27 5.27	7.71 7.73	39	219—220
IIIp	CH_2=(CH_3)C	4-F	$C_{17}H_{19}FN_2O_2$ 302.35	67.53 67.55	6.33 6.29	9.27 9.31	47	98—99
IIIq	CH_2=(CH_3)C	4-CH_3O	$C_{18}H_{22}N_2O_3$ 315.37	68.77 68.76	7.05 7.08	8.91 9.00	60	109—110
IIIr	CH_2=(CH_3)C	3-CH_3O	$C_{18}H_{22}N_2O_3$ 315.37	68.77 68.72	7.05 7.01	8.91 8.88	50	111—112
IIIs	CH_2=(CH_3)C	4-Ph	$C_{23}H_{24}N_2O_2$ 360.46	76.64 76.59	6.71 6.73	7.77 7.69	35	165—167
IIIt	$COCH_3$	H	$C_{16}H_{18}N_2O_3$ 286.34	67.12 67.05	6.34 6.28	9.78 9.73	85	114—115
IIIu	$COCH_3$	3-NO_2	$C_{16}H_{17}N_3O_5$ 331.37	58.00 57.98	5.17 5.19	12.68 12.60	60	140—142
IIIv	$COCH_3$	4-CH_3O	$C_{17}H_{20}N_2O_4$ 316.37	64.54 64.61	6.37 6.35	8.85 8.87	77	128—130
Va	H	–	$C_{16}H_{14}Cl_2N_2O_3$ 341.17	52.80 53.01	4.13 4.10	8.21 8.30	30	161—163
Vb	Boc	–	$C_{20}H_{22}Cl_2N_2O_5$ 440.55	54.43 54.65	5.03 5.07	6.35 6.39	45	118—119

one ring. Moreover, the ^{1}H NMR spectrum showed the isoxazoline ring H_2-4 protons in the region δ = 3.00—4.01, which is completely consistent with an isoxazoline unsubstituted at the position 4. If the spiro atom were at the position 4 of the isoxazoline ring (the possible regioisomer *IV*), the protons at the position 5 would appear at lower fields [12].

We have shown that NMR spectra indicate the regiochemistry of the cycloadducts *III* which are formed by the attack of the carbon of the nitrile oxide at the CH_2 terminus of the exocyclic double bond. The observed regiochemistry seems to be independent of the electronic structure of the substituent on the pyrrolidinone *I* as well as nitrile oxide *II*.

Therefore we have performed an FMO analysis of AM1 calculated [13] frontier orbitals. Geometries of reactants were fully optimized, the results of the calculations are summarized in Tables 2 and 3. Inspection of energy levels shows that the cycloaddition to parent *Ia* as well as to alkenyl derivative *Id* is governed by the LUMO dipole, whereas the addition to pyrrolidinones *Ic* and *Ie,* both possessing electron-withdrawing groups on the nitrogen, is governed by both frontier orbital interactions. The FMO arguments predict correct regioselectivity, the preferential attack of dipole oxygen at the spiro carbon in the LUMO controlled 1,3-dipolar cycloaddition to *Ia, Ib,* and *Id.* On the other hand, the regiochemistry of the cycloaddition of nitrile oxides to *Ic* and *Id*, where the second dominant HOMO dipole interaction can form the second possible regioisomer *IV*, seems to be controlled not only by frontier orbital interaction, but also by the steric effects of the methyl groups at the ring junction. From Dreiding models it is obvious that the bulky methyl groups at the position 5 of *I* prevent the attack to give spiroisoxazoline *IV*.

The 1,3-dipolar cycloaddition of arylnitrile oxides to alkenyl derivative *Id* proceeded fully chemoselectively, only the cycloadducts to the exocyclic double bond were formed. The cycloadducts which could be formed by the attack of nitrile oxides to the double bond of alkenyl chain in *Id* have not been detected in the crude reaction mixture by NMR spectroscopy. This can be explained by the well known fact that angular strain in a dipolarophile increases its reactivity [14].

