CYCLOADDITIONS OF 2,5-DIMETHYL-3-FURANNITRILE OXIDE TO ALKENES AND ALKYNES

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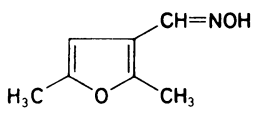
Regioselectivity of 1,3-dipolar cycloadditions of 2,5-dimethyl-3-furannitrile oxide (*IIa*) to alkenes or alkynes is described. Nitrile oxide *IIa* generated in situ reacts with monosubstituted alkenes or alkynes to give exclusively 5-substituted 3-(5-dimethyl-3-furyl)-2-isoxazolines *IV* and isoxazoles *V*, 2,5-disubstiuted alkenes sometimes afforded a mixture of regioisomeric isoxazolines. Reactivity of furannitrile oxides *II* and *III* in cycloadditions to ethene was studied by the MNDO method.

Cycloadditions of nitrile oxides have been studied for a long time, but the regioselectivity and reactivity were first investigated by Huisgen[1,2] after the pioneering work by Quilico and Grünanger[3]. The FMO theory of reactivity and regioselectivity applied by Sustmann[4] and Houk[5] seemingly finished proceeding in this field. Nevertheless, 1,3-dipolar cycloadditions revived in the last few years and were employed for preparations of the required products for further syntheses[6]. Of greatest interest were regioselective cycloadditions of nitrile oxides[7] generally leading to isoxazoles and isoxazolines. Of furan derivatives especially those substituted in β-position are of interest because of their biological activity; the latter are, however, inconveniently accessible by classical methods.

A characteristic feature of some commercial fungicides is the 2,5-dimethyl-3-furyl building block (e.g. Furcarbanil, N-phenyl-2,5-dimethyl-3-furancarboxamide, Furmecyclox, N-cyclohexyl-N-methoxy-2,5-dimethyl-3-furancarboxamide)[8], and therefore, we have made use of products originating from 1,3-dipolar cycloadditions leading to isoxazoles and isoxazolines substituted by the above-mentioned building block. So far, preparation of any 3-furannitrile oxide has not been reported; this paper describes the synthesis of 2,5-dimethyl-3-furannitrile oxide (*IIa*), its reactivity and regioselectivity in 1,3-dipolar cycloadditions to some alkenes and alkynes, and also quantum chemical calculations for *IIa* in comparison with the substituted 2-furannitrile oxides *IIIa*–*IIId* (ref.[9]) and 3-furannitrile oxides *IIb*–*IId*.

2,5-Dimethyl-3-furannitrile oxide (*IIa*) was generated in situ from 2,5-dimethyl-3-

-furancarboxaldoxime (*I*) and sodium hypochlorite under catalysis of triethylamine[10] in the presence of dipolarophiles because the orthodox way involving dehydrochlorination of 2,5-dimethyl-3-furanhydroximic chloride was disadvantageous due to its instability.



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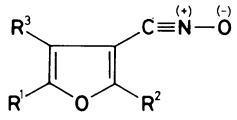
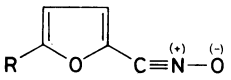
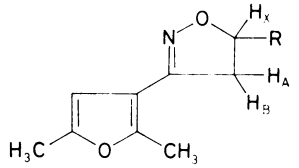


IIa, $R^1 = R^2 = CH_3$; $R^3 = H$
IIb, $R^1 = R^2 = R^3 = CH_3$
IIc, $R^1 = R^2 = R^3 = H$
IId, $R^1 = R^3 = H$; $R^2 = CH_3$



IIIa, R = CH_3
IIIb, R = H
IIIc, R = NO_2
IIId, R = 4-NO_2—C_6H_4

Cycloadditions of the nitrile oxide *IIa* to various alkenes added directly to the mixture where *IIa* was generated in situ were studied in detail; as found, all types of olefins well reacted under like conditions. The reaction with ethyl 2-propenoate, acrylonitrile, chlorovinyl ether, vinyl acetate, styrene, 1-hexene, allyl alcohol, allyl bromide, and 1,1-dichloroethene was regioselective to give 5-substituted 3-(2,5-dimethyl-3-furyl)isoxazolines *IVa*–*IVh* in good to very good yields (Table I). Better yields were obtained when employing more than one equivalent of the dipolarophile.



