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Reaction of Allyl Phenylcarbamate with Benzaldehyde Oximes in the Presence of *N*-Chlorobenzenesulfonamide Sodium Salt

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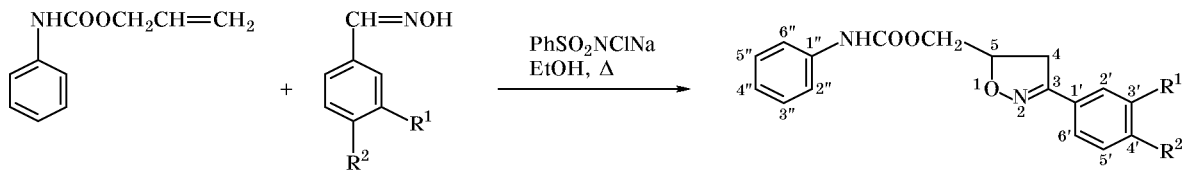
Abstract—Allyl phenylcarbamate reacts with benzaldehyde oxime and ring-substituted benzaldehyde oximes in ethanol in the presence of *N*-chlorobenzenesulfonamide sodium salt to give the corresponding 3-aryl-5-(phenylcarbamoyloxymethyl)-4,5-dihydroisoxazoles.

Chloramine-T and other related *N*-halogen reagents are widely used in organic syntheses [1]. Hassner and Rei [2] proposed a procedure for preparation of nitrile oxides from some aliphatic and aromatic aldehyde oximes using *N*-chloro-4-methylbenzenesulfonamide sodium salt (Chloramine-T). This procedure was succesfully applied to generation of nitrile oxides *in situ* with subsequent cycloaddition to olefins; as a result, 4,5-dihydroisoxazoles were obtained in fairly high yields (up to 80%). However, the synthetic potential of the proposed method was demonstrated on a limited number of aldehyde oximes: only 3,4,5-trimethoxybenzaldehyde oxime, *p*-methoxybenzaldehyde oxime, and butanal oxime were involved. Moreover, there are no sufficient published data on the effect of substituent at the double bond of olefin on the regioselectivity of cycloaddition. It is known [3] that reactions of nitrile oxides with terminal alkenes provide an example of highly regioselective 1,3-dipolar cycloaddition resulting in formation of 3,5-disubstituted 4,5-dihydroisoxazoles. When a strong electron-acceptor substituent (such as CO_2Alk, SO_2R, or CF_3 group) is present at the double bond, the yield of 3,4-disubstituted 4,5-dihydroisoxazoles is as low as 4–7%. The data of [4, 5] also count in favor of high regioselectivity of the process.

In continuation of our studies on the synthesis of new polyfunctional heterocyclic carbamate derivatives [6], in the present work we examined reactions of allyl phenylcarbamate (**I**) with benzaldehyde oxime (**IIa**), 4-methoxybenzaldehyde oxime (**IIb**), 3,4-methylenedioxybenzaldehyde oxime (**IIc**), 4-chlorobenzaldehyde oxime (**IId**), 4-bromobenzaldehyde oxime (**IIe**), 3-nitrobenzaldehyde oxime (**IIf**), and 4-nitrobenzaldehyde oxime (**IIg**) in the presence of *N*-chlorobenzenesulfonamide sodium salt (Chloramine-B). The reactions were carried out in boiling ethanol for 6 h.

The structure of the products was established on the basis of their IR, ^1H and ^{13}C NMR, and mass spectra. It was found that the cycloaddition of substituted (as well as of unsubstituted) benzonitrile oxides to the allyl group of **I** is strictly regioselective; as a result, the corresponding 3-aryl-5-(phenylcarba-

Scheme 1.



I **IIa–IIg** **IIIa–IIIg**

II, **III**: $R^1 = R^2 = H$ (**a**); $R^1 = H$, $R^2 = OMe$ (**b**); $R^1R^2 = OCH_2O$ (**c**); $R^1 = H$, $R^2 = Cl$ (**d**); $R^1 = H$, $R^2 = Br$ (**e**); $R^1 = NO_2$, $R^2 = H$ (**f**); $R^1 = H$, $R^2 = NO_2$ (**g**).