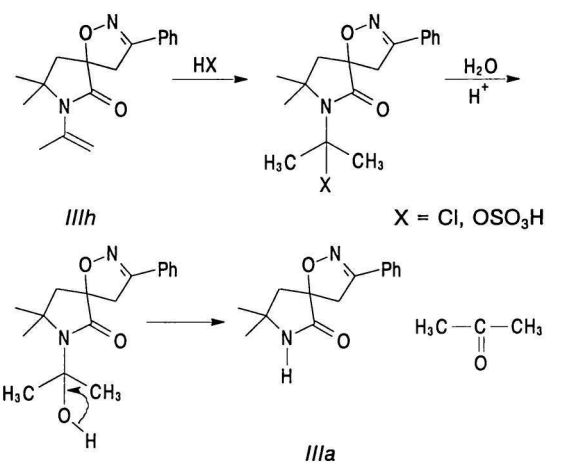
The attempt to obtain the derivatives structurally related to the GABA analogues by means of the ring opening of the pyrrolidinone moiety was unsuccessful. The cycloadducts *III* are totally stable by heating with concentrated HCl, H_2SO_4, NaOH, and LiOH. Only in the case of the alkenyl-substituted derivatives of *III* the 1-methylethenyl chain on nitrogen is removed by treatment with concentrated HCl or H_2SO_4 under the formation of the cycloadducts, which have been prepared by the cycloaddition to the parent derivative *Ia*. The possible mechanism is demonstrated in Scheme 1.

Table 2. Relevant Electronic Parameters of Pyrrolidinones *Ia, Ic—Ie* Calculated with AM1

Compound	E_{HO} / eV	E_{LU} / eV	E_{HO-1} / eV	N	C_α HO	C_β HO	C_α LU	C_β LU	C_α HO −1	C_β HO −1
Ia	− 9.94	0.37	− 10.44	0.76	− 0.18	− 0.21	− 0.51	0.66	0.58	0.60
Ic	− 10.74	− 0.09	− 10.77	0.66	− 0.28	− 0.31	0.46	− 0.63	0.53	0.59
Id	− 8.74	0.15	− 10.48	0.54	− 0.37	− 0.62	0.46	− 0.63	0.59	0.62
Ie	− 10.32	− 0.14	− 10.75	− 0.67	0.26	0.29	− 0.43	0.61	0.54	0.56

Table 3. Relevant Electronic Parameters of Benzonitrile Oxide (BNO) and 2,4-Dichlorobenzoylnitrile oxide (BzNO)

Compound	E_{HO} / eV	E_{LU} / eV	E_{LU+1} / eV	C HO	O HO	C LU	O LU	C LU + 1	O LU + 1
BNO	− 9.38	− 0.50	–	0.37	− 0.49	0.23	0.21	–	–
BzNO	− 10.79	− 1.06	0.18	0.61	− 0.68	0.15	0.19	− 0.37	− 0.28



Scheme 1

EXPERIMENTAL

Melting points were determined on a Kofler hot plate apparatus and are uncorrected. ^{1}H NMR spectra of deuterochloroform solutions were recorded on a Varian VXR 300 and Tesla BS 487 C (80 MHz) instruments, respectively, and ^{13}C NMR spectra of deuterochloroform solutions on Varian VXR 300 spectrometer (TMS as internal standard, $CDCl_3$). All reagents were purified and dried if necessary prior to use. TLC analyses were carried out with Lachema UV_{254} silica gel plates.

3,3-Methylene-5,5-dimethyl-2-pyrrolidinone *Ia* and 1-(1-methylethenyl)-3,3-methylene-5,5-dimethyl-2-pyrrolidinone *Id* were prepared according to Ref. [9].