IVa, R = C_6H_5
IVb, R = $CH_3(CH_2)_3$
IVc, R = CH_2OH
IVd, R = CH_2Br
IVe, R = CN
IVf, R = OCH_2CH_2Cl
IVg, R = $COOC_2H_5$
IVh, R = $OCOCH_3$

The structure of isoxazolines *IVa*–*IVh* was determined by comparing the chemical shift data for H-5 methine and H-4 methylene protons with those published for the analogous 3-phenyl substituted derivatives[11] *IV* and by analyses of the ^{13}C NMR spectra. The individual signals were ascribed by means of *J*-resolved[20] and hetero-correlated[20] NMR spectroscopies (Tables II–IV).

Dipolar cycloadditions to monosubstituted alkenes prevalently led to 5-substituted isoxazolines[12] and only some afforded 4-substituted regioisomers provided a strong electron-accepting group was attached to the alkene. Thus e.g., the reaction of ben-

zenenitrile oxide with methyl 2-propenoate was reported to proceed in a 96 : 4 ratio in favour of the 5-substituted isoxazoline[13]. The FMO theory learns[5] that the 4-substituted regioisomers should be obtained in a higher yield the greater is the interaction of frontier HOMO(dipole)–LUMO(dipolarophile).

TABLE I
Physicochemical data of isoxazolines *IV* and isoxazoles *V*

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found		
			% C	% H	% N
IVa	$C_{15}H_{15}NO_2$	[a]	74·66	6·27	5·80
	(241·3)	52	74·47	6·39	5·69
IVb	$C_{13}H_{19}NO_2$	oil	66·35	8·14	5·95
	(235·2)	53	66·03	7·92	6·14
IVc	$C_{10}H_{12}NO_3$	120—122	61·83	6·22	7·21
	(194·2)	83	61·89	6·39	7·27
IVd	$C_{10}H_{11}BrNO_2$	59—61	46·71	4·30	5·44
	(257·1)	85	46·82	4·48	5·40
IVe	$C_{10}H_{10}N_2O_2$	oil	63·14	5·30	14·72
	(190·2)	84	63·29	5·10	14·61
IVf	$C_{11}H_{13}ClNO_3$	[b]	54·44	5·39	5·77
	(242·7)	78	54·23	5·28	5·71
IVg	$C_{12}H_{15}NO_4$	[c]	60·75	6·36	5·90
	(237·2)	81	60·39	6·25	5·82
IVh	$C_{11}H_{13}NO_4$	oil	59·19	5·87	6·27
	(223·2)	68	58·96	5·93	6·15
Va	$C_{15}H_{13}NO_2$	35—38	75·28	5·48	5·85
	(239·3)	71	75·06	5·27	5·71
Vb	$C_{13}H_{17}NO_2$	oil[f]	67·20	7·35	6·06
	(233·3)	54	67·06	7·12	5·94
Vc	$C_{10}H_{11}NO_3$	115—116	62·67	5·74	7·24
	(193·2)	72	62·43	5·59	7·02
Vd	$C_{10}H_{10}BrNO_2$[d]	83—84	46·89[d]	3·93	5·46
	(256·1)	41	46·38	3·56	5·39
Ve	$C_9H_8ClNO_2$[e]	oil	54·70	4·08	7·08
	(197·6)	51	54·31	3·82	6·98

[a] b.p. 120—130°C/6 Pa; [b] b.p. 100—110°C/6 Pa; [c] b.p. 110—120°C/6 Pa; [d] % Br calculated/found: 31·20/31·12; [e] % Cl calculated/found: 17·94/17·79; [f] b.p. 82—87°C/1 Pa.

Aiming to interprete the course of cycloaddition reactions of nitrile oxide *IIa* on theoretical terms, electronic structures of it and of further model methyl substituted 2- and 3-furannitrile oxides *II*–*III* were examined by the MNDO method[14,15] under a full optimization of geometric parameters. This semiempiric access was backed mainly by the fact that nitrile oxides are generally considered 1,3-dipoles with a zwitterionic character[5], the electronic structure and the reactivity of which could satisfactorily be described by the closed-shell RHF approximation[14,15]; this approximation constitutes the base for the MNDO method. Table V lists the data of selected geometric and energetic parameters of molecules *II*–*III*.

