

Reaction of 2-Propynyl Phenylcarbamate with Benzaldehyde Oximes in the Presence of *N*-Chlorobenzenesulfonamide Sodium Salt

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Received March 13, 2001

Abstract—2-Propynyl phenylcarbamate reacts with substituted benzaldehyde oximes on heating in ethanol in the presence of *N*-chlorobenzenesulfonamide sodium salt, yielding the corresponding 3-aryl-5-(phenylcarbamoyloxymethyl)isoxazoles.

We previously [1] reported on the synthesis of 3-aryl-5-(phenylcarbamoyloxymethyl)-4,5-dihydroisoxazoles by reactions of allyl phenylcarbamate with substituted benzaldehyde oximes in the presence of *N*-chlorobenzenesulfonamide sodium salt (Chloramine-B). The process is characterized by high regioselectivity. In continuation of these studies we now report on analogous reactions of 2-propynyl phenylcarbamate (**I**). It should be noted that alkynyl arylcarbamates and their derivatives are of great interest as intermediate products in the synthesis of various polyfunctional systems [2, 3]; some of them have found practical application [4].

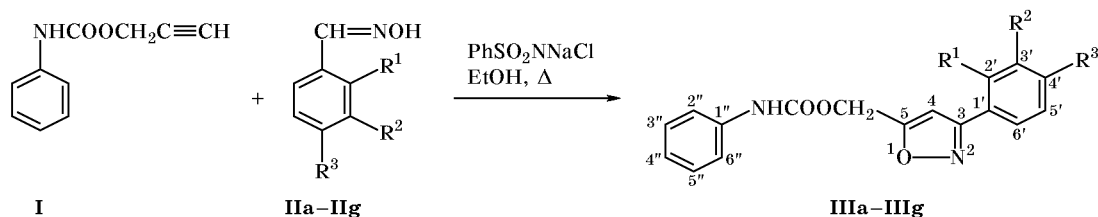
Unlike internal olefins and acetylene derivatives, reactions of terminal alkenes and alkynes with nitrile oxides are known [5] to show some similar relations. As a rule, such reactants lead to formation of 3,5-disubstituted isomers [6], while from internal alkenes and alkynes both possible isomers are formed [7]. It is also known that 1-phenylpropyne does not react

with nitrile oxides generated from arenehydroximoyl chlorides by the action of triethylamine [8].

The synthetic potential of 1,3-dipolar cycloaddition of acetylene derivatives to nitrile oxides generated *in situ* by the action of *N*-chlorobenzenesulfonamide sodium salt on benzaldehyde oximes, as well as general relations holding in this process, was explored very poorly. In order to fill this gap we examined the reaction of 2-propynyl phenylcarbamate (**I**) with benzaldehyde oxime **IIa** and *p*-methoxy-, *o*-methoxy-, *p*-bromo-, *m*-nitro-, *p*-nitro-, and 3,4-methylenedioxybenzaldehyde oximes **IIb–IIg** in the presence of *N*-chlorobenzenesulfonamide sodium salt. The reactions were carried out by heating the reactants in boiling ethanol for 5 h.

The structure of the products was established on the basis of their IR, ¹H NMR, and mass spectra. According to the spectral data, cycloaddition of substituted benzonitrile oxides to 2-propynyl phenylcarbamate occurs with high regioselectivity, yielding

Scheme 1.



II, III, $\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{H}$ (**a**); $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{OMe}$ (**b**); $\text{R}^1 = \text{OMe}$, $\text{R}^2 = \text{R}^3 = \text{H}$ (**c**); $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{Br}$ (**d**); $\text{R}^1 = \text{R}^3 = \text{H}$, $\text{R}^2 = \text{NO}_2$ (**e**); $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{NO}_2$ (**f**); $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{R}^3 = \text{OCH}_2\text{O}$ (**g**).

