2,5-DIMETHOXY-2,5-DIHYDROFURANS IN 1,3-DIPOLAR CYCLOADDITION REACTIONS

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It is shown that 2,5-dimethoxy-2,5-dihydrofurans enter into 1,3-dipolar cycloaddition with benzonitrile N-oxides and with diphenylnitrilimines to form derivatives of 1,3-dimethoxy-6-phenyl-1,3,3a,6a-tetrahydrofuro[3,4-d]isoxazole and 1,3-dimethoxy-4,6-diphenyl-1,3,3a,-6a-tetrahydrofuro[3,4-d]pyrazole, respectively.

Furan and dihydrofurans are capable of acting as the dipolarophile in reactions with benzonitrile N-oxides and diphenylnitrilimines [1-3].

We have found that 2,5-dimethoxy-2,5-dihydrofuran reacts with benzonitrile N-oxides and diphenylnitrilimines to give, respectively, derivatives of 1,3-dimethoxy-6-phenyl-1,3,3a,6a-tetrahydrofuro[3,4-d]-isoxazole and 1,3-dimethoxy-4,6-diphenyl-1,3,3a,6a-tetrahydrofuro[3,4-d]pyrazole in satisfactory yields. Methoxylated α-methylfuran and 2,5-dimethylfuran do not react under similar conditions. However, 2,5-dimethoxy-2-carbomethoxy-2,5-dihydrofuran forms adducts in low yields. The yields and analytical data for the compounds obtained are presented in Table 1.

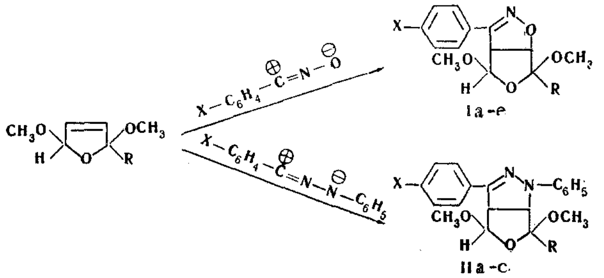

TABLE 1

Compound	X	R	mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
					C	H	N	C	H	N	
I a	H	H	86—86,5[1]	$C_{13}H_{15}NO_4$	62,60	5,78	5,74	62,65	6,02	5,62	50
I b	Br	H	134—135[1]	$C_{13}H_{14}N_2O_6$	47,63	4,27	4,47	47,58	4,30	4,26	61
I c	NO_2	H	185—186[2]	$C_{13}H_{14}NO_4Br$	52,91	4,91	9,61	53,06	4,79	9,52	63
I d	H	$COOCH_3$	162—163[1]	$C_{15}H_{17}NO_6$	58,65	5,67	4,71	58,62	5,52	4,56	11
I e	NO_2	$COOCH_3$	189—190[2]	$C_{15}H_{16}N_2O_8$	51,22	4,79	7,83	51,14	4,57	7,95	15
II a	H	H	170—170,5[3]	$C_{19}H_{20}N_2O_3$	70,51	6,27	9,00	70,36	6,22	8,64	62
II b	Br	H	164—165[3]	$C_{19}H_{19}N_2O_3Br$	56,70	4,92	6,86	56,58	4,75	6,95	62
II c	H	$COOCH_3$	174—174,5[3]	$C_{21}H_{22}N_2O_5$	66,19	6,09	7,41	65,94	5,80	7,33	35

[1] From petroleum ether.
[2] From benzene–petroleum ether.
[3] From alcohol.

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EXPERIMENTAL

Tetrahydrofuroisoxazoles. A) A solution of 0.03 mole of triethylamine in absolute ether was added slowly to a refluxing solution of 0.02 mole of dimethoxydihydrofuran and 0.02 mole of benzohydroxamyl chloride [4] in absolute ether. The mixture was refluxed for another hour and allowed to stand overnight. The precipitate of triethylamine hydrochloride was removed by filtration, the solvent was removed in vacuo, and Ia and Id were obtained after prolonged standing (10-20 h). Diphenylfuroxan (mp 114-115 deg) was isolated by subsequent freezing out.

B) p-Bromo- [5] or p-nitrobenzonitrile N-oxide [6] (0.001 mole) was mixed with 0.008 mole of dimethoxydihydrofuran, 5 ml of absolute ether was added to completely dissolve them, and the mixture was refluxed for 2 h, after which it was allowed to stand for a day. After removal of the solvent by distillation, the corresponding tetrahydrofuroisoxazole (Ib,c,e) crystallized out in the course of several hours.

Tetrahydrofuropyrazoles (IIa-c). Triethylamine (0.02 mole) was added rapidly to a solution of 0.01 mole of N^1-α-chlorobenzylidenephenylhydrazine [7] and 0.03 mole of dimethoxydihydrofuran in 30 ml of absolute benzene. The reaction mixture was refluxed for 4-8 h and allowed to stand overnight. The corresponding tetrahydrofuropyrazole was obtained after removal of the triethylamine salt and removal of the solvent by distillation.

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