Comparison of the R—C—N valency angles for the particular systems brings evidence for a linear structure of the R—C≡N$^+$—O$^-$ functional group, this being in agreement with the structure as determined for an unsubstituted formonitrile oxide by the ab initio calculations[16]. At the same time, it has been stressed that the linear

TABLE II

^{1}H NMR spectral data (δ, ppm; J, Hz in parentheses) of 3-(2,5-dimethyl-3-furyl)-5-R-substituted isoxazolines *IV*

Compound	CH_3 CH_3	H-4′	H_A (J_{AB})	H_B (J_{BX})	H_X (J_{AX})	Other protons
IVa	2·22 s 2·41 s	6·10 s	3·64 dd (16·2)	3·15 dd (8·30)	5·39 (10·6)	7·33 s (H-arom.)
IVb	2·23 s 2·41 s	6·08 s	3·26 dd (16·3)	2·83 dd (8·16)	4·58 dd (10·2)	0·81–1·60 m (9 H, butyl)
IVc	2·23 s 2·42 s	6·08 s	3·26 dd (16·5)	3·14 dd (7·82)	4·75 dd (10·47)	2·48 s (OH); 3·81 dd 1 H (H_C, J 3·36 Hz); 3·64 dd 1 H (H_D, J 4·68 Hz, J_{CD} 12·1 Hz)
IVd	2·25 s 2·42 s	6·10 s	3·39 dd (16·8)	3·17 dd (6·24)	4·88 dd (10·3)	3·53 dd, 1 H (H_C, J 4·28 Hz); 3·36 dd (H_D, J 8·3 Hz, J_{CD} 10·26 Hz)
IVe	2·22 s 2·40 s	6·09 s	3·67 dd (16·7)	3·56 dd (5·7)	5·34 dd (10·7)	
IVf	2·23 s 2·42 s	6·09 s	— 	 (2·2)	5·63 dd (6·16)	3·02–4·17 m, 6H (H_A, H_B, 2 × CH_2)
IVg	2·23 s 2·43 s	6·08 s	3·51 d	3·51 d (8·9)	5·03 dd (9·30)	1·31 t, 3 H (CH_3); 4·23 q, 2 H (CH_2, J 7·1 Hz)
IVh	2·28 s 2·47 s	6·10 s	3·52 dd (17·4)	3·16 dd (2·4)	6·73 dd (6·40)	2·07 s, 3 H (CH_3)

structure of substituted nitrile oxides can be, to some extent, also due to overrating the repulsion interactions for medium internuclear distances within the MNDO method. The N—O bond distance values indicate a weakening of the multiple bond in comparison with that of H—C≡N$^+$—O$^-$, and consequently, a relatively low π-order of the above-mentioned bond (0·438 – 0·473). The measure of polarization, likewise the absolute magnitude of charges at nitrogen and oxygen, are subject to both substitution and position of the nitrile oxide group at the furan ring.

Cycloadditions of nitrile oxides belong, according to Sustmann's classification[4], to type II, in other words both frontier interactions HOMO(dipole)–LUMO (dipolarophile) and LUMO (dipole)–HOMO (dipolarophile) came into effect. Both electron-donating and electron-accepting substituents in the dipolarophile accelerate the rate of cycloadditions with respect to ethene, whereas substitution at the 1,3--dipole enhanced its nucleophilic or electrophilic character depending on the nature of substituents. This fact was substantiated by energies of the frontier orbitals (Table V) showing energetic changes HOMO and LUMO of molecules *II*–*III* in relation with the substitution when contrasted with those for unsubstituted HCNO.

As follows from values of HOMO and LUMO energies, substitution by a phenyl fragmen (*IIc*, *IIIb*) contributed to lowering of the difference between the frontier orbital values, this being typical of substituents able to undergo conjugation. This approximation becomes more pronounced with 2-furannitrile oxide (*IIIb*) what is in line with the more effective conjugation of the nitrile oxide grouping in position 2 at the furan ring than in position 3. The secondary substitution with electron-accepting nitro (*IIIc*) or 4-nitrophenyl (*IIId*) groups at the furan ring contributes to

TABLE III

^{1}H NMR spectral data (δ, ppm) of 3-(2,5-dimethyl-3-furyl)-5-R-substituted isoxazoles *V*