1-n-Butyl-3,3-methylene-5,5-dimethyl-2-pyrrolidinone (*Ia*): Sodium hydride (19 mmol) was added portionwise at 0 °C to a stirred solution of *Ia* (18.4 mmol) in dry DMF (50 cm^3) under nitrogen. The reaction mixture was allowed to warm to 50 °C and was stirred for 30 min. Then this solution was cooled again at 0 °C and n-butyl chloride (18.4 mmol) in DMF (15 cm^3) was added, followed by stirring at 50 °C for 1 h. The mixture was then poured into 100 cm^3 of ice-cooled water and extracted with ether. The extract was dried and evaporated to obtain yellow oil in 75 % yield. ^{1}H NMR spectrum, δ: 5.88 (dd, 1H, =CH), 5.19 (dd, 1H, =CH), 3.13 (t, 2H, H_2-1′), 2.51 (dd, 2H, H_2-4), 1.47—1.58 (m, 2H, H_2-2′), 1.24—1.33 (m, 2H, H_2-3′), 1.18 (s, 6H, 2 × CH_3), 0.86 (t, 3H, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ: 167.26 (s, C-2), 139.20 (s, C-3), 114.45 (t, $=CH_2$), 57.90 (s, C-5), 41.13 (t, C-4), 39.44 (t, C-1′), 31.42 (t, C-2′), 27.23 (q, CH_3), 20.30 (t, C-3′), 13.56 (q, CH_3).

1-(1,1-Dimethylethoxycarbonyl)-3,3-methylene-5,5-dimethyl-2-pyrrolidinone (*Ic*) was prepared according to the procedure described in Ref. [15]. Di-*tert*-butyldicarbonate (15 mmol) in acetonitrile (10 cm^3) was added dropwise at room temperature to the stirred solution of pyrrolidinone *Ia* (10 mmol) and 4-dimethylaminopyridine (1 mmol) in acetonitrile (30 cm^3). The reaction mixture was stirred at room temperature for about 4 h (TLC), then it was concentrated under diminished pressure to obtain colourless crystals in 90 % yield, m.p. = 62—63 °C. ^{1}H NMR spectrum, δ: 6.17 (dd, 1H, =CH), 5.45 (dd, 1H, =CH), 2.60 (dd, 2H, H_2-4), 1.56 (s, 9H, 3 × CH_3), 1.49 (s, 6H, 2 × CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ: 166.71 (s, C-2), 150.61 (s, OC=O), 138.13 (s, C-3), 119.34 (t, $=CH_2$), 82.71 (s, *t*-Bu), 59.55 (s, C-5), 41.75 (t, C-4), 28.02, 27.28 (q, q, 2 × CH_3).

1-Acetyl-3,3-methylene-5,5-dimethyl-2-pyrrolidinone (*Ie*): The stirred solution of pyrrolidinone *Ia* (12 mmol) and sodium acetate (12 mmol) in acetic anhydride (16 cm^3) was refluxed for 3 h. Acetic anhydride was removed *in vacuo* and the residue was extracted with boiling toluene. The extracts were evaporated and chromatographed on a short column of silica gel to obtain *Ie* in 60 % yield, m.p. = 48—49 °C. The compound *Ie* is polymerized by standing. ^{1}H NMR spectrum, δ: 6.21 (dd, 1H, =CH), 5.52 (dd, 1H, =CH), 2.63 (dd, 2H, H_2-4), 2.53 (s, 3H, $COCH_3$), 1.52 (s, 6H, 2 × CH_3). ^{13}C NMR spectrum, δ: 172.58 (s, $COCH_3$), 168.39 (s, C-2), 138.30 (s, C-3), 120.44 (t, $=CH_2$), 60.42 (s, C-5), 41.91 (t, C-4), 27.09, 27.00 (q, q, 2 × CH_3).

Spiroisoxazolines *IIIc—IIIg*, *Va*, *Vb*

Triethylamine (13 mmol) in ether (30 cm^3) was added to a stirred solution of arylhydroximoyl chloride (10 mmol) and the dipolarophile *I* (10 mmol) in ether at 0—5 °C within 1 h. The reaction mixture was stirred overnight at room temperature, the separated triethylammonium chloride was filtered off, removed by dissolving in water and organic material was evaporated under diminished pressure, dried, and separated by chromatography on a silica gel column and purified by crystallization. Characterization of the synthesized compounds is given in Table 1.