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Table 1. Yields, melting points, and elemental analyses of 3-aryl-5-(phenylcarbamoyloxymethyl)-4,5-dihydroisoxazoles **IIIa**–**IIIg**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIIa	87	149	69.29	5.13	9.87	$C_{17}H_{16}N_2O_3$	68.92	5.41	9.46
IIIb	92	143	65.98	6.01	8.72	$C_{18}H_{18}N_2O_4$	66.26	5.52	8.59
IIIc	83	150	63.11	5.08	7.89	$C_{18}H_{16}N_2O_5$	63.53	4.71	8.24
IIId	86	159	61.02	4.81	8.13	$C_{17}H_{15}N_2O_3Cl$	61.73	4.54	8.47
IIIe	85	172	54.12	4.42	7.36	$C_{17}H_{15}N_2O_3Br$	54.40	4.00	7.47
IIIf	89	165	59.29	4.11	11.83	$C_{17}H_{15}N_3O_5$	59.82	4.40	12.32
IIIg	90	192	59.34	4.62	12.16	$C_{17}H_{15}N_3O_5$	59.82	4.40	12.32

Table 2. IR and ^{1}H NMR spectra of 3-aryl-5-(phenylcarbamoyloxymethyl)-4,5-dihydroisoxazoles **IIIa**–**IIIg**

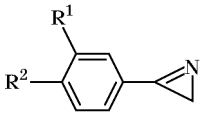
Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm
IIIa	3300 (NH), 1740 (C=O), 1610, 1570 (C=C_{arom})	8.51 br.s (1H, NH), 7.21–7.32 m (10H, H_{arom}), 4.90 m (1H, 5-H), 4.20 m (2H, OCH_2), 3.39 d.d (1H, 4-H, *J* = 12, 10 Hz), 3.18 d.d (1H, 4-H, *J* = 9.8, 8.5 Hz)
IIIb	3405 (NH), 1730 (C=O), 1620, 1610, 1550 (C=C_{arom})	8.51 br.s (1H, NH), 7.51 d (2H, 2″-H, 6″-H, *J* = 10 Hz), 7.44 d (2H, 2′-H, 6′-H, *J* = 9 Hz), 7.16 t (2H, 3″-H, 5″-H, *J* = 6.5 Hz), 6.91 t (1H, 4″-H, *J* = 6.5 Hz), 6.85 d (2H, 3′-H, 5′-H, *J* = 10 Hz), 4.83 m (1H, 5-H), 4.18 m (2H, OCH_2), 3.78 s (3H, OCH_3), 3.37 d.d (1H, 4-H, *J* = 12, 10 Hz), 3.13 d.d (1H, 4-H, *J* = 9.7, 8.5 Hz)
IIIc	3340 (NH), 1700 (C=O), 1620, 1558 (C=C_{arom})	8.57 br.s (1H, NH), 7.43 d (2H, 2″-H, 6″-H, *J* = 9 Hz), 7.18 d (2H, 3″-H, 5″-H, *J* = 9 Hz), 7.15 s (1H, 2′-H), 7.02 d (1H, 6′-H, *J* = 9 Hz), 6.91 t (1H, 4″-H, *J* = 6.1 Hz), 6.77 d (1H, 5′-H, *J* = 9 Hz), 5.97 s (2H, OCH_2O), 4.85 m (1H, 5-H), 4.18 m (2H, OCH_2), 3.39 d.d (1H, 4-H, *J* = 12, 10 Hz), 3.14 d.d (1H, 4-H, *J* = 9.7, 8.5 Hz)
IIId	3415 (NH), 1735 (C=O), 1620, 1555 (C=C_{arom})	8.24 br.s (1H, NH), 7.63 d (2H, 2″-H, 6″-H, *J* = 10 Hz), 7.43 d (2H, 3′-H, 5′-H, *J* = 10 Hz), 7.36 d (2H, 2″-H, 6″-H, *J* = 10 Hz), 7.17 t (2H, 3″-H, 5″-H, *J* = 6.3 Hz), 6.86 t (1H, 4″-H, *J* = 6.3 Hz), 4.91 m (1H, 5-H), 4.20 m (2H, OCH_2), 3.43 d.d (1H, 4-H, *J* = 13.3, 10 Hz), 3.20 d.d (1H, 4-H, *J* = 9.7, 8.5 Hz)
IIIe[a]	3405 (NH), 1730 (C=O), 1620, 1575, 1560 (C=C_{arom})	8.52 br.s (1H, NH), 7.54 d (2H, 3′-H, 5′-H, *J* = 6 Hz), 7.52 d (2H, 2′-H, 6′-H, *J* = 6 Hz), 7.44 d (2H, 2″-H, 6″-H, *J* = 7 Hz), 7.17 t (2H, 3″-H, 5″-H, *J* = 6.1 Hz), 6.92 t (1H, 4″-H, *J* = 6.1 Hz), 4.91 m (1H, 5-H), 4.20 m (2H, OCH_2), 3.43 d.d (1H, 4-H, *J* = 13.3, 10 Hz), 3.19 d.d (1H, 4-H, *J* = 9.7, 8.5 Hz)
IIIf	3300 (NH), 1730 (C=O), 1605, 1540 (C=C_{arom}), 1530, 1355 (NO_2)	8.69 br.s (1H, NH), 7.59–7.62 m (4H, 2′-H, 4′-H, 5′-H, 6′-H), 7.38 d (2H, 2″-H, 6″-H, *J* = 7 Hz), 7.17 t (2H, 3″-H, 5″-H, *J* = 6.1 Hz), 6.90 t (1H, 4″-H, *J* = 6.1 Hz), 4.90 m (1H, 5-H), 4.19 m (2H, OCH_2), 3.41 d.d (1H, 4-H, *J* = 11.5, 10 Hz), 3.19 d.d (1H, 4-H, *J* = 9.8, 8.5 Hz)
IIIg	3400 (NH), 1735 (C=O), 1610, 1600, 1580 (C=C_{arom}), 1530, 1355 (NO_2)	8.57 br.s (1H, NH), 7.72 d (2H, 2′-H, 6′-H, *J* = 10 Hz), 7.58 d (2H, 3′-H, 5′-H, *J* = 10 Hz), 7.34 d (2H, 2″-H, 6″-H, *J* = 10 Hz), 7.17 t (2H, 3″-H, 5″-H, *J* = 6.3 Hz), 6.87 t (1H, 4″-H, *J* = 6.3 Hz), 4.92 m (1H, 5-H), 4.18 m (2H, OCH_2), 3.39 d.d (1H, 4-H, *J* = 11.2, 10 Hz), 3.15 d.d (1H, 4-H, *J* = 9.8, 8.5 Hz)