Compound	CH_3	CH_3	H-4′	H-4	Other protons
Va	2·22 s	2·47 s	6·21 s	6·53 s	6·85—7·68 m, 5 H (H-arom.)
Vb	2·26 s	2·47 s	6·03 s	6·16 s	0·94 t, 3 H (CH_3), 1·27—1·80 m, 4 H (2 · CH_2) 2·75 t, 2 H (CH_2)
Vc	2·21 s	2·28 s	6·16 s	7·99 s	4·23 d, 2 H (CH_2) 6·08 s, 1 H (OH)
Vd	2·36 s	2·47 s	6·52 s	6·73 s	4·47 d, 2 H (CH_2)
Ve[a]	2·25 s	2·45 s	6·12 s	6·22 s	

[a] ^{13}C NMR spectrum: 12·94 q (CH_3), 13·17 q (CH_3), 99·81 d (C-4), 105·08 d (C-4′), 109·58 s (C-3′), 150·65 and 149·89 s (C-2′, C-5′), 153·98 s (C-3), 158·72 s (C-5).

TABLE IV
^{13}C NMR spectral data (δ, ppm) of *IV*

Compound	CH_3	CH_3	C-2′ and C-5′	C-4′	C-3′	C-3	C-4	C-5
IVa[a]	12·99	13·58	150·36 150·31	105·31	111·1	150·9	44·59	81·32
IVb[b]	12·89	13·20	149·56 149·15	104·95	111·2	150·7	40·92	79·7
IVc[c]	13·23	13·76	150·61 150·61	105·44	111·26	152·12	38·04	80·2
IVd[d]	13·12	13·7	150·6 150·8	105·35	110·8	150·96	33·15	78·6
IVe[e]	12·56	13·20	150·7 151·2	104·9	109·2	151·44	41·92	65·52
IVf[f]	12·94	13·52	150·54 150·42	105·2	110·64	151·94	42·60	102·1
IVg[g]	13·41	13·76	150·7 150·36	103·7	110·17	154·57	40·08	76·7
IVh[h]	12·30	12·52	149·1 150·06	105·15	109·5	151·7	42·0	102·56

[a] Aromatic carbons: 128·4, 127·8, 125·6; [b] CH_3 and CH_2: 12·38, 21·9, 27·15, 34·24; [c] CH_2OH: 63·5; [d] CH_2Br: 41·1; [e] C=N: 117·35; [f] CH_2Cl and CH_2O: 43·12, 67·75; [g] CH_3, OCH_2, C=O: 12·82, 61·49, 170·1; [h] CH_3 and C=O: 19·81, 175·38.

a further drop in LUMO energy; an electron-donating substituent (*IIa*, *IIb*, *IId*, *IIIa*) increases nucleophilicity of the 1,3-dipole resulting in a mild enhancement of HOMO energies in comparison with the unsubstituted furannitrile oxides *IIc*, *IIIb*. Analysis of electronic density distribution in frontier orbitals offers a more detailed view on the course and regioselectivity of cycloaddition processes (Table VI). In addition to expansion (atom-orbital) coefficients of 1,3-dipoles and the model dipolarophile ethene also values of an effective overlap of the corresponding orbitals of reacting molecules determined from a simple quantitative relation

$$\gamma = \frac{C_1^{\mathrm{HOMO}} \cdot C_2^{\mathrm{LUMO}} + C_2^{\mathrm{HOMO}} \cdot C_1^{\mathrm{LUMO}}}{E_{\mathrm{HOMO}} - E_{\mathrm{LUMO}}}$$

are listed in Table VI. Comparison of the above-mentioned values showed that the frontier interaction HOMO(dipole)–LUMO(ethene) prevailed, but are not dominant. The absolute overlap magnitude of the proper frontier orbitals indicated an enhanced reactivity of 3-furannitrile oxides *IIa*–*IId*. Substitution by a methyl group lowered the overlap magnitude and therefore, no formation of a 4-substituted isoxazoline could be expected with the cycloaddition of nitrile oxide *IIa* to ethyl 2-propenoate. An electron-accepting substituent at the furyl residue contributed to the electron density in the active centre (*IIIb*, *IIIc*), whilst probably a conjugation effect of the arylfuryl group, dominating over the electron-accepting effect of the nitro group in *IIId* was involved in lowering the overlap values of HOMO and LUMO. The second frontier interaction LUMO (dipole)–HOMO (ethene) values concurrently revealed that the afore-mentioned interaction also noticeably contributed to the cycloaddition with a relatively more remarkable effect of 2-furannitrile oxides *III*.