Va: ^{1}H NMR spectrum, δ: 7.27—7.57 (m, 3H, H_{arom}), 3.82 (d, J_{AB} = 17.7 Hz, 1H, H_B-4), 3.23 (d, 1H, H_A-4), 2.48 (d, J_{AB} = 14.4 Hz, 1H, H_B-9), 2.08 (d, 1H, H_A-9), 1.43 (s, 3H, CH_3), 1.36 (s, 3H, CH_3). ^{13}C NMR spectrum, δ: 186.21 (s, C=O), 171.45 (s, C-6), 157.38 (s, C-3), 137.93, 134.77, 133.09, 131.35, 130.36, 126.86 (C_{arom}), 91.99 (s, C-5), 54.44 (s, C-8), 48.50 (t, C-4), 40.22 (t, C-9), 29.74, 29.68 (q, q, 2 × CH_3).

IIIc: ^{1}H NMR spectrum, δ: 7.34—7.67 (m, 5H, H_{arom}), 3.92 (d, J_{AB} =16.5 Hz, 1H, H_B-4), 3.19—3.30 (m, 2H, H_2-1′), 3.15 (d, 1H, H_A-4), 2.44 (d, J_{AB} = 13.8 Hz, 1H, H_B-9), 1.96 (d, 1H, H_A-9), 1.58—1.66 (m, 2H, H_2-2′), 1.40 (s, 3H, CH_3), 1.33—1.38 (m, 2H, H_2-3′), 1.31 (s, 3H, CH_3), 0.94 (t, 3H, CH_3-4′). ^{13}C NMR spectrum, δ: 170.43 (s, C-6), 155.73 (s, C-3), 130.03, 129.21, 128.59, 126.72 (C_{arom}), 87.28 (s, C-5), 58.38 (s, C-8), 48.44 (t, C-9), 42.73 (t, C-1′), 40.02 (t, C-4), 31.33 (t, C-2′), 28.12, 27.43 (q, q, 2 × CH_3), 20.43 (t, C-3′), 13.71 (q, CH_3).

IIId: ^{1}H NMR spectrum, δ: 8.25 (d, 2H, H_{2arom}), 7.82 (d, 2H, H_{2arom}), 3.94 (d, J_{AB} = 16.8 Hz, 1H, H_B-4), 3.19—3.25 (m, 2H, H_2-1′), 3.19 (d, 1H, H_A-4), 2.49 (d, J_{AB} = 13.8 Hz, 1H, H_B-9), 2.02 (d, 1H, H_A-9), 1.58—1.66 (m, 2H, H_2-2′), 1.43 (s, 3H, CH_3), 1.36—1.40 (m, 2H, H_2-3′), 1.35 (s, 3H, CH_3), 0.94 (t, 3H, CH_3-4′). ^{13}C NMR spectrum, δ: 170.43 (s, C-6), 155.73 (s, C-3), 130.03, 129.21, 128.59, 126.72 (C_{arom}), 87.28 (s, C-5), 58.38 (s, C-8), 48.44 (t, C-9), 42.73 (t, C-1′), 40.02 (t, C-4), 31.33 (t, C-2′), 28.12, 27.43 (q, q, 2 × CH_3), 20.43 (t, C-3′), 13.71 (q, CH_3).

Vb: ^{1}H NMR spectrum, δ: 7.28—7.55 (m, 3H, H_{arom}), 3.86 (d, J_{AB} = 14.7 Hz, 1H, H_B-4), 3.24 (d, 1H, H_A-

4), 2.46 (d, J_{AB} = 14.1 Hz, 1H, H_B-9), 2.06 (d, 1H, H_A-9), 1.63 (s, 3H, CH_3), 1.57 (s, 6H, 2 × CH_3), 1.55 (s, 6H, 2 × CH_3). ^{13}C NMR spectrum, δ: 186.10 (s, C=O), 169.81 (s, C-6), 157.36 (s, C=OO*t*-Bu), 138.07, 133.17, 131.35, 130.39, 126.91 (C_{arom}), 90.18 (s, C-5), 84.06 (s, C—*t*-Bu), 60.41 (s, C-8), 47.00 (t, C-9), 40.31 (t, C-4), 28.34 (q, CH_3), 28.03 (q, 2 × CH_3), 27.06 (q, CH_3).

