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Heterocyclizations of Functionalized Heterocumulenes with C,N- and C,O-Dinucleophiles: III.* Cyclization of *N*-(1-Aryl-1-chloro-2,2,2-trifluoroethyl)-*N'*-arylcarbodiimides with 3-Substituted 1-Phenylpyrazol-5-ones

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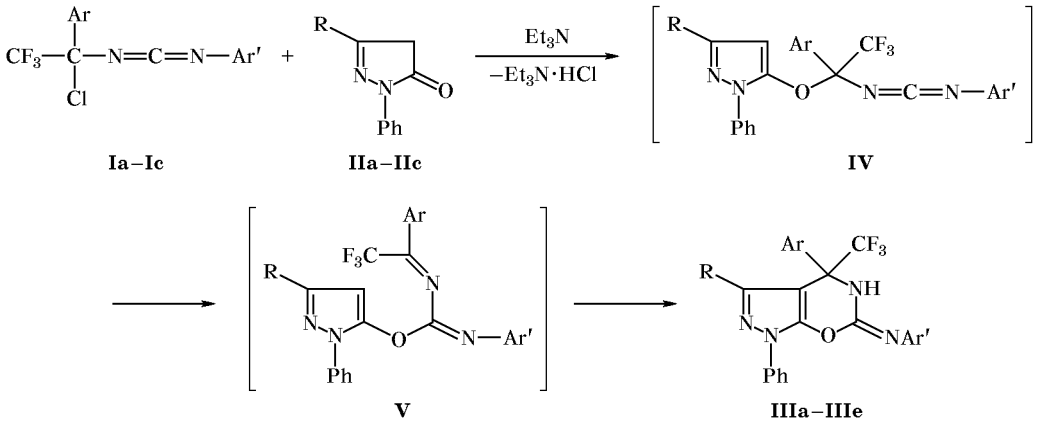
Abstract—Cyclization of *N*-(1-aryl-1-chloro-2,2,2-trifluoroethyl)-*N'*-arylcarbodiimides with 3-substituted 1-phenylpyrazol-5-ones yields 6-aryl-4-arylimino-1-phenyl-6-trifluoromethyl-1,4,5,6-tetrahydropyrazolo-[4,3-*e*][1,3]oxazines.

N-(1-Chloroalkyl)carbodiimides are used as 1,3-dielectrophilic components in the synthesis of various nitrogen-containing heterocyclic compounds [2, 3]. In particular, we previously showed that condensation of these reagents with 1,3-diketones (which act as O,C-dinucleophiles) yields 1,3-oxazine derivatives [4].

With the goal of synthesizing relatively difficultly accessible fused pyrazolo[4,3-*e*][1,3]oxazine systems [5], in the present work we examined reactions of *N*-(1-aryl-1-chloro-2,2,2-trifluoroethyl)-*N'*-arylcarbodiimides **Ia**–**Ic** with such O,C-dinucleophiles as 3-substituted 1-phenylpyrazol-5-ones **IIa**–**IIc**. We have found that *N*-(1-chloroalkyl)carbodiimides **Ia**–**Ic** react with 1-phenylpyrazol-5-ones **IIa**–**IIc** containing an electron-acceptor substituent R in position *3* to afford 3-R-4-aryl-6-arylimino-1-phenyl-4-trifluoromethyl-1,4,5,6-tetrahydropyrazolo[4,3-*e*][1,3]oxazines **IIIa**–**IIIe** (Scheme 1). The reactions occur in benzene in the presence of triethylamine at room temperature and take 3 days.

Scheme 1.