Similarly, furannitrile oxide *IIa* reacted regioselectively with monosubstituted alkynes to afford 5-substituted isoxazoles *V*. 3-(2,5-Dimethyl-3-furyl)-5-R-substituted isoxazoles (*Vb*–*Vd*) (Table I) were obtained by cycloaddition of *IIa* to propargyl alcohol, propargyl bromide or 1-hexyne in fair yields. Because of lower reactivity of alkynes[3] with respect to alkenes, a 5-fold excess of the dipolarophile was employed in dipolar cycloadditions.

Cycloaddition of *IIa* to phenylacetylene furnished exclusively 5-phenyl-3-(2,5-dimethyl-3-furyl)isoxazole (*Va*) in 71% yield; on the other hand, the alternative 1,3-addition product *VI* (acetylene oxime) described with the reaction with benzenenitrile oxide[3,17,18] was not found nor in the crude reaction mixture. Formation of such oximes was rationalized by an electrophilic attack through carbon atom of the nitrile oxide to the phenylacetylene triple bond[3]. Thus, origination of the 1,3-addition product will rise with the electrophilicity of the 1,3-dipole. As showed the MNDO calculations (Tables V, VI), substitution by two methyl groups in *IIa* resulted in an increase of its nucleophilicity; this well explains, why the 1,3-addition product *VI* did not originate.

TABLE V

Selected MNDO values of geometric and energy parameters of furannitrile oxides *II* and *III*

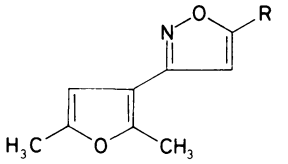
Compound	R–C–N[a]	N–O[b]	N[c]	O[c]	N–O[d]	HOMO[e]	LUMO[a]
IIa	179·8	1·7111	0·268	−0·311	0·4385	−9·1390	−0·3654
IIb	179·5	1·1710	0·288	−0·296	0·4441	−9·0751	−0·5399
IIc	179·6	1·1716	0·268	−0·309	0·4387	−9·2746	−0·2848
IId	179·7	1·1708	0·269	−0·310	0·4393	−9·1906	−0·3667
IIIa	179·5	1·1713	0·289	−0·295	0·4451	−9·0782	−0·5459
IIIb	179·3	1·1701	0·289	−0·296	0·4448	−9·1547	−0·5169
IIIc	179·8	1·1722	0·319	−0·262	0·4732	−10·0289	−1·8520
IIId	179·6	1·1711	0·299	−0·283	0·4539	−9·2449	−1·8187

[a] bond angle, deg; [b] bond length, Å; [c] charge; [d] π-bond order; [e] energy.

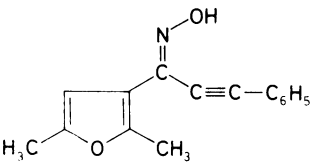
TABLE VI

Orbital coefficients of furannitrile oxides *II* and *III* and overlap of their HOMO and LUMO with ethene

Compound		c_C	c_O	Overlap
IIa	HOMO	0·304	−0·454	0·0512
	LUMO	−0·230	−0·194	0·0306
IIb	HOMO	−0·273	0·423	0·0473
	LUMO	−0·265	−0·223	0·0357
IIc	HOMO	−0·354	0·516	0·0580
	LUMO	−0·259	−0·209	0·0335
IId	HOMO	0·325	−0·480	0·0540
	LUMO	0·241	0·203	0·0320
IIIa	HOMO	−0·279	0·430	0·0481
	LUMO	−0·266	−0·225	−0·0360
IIIb	HOMO	−0·296	0·451	0·0504
	LUMO	0·274	0·230	0·0368
IIIc	HOMO	−0·362	0·498	0·0536
	LUMO	0·137	0·175	0·0265
IIId	HOMO	−0·234	0·365	0·0400
	LUMO	−0·072	−0·094	0·0140



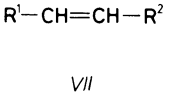
Va, R = C_6H_5
Vb, R = $CH_3(CH_2)_3$
Vc, R = CH_2OH
Vd, R = CH_2Br
Ve, R = Cl



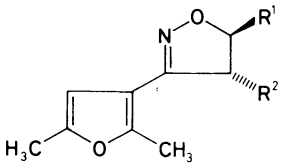
VI

Only 3-(2,5-dimethyl-3-furyl)-5-chloroisoxazole (*Ve*) was isolated in 51% yield from the product when reacting nitrile oxide *IIa* with 1,1-dichloroethene; 3-(2,5-dimethyl-3-furyl)-5,5-dichloroisoxazoline, the precursor of *Ve* was not found. A similar dehydrohalogenation, as a result of the action of bases, was observed with several isoxazolines substituted by bromine or chlorine[19,20] in position 5. The structure of *Ve* was unambiguously evidenced by ^1H and ^{13}C spectral experiments.