IIIe: ^{1}H NMR spectrum, δ: 7.53 (d, 2H, H_{2arom}), 7.19 (d, 2H, H_{2arom}), 3.92 (d, J_{AB} = 16.8 Hz, 1H, H_B-4), 3.18 (d, 1H, H_A-4), 2.44 (d, J_{AB} = 14.0 Hz, 1H, H_B-9), 2.37 (s, 3H, CH_3), 2.00 (d, 1H, H_A-9), 1.56 (s, 6H, 2 × CH_3), 1.54 (s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 171.16 (s, C-6), 155.79 (s, OC=O), 149.99 (s, C-3), 140.62, 129.42, 126.79, 125.98 (C_{arom}), 90.18 (s, C-5), 84.06 (s, C—*t*-Bu), 60.41 (s, C-8), 47.00 (t, C-9), 40.31 (t, C-4), 28.34 (q, CH_3), 28.03 (q, 2 × CH_3), 27.06 (q, CH_3).

IIIf: ^{1}H NMR spectrum, δ: 7.71—7.75 (m, 4H, H_{arom}), 3.93 (d, J_{AB} = 17.0 Hz, 1H, H_B-4), 3.21 (d, 1H, H_A-4), 2.48 (d, J_{AB} = 16.1 Hz, 1H, H_B-9), 2.10 (d, 1H, H_A-9), 1.67 (s, 3H, CH_3), 1.56 (s, 12H, 4 × CH_3). ^{13}C NMR spectrum, δ: 170.65 (s, C-6), 154.61 (s, OC=O), 149.76 (s, C-3), 132.46, 132.42, 127.25, 127.07, 113.67 (C_{arom}), 118.19 (s, C=N), 87.85, 83.86 (s, s, C-5, C—*t*-Bu), 60.40 (s, C-8), 47.23, 41.99 (t, t, C-9, C-4), 28.49 (q, CH_3), 28.38 (q, 2 × CH_3), 27.99 (q, CH_3), 26.94 (q, CH_3).

IIIg: ^{1}H NMR spectrum, δ: 6.90 (s, 1H, H_{arom}), 3.76 (d, J_{AB} =17.5 Hz, 1H, H_B-4), 3.00 (d, 1H, H_A-4), 2.50 (d, J_{AB} = 13.9 Hz, 1H, H_B-9), 2.30 (s, 9H, 3 × CH_3), 2.03 (d, 1H, H_A-9), 1.58 (s, 6H, 2 × CH_3), 1.55 (s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 171.33 (s, C-6), 156.89 (s, OC=O), 149.99 (s, C-3), 139.01, 136.86, 128.44, 125.26 (C_{arom}), 86.03, 83.60 (s, s, C-5, C—*t*-Bu), 60.36 (s, C-8), 47.30, 46.66 (t, t, C-9, C-4), 28.61 (q, CH_3), 28.07 (q, 2 × CH_3), 26.94 (q, CH_3), 21.08, 19.67 (q, CH_3).

Spiroisoxazolines *IIIh—IIIv*

To the stirred mixture of dipolarophile (21 mmol), triethylamine (2 mmol), 11 % aqueous solution of sodium hypochlorite (20 cm^3; 34 mmol), and dichloromethane (15 cm^3) solution of respective benzaldehyde oxime (21 mmol) in dichloromethane (20 cm^3) was added at 0 °C during 15 min. Stirring was continued overnight, organic layer separated and concentrated *in vacuo*. The residue was triturated or crystallized.

IIIh: ^{1}H NMR spectrum, δ: 7.26—7.69 (m, 5H, H_{arom}), 5.25 (s, 1H, H_{vinyl}), 4.96 (s, 1H, H_{vinyl}), 3.99 (d, J_{AB} = 16.5 Hz, 1H, H_A-4), 3.19 (d, 1H, H_B-4), 2.54 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.05 (d, 1H, H_B-9), 2.01, 1.49, 1.37 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.22 (s, C-6), 155.82 (s, C-3), 139.59, 130.17, 128.76, 128.68, 126.81, 115.73 (C_{arom}, C_{vinyl}), 87.32 (s, C-5), 60.06 (s, C-8), 48.96 (t, C-9), 42.72 (t, C-4), 28.75, 28.09, 21.90 (q, q, q, 3 × CH_3).