[a] ^{13}C NMR spectrum, δ_C, ppm: 37.14 (C^4), 65.98 (OCH_2), 80.21 (C^5), 119.31 ($C^{2''}$, $C^{6''}$), 123.65 ($C^{4''}$), 129.38 ($C^{4'}$), 129.70 ($C^{3''}$, $C^{5''}$), 130.13 ($C^{2'}$, $C^{6'}$), 132.78 ($C^{3'}$, $C^{5'}$), 140.11 ($C^{1''}$), 154.27 (C=N), 156.50 (C=O).

moyloxymethyl)-4,5-dihydroisoxazoles **IIIa**–**IIIg** are formed (Scheme 1). Their yields, melting points, elemental analyses, and IR and ^{1}H NMR spectral parameters are collected in Tables 1 and 2. It should be noted that only one isomer was detected by ^{1}H NMR among the cycloadditions products.

The structure of compounds **IIIa**–**IIIg** as 3,5-disubstituted 4,5-dihydroisoxazoles rather than the corresponding 3,4-disubstituted isomers follows from the ^{1}H NMR and mass spectra and also from the ^{13}C NMR spectra recorded for compounds **IIIb** and **IIIe**. In the ^{1}H NMR spectra of **IIIa**–**IIIg** we observed a multiplet at δ 4.8–4.9 ppm which belongs to 5-H of the isoxazole ring. The downfield shift of this signal relative to its usual position [7] can be explained by deshielding effect of the isoxazole oxygen atom. The structure of **IIIb** and **IIIe** is additionally confirmed by the ^{13}C NMR spectra, δ_C, ppm: **IIIb**: 37.64 (C^4), 65.79 (OCH_2), 55.79 (OCH_3), 79.44 (C^5), 115.01 ($C^{3'}$, $C^{5'}$), 119.29 ($C^{2''}$, $C^{6''}$), 123.30 ($C^{1'}$), 123.62 ($C^{4''}$), 129.31 ($C^{3''}$, $C^{5''}$), 129.68 ($C^{2'}$, $C^{6'}$), 140.13 ($C^{1''}$), 154.31 (C=N), 156.62 (C=O), 162.09 ($C^{4'}$). The ^{13}C chemical shifts of **IIIe** are given in Table 3. The observed spectral pattern is consistent with published data for structurally related compounds [1, 8, 9].