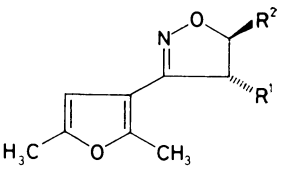
Cycloadditions of nitrile oxide *IIa* to 1,2-disubstituted alkenes *VII* proceeded at the same conditions to give regioisomeric products: with ethyl 2-butenoate (*VIIa*) 5-methylisoxazoline *VIIIa* (71%), and 4-methylisoxazoline *IXa* (29%) in a 75% overall yield and with ethyl 3-phenyl-2-propenoate (*VIIb*) *VIIIb* (70%) and *IXb* (30%) in both cases unseparable mixtures by column chromatography were obtained. Cycloadditions of benzenenitrile oxide to the above-mentioned esters[21] likewise led to 5-substituted derivatives as main products (66 : 34 and 70 : 30, respectively).



VII



VIII



IX

In formulae *VII*, *VIII* and *IX*: *a*, $R^1 = CH_3$; $R^2 = COOC_2H_5$ *b*, $R^1 = C_6H_5$; $R^2 = COOC_2H_5$
c, R^1 = 2-furyl; $R^2 = COOCH_3$ *d*, R^1 = 5-NO_2-2-furyl; $R^2 = COOCH_3$

Cycloaddition of *IIa* to methyl 3-(2-furyl)-2-propenoate (*VIIc*) and 3-(5-nitro-2-furyl)-2-propenoate (*VIId*) surprisingly afforded only 5-substituted isoxazolines *VIIIc* (84%) and *VIIId* (92%); the regioisomeric adducts *IXc* and *IXd* were not detected in the crude mixture by NMR spectroscopy. Structures *VIIIc* and *VIIId* were ascribed on the basis of a high chemical shift value for H-5 (5·90 and 5·93 for *VIIIc* and *VIIId*, respectively), what could be rationalized by a simultaneous shielding

by the heteroatom oxygen and furyl residue. The difference in regioselectivity of these cycloaddition reactions can be explained from the model for HOMO–LUMO interactions of the reacting components[5]. The presence of an electron-accepting group lowers the HOMO and LUMO energies of the dipolarophile what means that the reaction is controlled by a HOMO(*IIa*)–LUMO(dipolarophile) interaction. A regioisomeric transition state in which oxygen (a greater atom-orbital coefficient in HOMO *IIa*) interacts with an R-substituted carbon, and the carbon atom of nitrile oxide *IIa* interacts with that bearing an ethoxycarbonyl residue. R-Furyl and 5-nitro-2-furyl substituents lower the LUMO energies more markedly than the respective phenyl and methyl substituents; as a result, only regioisomers *VIIIc* and *VIIId* were formed.

EXPERIMENTAL

Melting points are uncorrected, the ^{1}H and ^{13}C NMR spectra (δ, ppm; J, Hz) of deuterochloroform solutions containing tetramethylsilane as an internal standard were measured with Jeol JX-100 and Varian VXR-300 instruments, respectively. The IR spectra in KBr (ν, cm^{-1}) were recorded with a Specord 71 IR (Zeiss, Jena) apparatus, and the UV spectra of methanolic solutions (λ, nm; ε, m^2 mol^{-1}) with an M-40 (Zeiss, Jena) spectrophotometer. The reaction course was monitored by thin-layer chromatography on Silufol sheets (chloroform, cyclohexane–ethyl acetate 4 : 1, detection by UV 254 nm light). The products were purified by column chromatography on silica gel (chloroform).