IIIi: ^{1}H NMR spectrum, δ: 8.15 (d, 2H, H_{arom}), 7.73 (d, 2H, H_{arom}), 5.15 (s, 1H, H_{vinyl}), 4.86 (s, 1H, H_{vinyl}), 3.88 (d, J_{AB} = 16.5 Hz, 1H, H_A-4), 3.10 (d, 1H, H_B-4), 2.45 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.00 (d, 1H, H_B-9), 1.90, 1.39, 1.28 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.20 (s, C-6), 154.40 (s, C-3), 139.40, 133.24, 127.56, 124.31, 124.00, 116.00 (C_{arom}, C_{vinyl}), 88.53 (s, C-5), 60.24 (s, C-8), 48.65 (t, C-9), 41.95 (t, C-4), 28.72, 28.12, 21.89 (q, q, q, 3 × CH_3).

IIIj: ^{1}H NMR spectrum, δ: 7.61—8.43 (m, 4H, H_{arom}), 5.27 (s, 1H, H_{vinyl}), 4.97 (s, 1H, H_{vinyl}), 4.01 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.26 (d, 1H, H_B-4), 2.57 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.12 (d, 1H, H_B-9), 2.02, 1.50, 1.39 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.23 (s, C-6), 154.22 (s, C-3), 139.39, 132.30, 130.99, 129.81, 124.63, 121.62, 115.91 (C_{arom}, C_{vinyl}), 88.21 (s, C-5), 60.16 (s, C-8), 48.62 (t, C-9), 42.12 (t, C-4), 28.69, 28.10, 21.85 (q, q, q, 3 × CH_3).

IIIk: ^{1}H NMR spectrum, δ: 7.56 (d, 2H, H_{arom}), 7.20 (d, 2H, H_{arom}), 5.24 (s, 1H, H_{vinyl}), 4.95 (s, 1H, H_{vinyl}), 3.96 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.17 (d, 1H, H_B-4), 2.52 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.03 (d, 1H, H_B-9), 2.01, 1.48, 1.36 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.81 (s, C-6), 155.81 (s, C-3), 140.43, 129.68, 129.40, 126.77, 126.32, 115.75 (C_{arom}, C_{vinyl}), 87.15 (s, C-5), 67.07 (s, C-8), 48.99 (t, C-9), 42.88 (t, C-4), 28.77, 28.11, 21.93 (q, q, q, 3 × CH_3).

IIIℓ: ^{1}H NMR spectrum, δ: 7.60 (d, 2H, H_{arom}), 7.38 (d, 2H, H_{arom}), 5.25 (s, 1H, H_{vinyl}), 4.96 (s, 1H, H_{vinyl}), 3.95 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.15 (d, 1H, H_B-4), 2.53 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.05 (d, 1H, H_B-9), 2.01, 1.49, 1.37 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.30 (s, C-6), 154.91 (s, C-3), 139.51, 136.23, 128.97, 128.01, 127.58, 115.75 (C_{arom}, C_{vinyl}), 87.60 (s, C-5), 60.01 (s, C-8), 48.83 (t, C-9), 42.47 (t, C-4), 28.73, 28.06, 21.87 (q, q, q, 3 × CH_3).

IIIm: ^{1}H NMR spectrum, δ: 7.21—7.66 (m, 3H, H_{arom}), 5.25 (s, 1H, H_{vinyl}), 4.95 (s, 1H, H_{vinyl}), 4.01 (d, J_{AB} = 17.1 Hz, 1H, H_A-4), 3.40 (d, 1H, H_B-4), 2.55 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.08 (d, 1H, H_B-9), 2.01, 1.49, 1.30 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.35 (s, C-6), 154.92 (s, C-3), 139.50, 136.37, 133.50, 131.57, 130.40, 127.46, 127.10, 115.75 (C_{arom}, C_{vinyl}), 88.16 (s, C-5), 60.10 (s, C-8), 48.51 (t, C-9), 42.72 (t, C-4), 28.71, 28.18, 21.91 (q, q, q, 3 × CH_3).