I, Ar = Ar′ = Ph (**a**); Ar = Ph, Ar′ = 4-MeC_6H_4 (**b**); Ar = 4-$MeOC_6H_4$, Ar′ = 4-MeC_6H_4 (**c**); **II**, R = CF_3 (**a**), MeOC(O) (**b**), EtOC(O) (**c**); **III**, R = CF_3, Ar = Ar′ = 4-MeC_6H_4 (**a**); R = MeOC(O), Ar′ = 4-MeC_6H_4, Ar = Ph (**b**); R = MeOC(O), Ar = 4-MeC_6H_4 (**c**); R = EtOC(O), Ar = Ar′ = Ph (**d**); R = EtOC(O), Ar = 4-$MeOC_6H_4$, Ar′ = 4-MeC_6H_4 (**e**).

* For communication II, see [1].

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Table 1. Yields, melting points, and elemental analyses of 4-aryl-6-arylimino-1-phenyl-4-trifluoromethyl-1,4,5,6-tetrahydropyrazolo[4,3-*e*][1,3]oxazines **IIIa**–**IIIe**

Comp. no.	Yield, %	mp, °C	Found, %				Formula	Calculated, %			
			C	H	N	Cl		C	H	N	Cl
IIIa	46	192–193	61.39	3.74	10.70	21.32	$C_{27}H_{20}F_6N_4O$	61.13	3.80	10.56	21.49
IIIb	47	222–223	64.76	4.36	10.81	11.45	$C_{27}H_{21}F_3N_4O_3$	64.03	4.18	11.06	11.25
IIIc	45	201–202	62.28	4.41	10.15	10.34	$C_{28}H_{23}F_3N_4O_4$	62.68	4.32	10.44	10.62
IIId	50	184–185	63.74	4.32	10.99	11.50	$C_{27}H_{21}F_3N_4O_3$	64.03	4.18	11.06	11.25
IIIe	53	167–168	63.07	4.45	10.38	10.14	$C_{29}H_{25}F_3N_4O_4$	63.27	4.58	10.18	10.35

Table 2. IR and NMR spectral parameters of 4-aryl-6-arylimino-1-phenyl-4-trifluoromethyl-1,4,5,6-tetrahydropyrazolo-[4,3-*e*][1,3]oxazines **IIIa**–**IIIe**

Comp. no.	IR spectrum (KBr), ν, cm^{-1}		^1H NMR spectrum, δ, ppm (*J*, Hz)	^{19}F NMR spectrum, δ_F, ppm
	C=N	N–H		
IIIa	1693	3450	2.32 s (3H, CH_3), 2.25 s (3H, CH_3), 7.05 d (2H, *J* = 8.1), 7.16 d (2H, *J* = 7.8), 7.34 d (2H, *J* = 7.8), 7.47 d (2H, *J* = 8.4), 7.51 d (1H, *J* = 7.5), 7.62 t (2H, *J* = 8.1), 7.92 d (2H, *J* = 8.01), 9.75 s (1H, NH)	–60.98, –74.41
IIIb	1690 1700[a]	3435	2.26 s (3H, CH_3), 3.58 s (3H, CH_3O), 7.05 d (2H, *J* = 8.01), 7.33 m (5H, H_{arom}), 7.60 t (2H, *J* = 8.0), 7.94 d (1H, *J* = 8.1), 9.63 s (1H, NH)	–74.45
IIIc	1685 1700[a]	3390	2.28 s (3H, CH_3), 3.66 s (3H, CH_3OCO), 3.77 s (3H, CH_3O), 6.82 d (2H, *J* = 8.7), 7.04 d (2H, *J* = 8.3), 7.48 m (5H, H_{arom}), 7.57 t (2H, *J* = 7.9), 7.97 d (2H, *J* = 8.3), 9.56 s (1H, NH)	–74.90
IIId	1690 1700[a]	3290	1.06 s (3H, CH_3, *J* = 7.2), 4.03 q (2H, CH_2O, *J* = 7.2), 6.97 t (1H, *J* = 7.2), 7.31 m (5H, H_{arom}), 7.53 m (7H, H_{arom}), 7.93 d (2H, *J* = 8.1), 9.8 s (1H, NH)	–73.74
IIIe	1695 1700[a]	3310	1.13 t (3H, CH_3, *J* = 7.1), 2.26 s (3H, $CH_3C_6H_4$), 3.76 s (3H, CH_3O), 4.09 q (2H, *J* = 7.1), 6.84 d (2H, *J* = 8.7), 7.05 d (2H, *J* = 8.4), 7.47 m (5H, H_{arom}), 7.60 t (2H, *J* = 8.0), 7.94 d (1H, *J* = 8.1), 9.63 s (1H, NH)	–74.45

[a] $\nu_{C=O}$.