Yields, melting points, IR and ^1H NMR spectra, and elemental analyses of substituted isoxazoles **IIIa–IIIg**^a

Comp. no.	Yield, %	mp, °C	IR spectrum, ν , cm^{-1}	^1H NMR spectrum, δ , ppm (J , Hz)
IIIa	83	111	3305 (NH), 1740 (C=O), 1600, 1540 (C=C, C=C _{arom})	8.94 br.s (1H, NH), 7.92 m (2H, 2''-H, 6''-H), 7.35 t (2H, 3''-H, 5''-H, 7.4), 7.62–7.44 m (5H, H _{arom}), 7.05 t (1H, 4''-H, 7.4), 7.00 s (1H, 4-H), 5.34 s (2H, OCH ₂)
IIIb	89	107	3320 (NH), 1710 (C=O), 1615, 1560, 1515 (C=C, C=C _{arom})	8.80 br.s (1H, NH), 7.83 d (2H, 2'-H, 6'-H, 8.2), 7.58 d (2H, 2''-H, 6''-H, 8.9), 7.32 t (2H, 3''-H, 5''-H, 8.9), 7.04 m (3H, 3'-H, 5'-H, 4''-H), 6.90 s (1H, 4-H), 5.35 s (2H, OCH ₂), 3.87 s (3H, OMe)
IIIc	85	109	3300 (NH), 1745 (C=O), 1610, 1560, 1510 (C=C, C=C _{arom})	8.80 br.s (1H, NH), 7.85 d.d (1H, 3'-H, 1.5, 7.4), 7.32 m (8H, H _{arom}), 6.96 s (1H, 4-H), 5.35 s (2H, OCH ₂), 3.93 s (3H, OMe)
III d	63	132	3300 (NH), 1715 (C=O), 1620, 1570, 1515 (C=C, C=C _{arom})	8.81 br.s (1H, NH), 7.85 d (2H, 2'-H, 6'-H, 8.2), 7.70 d (2H, 3'-H, 5'-H, 8.2), 7.58 d (2H, 2''-H, 6''-H, 7.4), 7.31 t (2H, 3''-H, 5''-H, 7.4), 7.09 m (1H, 4''-H), 6.99 s (1H, 4-H), 5.35 s (2H, OCH ₂)
IIIe	61	138	3365 (NH), 1720 (C=O), 1585, 1555, 1535 (C=C, C=C _{arom})	8.85 br.s (1H, NH), 8.70 s (1H, 2'-H), 8.34 m (2H, 4'-H, 6'-H), 7.85 t (1H, 5'-H, 7.4), 7.58 d (2H, 2''-H, 6''-H, 7.0), 7.29 t (2H, 3''-H, 5''-H, 7.0), 7.19 s (1H, 4-H), 7.05 t (1H, 4''-H, 7.0), 5.40 s (2H, OCH ₂)
III f	57	147	3410 (NH), 1745 (C=O), 1580, 1555, 1535 (C=C, C=C _{arom})	8.82 br.s (1H, NH), 8.38 d (2H, 2'-H, 6'-H, 7.4), 8.19 d (2H, 3'-H, 5'-H, 7.4), 7.54 d (2H, 2''-H, 6''-H, 6.7), 7.30 t (2H, 3''-H, 5''-H, 6.7), 7.14 s (1H, 4-H), 7.05 t (1H, 4''-H, 6.7), 5.41 s (2H, OCH ₂)
III g	85	120	3300 (NH), 1710 (C=O), 1610, 1560, 1515 (C=C, C=C _{arom})	8.78 br.s (1H, NH), 7.58 d (2H, 2''-H, 6''-H, 7.4), 7.35 m (4H, 2'-H, 3''-H, 4''-H, 5''-H), 7.00 m (2H, 5'-H, 6'-H), 6.90 s (1H, 4-H), 6.08 s (2H, OCH ₂ O), 5.33 s (2H, OCH ₂)

Comp. no.	Found, %			Formula	Calculated, %		
	C	H	N		C	H	N
IIIa	69.05	5.07	9.79	C ₁₇ H ₁₄ N ₂ O ₃	69.39	4.76	9.52
IIIb	66.26	5.15	8.53	C ₁₈ H ₁₆ N ₂ O ₄	66.67	4.94	8.64
IIIc	66.41	4.79	8.71	C ₁₈ H ₁₆ N ₂ O ₄	66.67	4.94	8.64
III d	54.36	3.84	7.65	C ₁₇ H ₁₃ BrN ₂ O ₃	54.69	3.49	7.51
IIIe	59.99	3.79	12.03	C ₁₇ H ₁₃ N ₃ O ₅	60.18	3.84	12.39
III f	60.09	4.00	11.94	C ₁₇ H ₁₃ N ₃ O ₅	60.18	3.84	12.39
III g	64.06	4.20	8.11	C ₁₈ H ₁₄ N ₂ O ₅	63.91	4.14	8.28

^a ^1H NMR spectrum of 2-propynyl phenylcarbamate (**I**), δ , ppm (J , Hz): 8.69 br.s (1H, NH), 7.55 d (2H, 2-H, 6-H, 7.4), 7.30 t (2H, 3-H, 5-H, 7.4), 7.02 t (1H, 4-H, 7.4), 4.76 d (2H, OCH₂, 2), 2.99 t (1H, $\equiv\text{CH}$, 2).

the corresponding 3-aryl-5-(phenylcarbamoyloxy-methyl)isoxazoles **IIIa–IIIg** (Scheme 1). Their yields, IR and ^1H NMR spectra, and elemental analyses are given in table.