Analysis of the mass spectra of dihydroisoxazoles **IIIa**–**IIIg** revealed some general relations holding in the fragmentation of their molecular ions under electron impact. All compounds **IIIa**–**IIIg** showed in the spectra the molecular ion peaks whose abundance ranges from 2 to 19%. The presence of strong ion peaks with *m*/*z* 177 (**IIIa**), 207 (**IIIb**), 221 (**IIIc**), 211.5 (**IIId**), 256 (**IIIe**), and 222 (**IIIf**, **IIIg**) in addition to the fragment ion peak with *m*/*z* 119 indicates that the fragmentation of **IIIa**–**IIIg** begins with elimination of phenyl isocyanate from the molecular ion. On the other hand, the mass spectra of **IIIa**–**IIIg** contain peaks of ions with *m*/*z* values of 117 (**IIIa**), 147 (**IIIb**), 161 (**IIIc**), 151.5 (**IIId**), 183 (**IIIe**), and 162 (**IIIf**, **IIIg**). Taking into account the data of [10], these ions correspond to 2-arylazirine species **A**.

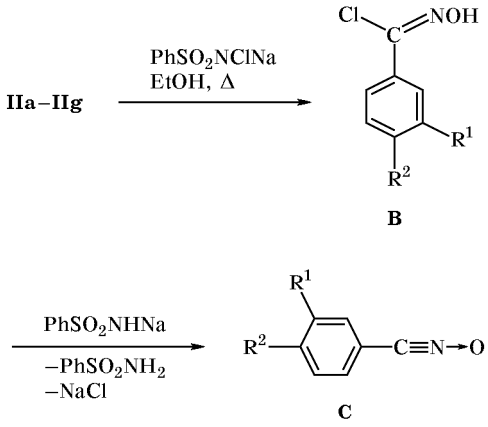


A

This fragmentation pathway provides an additional support for the structure of **IIIa**–**IIIg** as 3,5-disubstituted dihydroisoxazole derivatives.

The high regioselectivity in the addition of nitrile oxides to allyl phenylcarbamate (**I**) is consistent with charge distribution in the 1,3-dipole and dipolarophile. Presumably, *N*-chlorobenzenesulfonamide sodium salt in the above transformations acts as chlorinating agent which converts oximes **IIa**–**IIg** into the corresponding carbohydroximoyl chlorides **B**. Elimination of hydrogen chloride from the latter by the action of a base yields nitrile oxides **C** (Scheme 2).

Scheme 2.



EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian VXR-400 spectrometer (400 MHz) in acetone-d_6 using tetramethylsilane as internal reference. The ^{13}C NMR spectra were obtained on a Bruker WM-400 instrument at 100 MHz with complete decoupling from protons (solvent acetone-d_6). The mass spectra (70 eV) were run on an MKh-1306 mass spectrometer. The IR spectra were measured on an IKS-29 spectrophotometer in mineral oil; the spectral range 4000–400 cm^{-1} was examined. The purity of the products was checked by TLC on Silufol UV-254 plates.

Allyl phenylcarbamate was synthesized following the procedure reported in [11], by reaction of freshly distilled phenyl isocyanate with a small excess of allyl alcohol in carbon tetrachloride. The product was purified by recrystallization from hexane, mp 70°C [12].

3-Aryl-5-(phenylcarbamoyloxymethyl)-4,5-dihydroisoxazoles IIIa–**IIIg.** A mixture of 1.35 mmol of allyl phenylcarbamate (**I**), 1.35 mmol of benzaldehyde oxime **IIa**–**IIg**, and 1.35 mmol of *N*-chlorobenzenesulfonamide sodium salt trihydrate in 25 ml of anhydrous ethanol was refluxed for 6 h. The precipitate was filtered off, the filtrate was evaporated under

reduced pressure, and the residue was treated with methylene chloride (2 × 20 ml). The extract was washed with water (2 × 30 ml) and with 1 N aqueous sodium hydroxide (2 × 25 ml), dried over magnesium sulfate, and evaporated. Crystalline products **IIIa**–**IIIg** were washed on a filter with 5 ml of diethyl ether and were recrystallized from chloroform–petroleum ether (1 : 2).

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