Most probably, the reaction begins with attack by the more electrophilic α-carbon atom in 1-chloroalkylcarbodiimides **I** on the oxygen atom of pyrazol-5-ones **II** to give 1-(5-pyrazolyloxy)alkylcarbodiimides **IV** (cf. [3]) which then undergo rearrangement into intermediates **V** having a 2,4-diaza-1,3-diene structure. Cyclization of the latter occurs even at room temperature via attack by the highly electrophilic C=N carbon atom on the π-electron-rich C^4 carbon atom of the pyrazole ring. The proposed reaction sequence is supported by the IR and ^{19}F NMR spectra of the reaction mixture, which were recorded immediately after quantitative separation of triethylamine hydrochloride. In the ^{19}F NMR spectra we observed signals from CF_3 groups in intermediates **IV** and **V** at δ_F –81 ppm [4] and –68 ppm [6], respectively, which had almost equal intensities. The IR spectra contained absorption bands due to N=C=N fragment at 2160–2170 cm^{-1} and C=N bond at 1650–1660 cm^{-1}. The above ^{19}F NMR signals and IR bands disappeared on prolonged storage of the mixture (72 h at 25°C) or on heating for 2 h in benzene under reflux.

4-Aryl-6-arylimino-1-phenyl-4-trifluoromethyl-1,4,5,6-tetrahydropyrazolo[4,3-*e*][1,3]oxazines **IIIa**–**IIIe** (Tables 1, 2) are colorless high-melting crystalline substances. Their structure was proved by the IR

and ^1H and ^{19}F NMR spectra. In the IR spectra of **IIIa**–**IIIe** absorption bands due to exocyclic imino groups and endocyclic NH groups were present in the regions 1685–1695 and 3290–3450 cm^{-1}, respectively. Compounds **IIIa**–**IIIe** characteristically showed in the ^{19}F NMR spectra a singlet from the CF_3 group at δ_F –73.7 to –74.9 ppm, indicating that this group is linked to the C–**C**–N fragment [7]. Fusion at C^4 of the pyrazole ring is consistent with the ^1H NMR spectra which lack signal from proton in that position but contain a singlet at δ 9.56–9.75 ppm from the NH proton.

EXPERIMENTAL

The IR spectra of samples prepared as KBr pellets were recorded on a UR-20 spectrometer. The ^1H NMR spectra of solutions in DMSO-d_6 were measured on a Varian Gemini spectrometer at 300 MHz using HMDS as internal reference. The ^{19}F NMR spectra were obtained from solutions in DMSO-d_6 using a Varian Gemini instrument (188.28 MHz); CCl_3F was used as internal reference.

1-Chloroalkylcarbodiimides **Ia**–**Ic** were synthesized by the procedure reported in [7].

4-Aryl-6-arylimino-3-R-1-phenyl-4-trifluoromethyl)-1,4,5,6-tetrahydropyrazolo[4,3-*e*][1,3]oxazines IIIa–IIIe. A mixture of 0.005 mol of 1-chloroalkylcarbodiimide **Ia**–**Ic**, 0.005 mol of 1-phenylpyrazol-5-one **IIa**–**IIc**, and 0.006 mol of triethylamine in 20 ml of benzene was stirred for 2 h at room temperature, the precipitate of triethylamine hydrochloride was filtered off, the filtrate was heated for 2 h under reflux or was left to stand for 72 h. After removal of the solvent, the residue was recrystallized from 2-propanol–hexane (3 : 1).

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