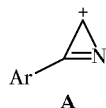
The formation of only one isomer follows from the ^1H NMR spectra of the products, which indicate that

the addition of nitrile oxide occurs at the C \equiv C bond. Unlike initial 2-propynyl phenylcarbamate (**I**), the ^1H NMR spectra of products **IIIa–IIIg** lack triplet signal at δ 2.99 ppm due to proton at the triple bond, but an olefinic proton signal appears as a singlet at δ 6.90–7.19 ppm. The band at 2140 cm^{-1} , belonging

to stretching vibrations of the triple bond in **I** [9], disappears from the IR spectra of isoxazoles **IIIa–IIIg**.

Thus analysis of the ^1H NMR spectra of the products and structurally related compounds [6, 7] leads us to conclude that the cycloaddition of substituted benzonitrile oxides to 2-propynyl phenylcarbamate occurs regioselectively with formation of 3,5-disubstituted isoxazoles **IIIa–IIIg**.

The electron impact mass spectra of compounds **IIIa–IIIg** contain the molecular ion peaks whose relative intensity ranges from 12 to 29%. The presence of abundant ions with m/z 175 (**IIIa**), 205 (**IIIb**, **IIIc**), 254 (**IIIId**), 220 (**IIIe**, **IIIIf**), and 219 (**IIIg**), in addition to the ion with m/z 119, indicates that the fragmentation of **III** begins with elimination of phenyl isocyanate from the molecular ion. Also, the mass spectra of the products contain the following ions, m/z 116 (**IIIa**), 146 (**IIIb**, **IIIc**), 195 (**IIIId**), 161 (**IIIe**, **IIIIf**), and 160 (**IIIg**); taking into account the data of [7], the presence of the above ions suggest formation of 2-arylazirinium ion **A**:



On the whole, the yields of isoxazoles **IIIa–IIIg** are smaller than the yields of their 4,5-dihydro analogs [1], which may be due to lower reactivity of the triple $\text{C}\equiv\text{C}$ bond as compared to double $\text{C}=\text{CH}_2$ bond. On the other hand, the yields of compounds **IIIb**, **IIIc**, and **IIIg**, which were obtained from benzonitrile oxides having electron-donor substituents, were considerably greater than those for benzonitrile oxides with electron-acceptor groups. These data are consistent with the polarization of the 1,3-dipole.

EXPERIMENTAL

The ^1H NMR spectra were recorded on a Bruker AC-200 spectrometer (200.13 MHz) using acetone- d_6 as solvent and TMS as internal reference. The mass spectra (70 eV) were obtained on a Kratos MS-30 instrument. The IR spectra were measured on an IKS-29 spectrometer in the range from 4000 to 400 cm^{-1} ; samples were dispersed in mineral oil. The purity of the products was checked by TLC on Silufol UV-254 plates.

2-Propynyl phenylcarbamate (I) was synthesized following the procedure reported in [10], by reaction of freshly distilled phenyl isocyanate with a slight excess of 2-propynyl alcohol in carbon tetrachloride. The product was purified by recrystallization from hexane, mp 64°C.

3-Aryl-5-(phenylcarbamoyloxymethyl)isoxazoles IIIa–IIIg. A mixture of 1.35 mmol of 2-propynyl phenylcarbamate (**I**), 1.35 mmol of benzaldehyde oxime **IIa–IIg**, and 1.35 mmol of *N*-chlorobenzene-sulfonamide sodium salt trihydrate in 25 ml of anhydrous ethanol was refluxed for 5 h. The precipitate was filtered off, the filtrate was evaporated under reduced pressure, and the residue was treated with methylene chloride (2 × 25 ml). The extract was washed with a 1 N aqueous solution of sodium hydroxide (2 × 25 ml) and water (2 × 30 ml) and dried over magnesium sulfate. The solvent was removed to obtain crystalline products **IIIa–IIIg** which were purified by recrystallization from a 1 : 1 diethyl ether–hexane mixture.

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