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Synthesis of Methyl (Hetarylalkyl) *N*-Allyl-*N*-phenylcarbamates and Their Transformation into 4,5-Dihydroisoxazole Derivatives

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Abstract—Alkylation of aromatic carbamates with allyl bromide under liquid-liquid phase transfer catalysis furnished the corresponding *N*-allyl derivatives of aryl carbamates in 63–71% yields. It was found that the cycloaddition of arene carbonitrile *N*-oxides, generated *in situ* from the corresponding oximes in the presence of chloramine T, to the allyl fragment upon boiling in ethanol led to the production of the corresponding 4,5-dihydroisoxazole derivatives in 89–96% yields.

Keywords: aromatic *N*-substituted carbamates, *N*-alkylation, allyl bromide, phase transfer catalysis, triethylbenzylammonium chloride, *N*-allyl-*O*-*R*-*N*-phenylcarbamates, 1,3-dipolar cycloaddition of arene carbonitrile *N*-oxides, 4,5-dihydroisoxazole derivatives

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INTRODUCTION

4,5-Dihydroisoxazole derivatives have a wide spectrum of biological activity. Among them, substances with antiparasitic [1], antimicrobial [2–6], anti-inflammatory [7], antiproliferative [8], antifungal and antioxidant [9], antitumor [10], antimalarial [11], antituberculosis [12] activity have been found; compounds of this series are also inhibitors of human transglutaminase 2 (TG2) [13].

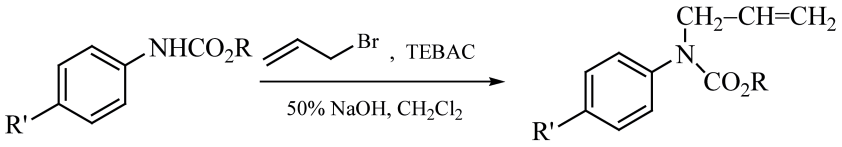
Methods for the synthesis of 4,5-dihydroisoxazole derivatives have been developed quite well. A method for obtaining 4,5-dihydroisoxazole derivatives by the reaction of α,β-unsaturated amides with nitrile oxides generated *in situ* from hydroxymoyl chlorides has been described [14]. In order to obtain 4,5-dihydrooxazole derivatives of the maleopimaric series, potentially biologically active compounds, the reaction of allyl-substituted derivatives of maleopimaric acid with aromatic nitrile oxides has been studied under the conditions of nitrile oxide synthesis from oximes by oxidation with sodium hypochlorite in the absence of or with ultrasonic activation. It has been shown that the reaction occurs under mild conditions and led to regiospecific formation of 4,5-dihydroisoxazol-5-ylmethyl derivatives of maleopimaric acid with yields of 77–99% [15]. It was found that without ultrasound, the reaction occurs at room temperature in a similar manner, but over a longer time (7 h) and with a higher yield (96%), therefore all further reactions were carried out without ultrasonic activation.

Chalcone derivatives are important intermediates and play the role of precursors in the synthesis of new isoxazolines. Thus, by fusing (2*E*)-1,3-bis(4-bromophenyl)prop-2-en-1-one with hydroxylamine hydrochloride in the presence of sodium hydroxide for 2 h in an oil bath, 3,5-bis(4-bromophenyl)-4,5-dihydroisoxazole was obtained [16]. Other examples of the synthesis of 4,5-dihydroisoxazole derivatives based on chalcones and hydroxylamine hydrochloride have been described earlier [17–19].

A synthesis of some Schiff bases containing an isoxazoline fragment has been proposed based on the reaction of hydroxylamine hydrochloride with chalcone in the presence glacial acetic acid in ethanol with boiling for 18–24 h [20]. One-pot condensation of pinacol with dialkyl oxalates and hydroxylamine hydrochloride afforded stable esters of 5-*tert*-butyl-5-hydroxy-4,5-dihydroisoxazole-3-carboxylic acid in preparative yields [21].