2,5-Dimethyl-3-furancarbaldoxime (*I*)

A solution of hydroxylammonium chloride (0·85 g, 12 mmol) and sodium acetate (1·2 g, 15 mmol) in water (15 ml) was poured into a solution of 2,5-dimethyl-3-furancarbaldehyde[22] (1·25 g, 10 mmol) in methanol (35 ml). The mixture was refluxed for 1 h, cooled, poured into water and the precipitate was crystallized from ethanol–water. Yield of the oxime *I* was 1·3 g (92%), m.p. 122°C. For $C_7H_9NO_2$ (139·1) calculated: 60·42% C, 6·52% H, 10·06% N; found: 60·33% C, 6·63% H, 10·21% N. IR spectrum: 955 (N–O); 1 655 (C=N); 3 320 (OH). UV spectrum: 261 (2·64). ^{1}H NMR spectrum: 2·23 s, 3 H (CH_3); 2·30 s, 3 H (CH_3); 6·19 s, 1 H (H-4); 8·02 s, 1 H (OH); 9·68 s, 1 H (CHO). ^{13}C NMR spectrum: 11·88 q (CH_3), 13·23 q (CH_3), 103·32 d (C-4), 114·50 s (C-3), 143·28 d (CH=N), 152·24 and 151·82 s, s (C-2, C-5).

3-(2,5-Dimethyl-3-furyl)-5-R-isoxazolines *IV* and
3-(2,5-Dimethyl-3-furyl)-5-R-isoxazoles *V*

A solution of 2,5-dimethyl-3-furancarbaldoxime (10 mmol) in dichloromethane (30 ml) was added to a stirred solution of the dipolarophile (50 mmol) in dichloromethane (25 ml), aqueous sodium hypochlorite (12% 15 ml) and triethylamine (0·2 ml) at 0°C during 1 h. The mixture was then stirred at 0°C for 1 h and at room temperature for 18 h. The organic layer was removed and the aqueous one was exhaustively extracted with dichloromethane. The combined organic layers were dried with $MgSO_4$, the solvent was distilled off and the crude product was purified by column chromatography on silica gel, or alternatively by crystallization or distillation under reduced pressure.

Isoxazolines *VIII* and *IX* from *IIa* and Alkenes

Starting from *IIa* and ethyl 2-butenoate (*VIIa*) and employing the above-mentioned procedure the crude product was distilled under diminished pressure b.p. 70–80°C/6 Pa, yield 75%. The *VIIIa* to *IXa* ratio was 71 : 29 (^{1}H NMR). For $C_{13}H_{17}NO_4$ (251·3) calculated: 52·14% C, 6·81% H, 5·57% N; found: 61·71% C, 7·35% H, 5·01% N. The ^{1}H NMR spectrum for *VIIIa*: 6·03 s, 1 H (H-4'); 4·95 m, 1 H (H-5, *J*(4, 5) 6·1 Hz); 4·18 d (H-4); 4·12 q, 2 H (OCH_2); 2·44 s, 3 H (CH_3); 2·29 s, 3 H (CH_3); 1·11–1·45 m, 6 H (2 × CH_3); for *IXa*: 6·03 s, 1 H (H-4'); 4·65 d. 1 H (H-5, *J*(4, 5) 4·1 Hz); 4·12 ,q 2 H (OCH_2); 3·86 m, 1 H (H-4); 2·44 s, 3 H (CH_3); 2·29 s, 3 H (CH_3); 1·11–1·45 m, 6 H (2 × CH_3).

The 70 : 30 mixture of *VIIIb* and *IXb* was obtained analogously from *IIa* and ethyl 2-phenyl-3--propenoate (*VIIb*), (b.p. 80–85°C/1 Pa), yield 72%. For $C_{18}H_{19}NO_4$ (313·4) calculated: 68·99% C, 6·11% H, 4·46% H; found: 69·45% C, 5·81% H, 4·85% N. The ^{1}H NMR spectrum for *VIIIb*: 7·35 s, 5 H (H-arom); 6·03 s, 1 H (H-4'); 5·90 d, 1 H (H-5, *J*(4, 5) 6·4 Hz); 4·11 to 4·39 m, 3 H (H-4, OCH_2); 2·45 s, 3 H (CH_3); 1·33 t, 3 H (CH_3); for *IXb*: 7·35 s, 1 H (H-arom); 5·82 s, 1 H (H-4'); 4·82 s, 2 H (H-5, H-4); 4·11–4·39 q, 2 H (OCH_2); 2·37 s, 3 H (CH_3); 2·11 s, 3 H (CH_3); 1·25 t, 3 H (CH_3).