IIIn: ^{1}H NMR spectrum, δ: 7.35 (q, 1H, H_{arom}), 7.30 (d, 2H, H_{arom}), 5.24 (s, 1H, H_{vinyl}), 4.96 (s, 1H, H_{vinyl}), 3.91 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.10 (d, 1H, H_B-4), 2.59 (d, J_{AB} = 14.4 Hz, 1H, H_A-9), 2.07 (d, 1H, H_B-9), 1.51, 1.48, 1.37 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.11 (s, C-6), 153.39 (s, C-3), 139.59, 135.23, 135.19, 131.125, 128.11, 115.72 (C_{arom},

C_{vinyl}), 87.86 (s, C-5), 60.12 (s, C-8), 49.26 (t, C-9), 45.34 (t, C-4), 28.73, 28.21, 21.96 (q, q, q, 3 × CH_3).

IIIo: ^{1}H NMR spectrum, δ: 7.53 (m, 4H, H_{arom}), 5.25 (s, 1H, H_{vinyl}), 4.96 (s, 1H, H_{vinyl}), 3.95 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.15 (d, 1H, H_B-4), 2.53 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.06 (d, 1H, H_B-9), 2.01, 1.48, 1.37 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.56 (s, C-6), 150.05 (s, C-3), 139.51, 131.96, 129.57, 128.26, 124.50, 115.88 (C_{arom}, C_{vinyl}), 87.67 (s, C-5), 60.14 (s, C-8), 48.84 (t, C-9), 42.43 (t, C-4), 28.76, 28.10, 21.91 (q, q, q, 3 × CH_3).

IIIp: ^{1}H NMR spectrum, δ: 7.68 (d, 2H, H_{arom}), 7.12 (d, 2H, H_{arom}), 5.25 (s, 1H, H_{vinyl}), 4.96 (s, 1H, H_{vinyl}), 3.96 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.17 (d, 1H, H_B-4), 2.53 (d, J_{AB} = 14.1 Hz, 1H, H_A-9), 2.06 (d, 1H, H_B-9), 2.01, 1.49, 1.36 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.68 (s, C-6), 154.92 (s, C-3), 162.12, 139.52, 128.85, 128.74, 116.01, 115.72 (C_{arom}, C_{vinyl}), 87.49 (s, C-5), 60.15 (s, C-8), 48.83 (t, C-9), 42.72 (t, C-4), 28.73, 28.10, 21.91 (q, q, q, 3 × CH_3).

IIIq: ^{1}H NMR spectrum, δ: 7.61 (d, 2H, H_{arom}), 6.92 (d, 2H, H_{arom}), 5.24 (s, 1H, H_{vinyl}), 4.95 (s, 1H, H_{vinyl}), 3.95 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.83 (s, 3H, OCH_3), 3.16 (d, 1H, H_B-4), 2.52 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.03 (d, 1H, H_B-9), 2.01, 1.48, 1.36 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.88 (s, C-6), 156.43 (s, C-3), 161.13, 139.64, 128.37, 121.73, 114.21, 114.14 (C_{arom}, C_{vinyl}), 87.05 (s, C-5), 60.08 (s, C-8), 55.36 (q, OCH_3), 48.99 (t, C-9), 43.01 (t, C-4), 28.78, 28.12, 21.94 (q, q, q, 3 × CH_3).

IIIr: ^{1}H NMR spectrum, δ: 6.97—7.30 (m, 4H, H_{arom}), 5.23 (s, 1H, H_{vinyl}), 4.94 (s, 1H, H_{vinyl}), 3.95 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.81 (s, 3H, OCH_3), 3.18 (d, 1H, H_B-4), 2.51 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.01 (d, 1H, H_B-9), 2.00, 1.47, 1.35 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.60 (s, C-6), 155.83 (s, C-3), 159.64, 139.57, 130.38, 129.67, 119.46, 116.51, 115.64, 111.43 (C_{arom}, C_{vinyl}), 87.40 (s, C-5), 60.03 (s, C-8), 55.30 (q, OCH_3), 48.85 (t, C-9), 42.73 (t, C-4), 28.65, 28.09, 21.87 (q, q, q, 3 × CH_3).

IIIs: ^{1}H NMR spectrum, δ: 7.37—7.76 (m, 8H, H_{arom}), 5.25 (s, 1H, H_{vinyl}), 4.96 (s, 1H, H_{vinyl}), 4.01 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.22 (d, 1H, H_B-4), 2.54 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.06 (d, 1H, H_B-9), 2.01, 1.49, 1.37 (s, s, s, 9H, 3 × CH_3). ^{13}C NMR spectrum, δ: 169.76 (s, C-6), 155.64 (s, C-3), 139.58, 128.89, 127.90, 127.82, 127.41, 127.35, 127.29, 127.05, 115.84 (C_{arom}, C_{vinyl}), 87.42 (s, C-5), 60.14 (s, C-8), 48.94 (t, C-9), 42.76 (t, C-4), 28.76, 28.13, 21.94 (q, q, q, 3 × CH_3).

IIIt: ^{1}H NMR spectrum, δ: 7.41—7.68 (m, 5H, H_{arom}), 3.91 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.28 (d, 1H, H_B-4), 2.53 (s, 3H, $COCH_3$), 2.47 (d, J_{AB} = 14.4 Hz, 1H, H_A-9), 2.11 (d, 1H, H_B-9), 1.66, 1.55 (s, s, 6H, 2 × CH_3). ^{13}C NMR spectrum, δ: 172.96 (s, $COCH_3$), 171.87 (s, C-6), 155.89 (s, C-3), 130.46, 128.73, 128.51, 128.78 (C_{arom}), 88.82 (s, C-5), 60.93 (s, C-8), 47.38 (t, C-9), 42.74 (t, C-4), 28.28, 27.04, 26.19 (q, q, q, 3 × CH_3).

IIIu: ^{1}H NMR spectrum, δ: 7.62—8.42 (m, 4H, H_{arom}), 3.93 (d, J_{AB} = 17.1 Hz, 1H, H_A-4), 3.34 (d, 1H, H_B-4), 2.52 (s, 3H, $COCH_3$), 2.50 (d, J_{AB} = 13.8 Hz, 1H, H_A-9), 2.16 (d, 1H, H_B-9), 1.66, 1.60 (s, s, 6H, 2 × CH_3). ^{13}C NMR spectrum, δ: 172.49 (s, $COCH_3$), 171.77 (s, C-6), 154.33 (s, C-3), 148.35, 132.30, 130.40, 129.92, 124.91, 121.62 (C_{arom}), 87.78 (s, C-5), 61.05 (s, C-8), 47.16 (t, C-9), 42.18 (t, C-4), 28.26, 27.04, 26.24 (q, q, q, 3 × CH_3).

IIIv: ^{1}H NMR spectrum, δ: 7.61 (d, 2H, H_{arom}), 6.93 (d, 2H, H_{arom}), 3.89 (d, J_{AB} = 16.8 Hz, 1H, H_A-4), 3.85 (s, 3H, OCH_3), 3.24 (d, 1H, H_B-4), 2.53 (s, 3H, $COCH_3$), 2.48 (d, J_{AB} = 14.1 Hz, 1H, H_A-9), 2.09 (d, 1H, H_B-9), 1.66, 1.60 (s, s, 6H, 2 × CH_3). ^{13}C NMR spectrum, δ: 173.20 (s, $COCH_3$), 171.98 (s, C-6), 155.51 (s, C-3), 161.35, 128.42, 121.10, 114.21 (C_{arom}), 86.58 (s, C-5), 60.99 (s, C-8), 55.37 (q, OCH_3), 47.49 (t, C-9), 43.07 (t, C-4), 28.38, 27.12, 26.25 (q, q, q, 3 × CH_3).

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