Methyl 3-(2,5-dimethyl-3-furyl)-5-(2-furyl)-4,5-dihydroisoxazole-4-carboxylate (VIIIc) *from IIa* and methyl 3-(2-furyl)-2-propenoate (*VIIc*), colourless viscous oil, 84%, b.p. 75–80°C/1 Pa. For $C_{15}H_{15}NO_5$ (289·3) calculated: 62·27% C, 5·23% H, 4·84% N; found: 62·48% C, 5·48% H, 5·24% N. ^{1}H NMR spectrum: 7·55 d, 1 H (H-5', *J*(4', 5') 2·0 Hz); 7·28 dd, 1 H (H-4'); 6·66 d, 1 H (H-3', *J*(3', 4') 3·5 Hz); 6·13 s, 1 H (H-4'); 5·90 d, 1 H (H-5, *J*(4, 5) 6·5 Hz); 4·71 d, 1 H (H-4); 3·81 s, 3 H ($COOCH_3$); 2·51 s, 3 H (CH_3); 2·28 s, 3 H (CH_3).

Methyl 3-(2,5-dimethyl-3-furyl)-5-(5-nitro-2-furyl)-4,5-dihydroisoxazole-4-carboxylate (VIIId) from *IIa* and methyl 3-(5-nitro-2-phenyl)-2-propenoate (*VIId*); yield 92%, m.p. 96–98°C. For $C_{15}H_{14}N_2O_7$ (334·3) calculated: 53·89% C, 4·22% H, 8·37% N; found: 54·25% C, 4·08% H, 8·59% N. ^{1}H NMR spectrum: 7·32 d, 1 H (H-4'); 6·67 d, 1 H (H-3', *J*(3', 4') 3·5 Hz); 6·08 s, 1 H (H-4'); 5·93 d, 1 H (H-5, *J*(4, 5) 5·3 Hz); 4·54 d, 1 H (H-4); 3·80 s, 3 H ($COOCH_3$); 2·47 s, 3 H (CH_3); 2·25 s, 3 H (CH_3).

REFERENCES

1. Huisgen R., Christl M.: Chem. Ber. *106*, 3291 (1973).
2. Huisgen R.: J. Org. Chem. *41*, 403 (1976).
3. Quilico A., Stagno d Alcontres G., Grünanger P.: Gazz. Chim. Ital. *80*, 479 (1950).
4. Sustmann R.: Pure Appl. Chem. *40*, 569 (1974).
5. Houk K. N., Sims J., Watts C. R., Luskus L. J.: J. Am. Chem. Soc. *95*, 7301 (1973).
6. Kozikowski A. P.: Acc. Chem. Res. *17*, 410 (1984).
7. Caramella P., Grünanger P. in: *1,3-Dipolar Cycloaddition Chemistry* (A. Padwa, Ed.), Vol. I, p. 291. Wiley, New York 1984.
8. Matocsy G., Nádasy M., Andriska V.: *Pesticide Chemistry*. Akadémiai Kiadó, Budapest 1988.
9. Jedlovská E., Fišera Ľ., Kováč J.: Chem. Papers *42*, 823 (1988).
10. Lee G. A.: Synthesis *1982*, 508.
11. Sustmann R., Huisgen R., Huber H.: Chem. Ber. *100*, 1802 (1967).
12. Bast K., Christl M., Huisgen R., Mack W., Sustmann R.: Chem. Ber. *106*, 3258 (1973).
13. Christl M., Huisgen R., Sustmann R.: Chem. Ber. *106*, 3275 (1973).
14. Dewar M. J. S., Thiel W. J.: J. Am. Chem. Soc. *99*, 4899 (1977).

15. Dewar M. J. S., Thiel W. J.: Theor. Chim. Acta *46*, 89 (1977).
16. Komornicky A., Goddard J. D., Schaefer H. F.: J. Am. Chem. Soc. *102*, 1763 (1980).
17. Morocchi S., Ricca A., Zanarotti A., Bianchi G., Gandolfi R., Grünanger P.: Tetrahedron Lett. *1969*, 3329.
18. Beltrame P., Sartirana P., Vintani C.: J. Chem. Soc., B *1971*, 814.
19. Tsuge O., Kanemasa S., Suga H., Nakagawa N.: Bull. Chem. Soc. Jpn. *60*, 2463 (1987).
20. Minami S., Matsumoto J.: Chem. Pharm. Bull. *15*, 366 (1967).
21. Christl M., Huisgen R.: Chem. Ber. *106*, 3345 (1973).
22. Bisagni F., Lhoste J. M., Nguyen Ch. H.: Bull. Soc. Chim. Fr. *1981*, 755.

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