The intramolecular cyclization of *N*-[(1*E*,3*S*)-1,3-diphenyl-3-(phenylsulfanyl)propylidene]hydroxylamine

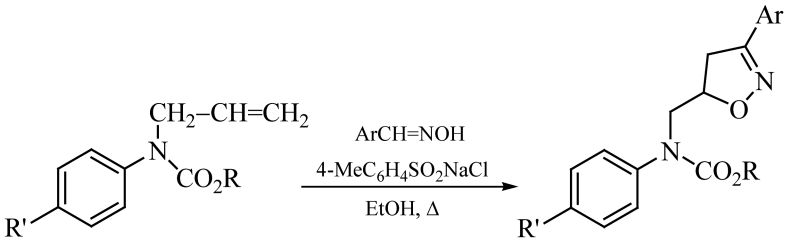
Scheme 1.



1a–1h **2a–2h**

R = Me, R = 4-Br (**e**); R = 2-furylmethyl, R = H (**f**), R = 2-morpholinoethyl, R = H (**g**); R = 2-(pyridin-2-yl)ethyl (**h**).

Scheme 2.



2a–2g **3a–3g**

R = Me, R = H, Ar = 3-$NO_2C_6H_4$ (**a**); R = Me, R = H, Ar = 3,4-$OCH_2OC_6H_3$ (**b**); R = Me, R = 4-Me, Ar = 4-BrC_6H_4 (**c**); R = Me, R = 4-MeO, Ar = 4-$MeOC_6H_4$ (**d**); R = 2-furanmethyl, R = H, Ar = 4-$MeOC_6H_4$ (**e**); R = 2-furanmethyl, R = H, Ar = 3-$NO_2C_6H_4$ (**f**); R = Me, R = 4-NO_2, Ar = 4-$MeOC_6H_4$ (**g**).

to a 4,5-dihydroisoxazole derivative under the action of sodium hydride in DMF has been described in [22]. A regioselective synthesis of 3,4-diaryl-5-carboxy-4,5-dihydroisoxazole-2-oxides has been developed by condensation of arylbenzaldehydes with arylnitromethanes followed by reaction with ethoxycarbonylmethylpyridinium bromide and intramolecular cyclization [23]. It was found that the obtained compounds exhibit antitumor activity.

The aim of this work was to study the possibility of synthesizing *N*-allyl derivatives from aromatic carbamates and transforming them into new derivatives of 4,5-dihydroisoxazole, among which compounds with potential biological activity can be found.

RESULTS AND DISCUSSION

In order to study the regioselectivity of 1,3-dipolar cycloaddition to *N*-allyl derivatives of *N*-phenylcarbamates of arenecarbonitrile *N*-oxides generated *in situ* from the corresponding oximes under the action of chloramine T, we synthesized methyl (hetarylalkyl) *N*-allyl-*N*-phenylcarbamates **2a**–**2h** by the alkylation reaction of the corresponding carbamates **1a**–**1h** with allyl bromide under the liquid-liquid phase-transfer catalysis (Scheme 1).

N-Allylation was carried out by stirring a mixture of *N*-substituted aromatic carbamates and allyl bromide in methylene chloride in the presence of 50% aqueous alkali and triethylbenzylammonium chloride (TEBAC) as a phase transfer catalyst at 20°C, monitoring the reaction progress by TLC analysis. The optimal process duration was found to be 7 h. After completion of the reaction, the resulting mixture was acidified with hydrochloric acid. The organic layer was separated, and the aqueous layer was extracted with methylene chloride. The combined organic phases were dried and concentrated. The residue was chromatographed on a silica gel column using benzene as an eluent. Compounds **2a**–**2h** were isolated as light yellow oils in 63–71% yields. The structure of methyl (hetarylalkyl) *N*-allyl-*N*-phenylcarbamates **2a**–**2h** was confirmed by IR and ^{1}H NMR spectroscopy method, and the composition was confirmed by elemental analysis.

Note that we previously studied the regularities of the 1,3-dipolar cycloaddition reaction of carbonitrile *N*-oxides to allyl and propargyl *N*-phenylcarbamates and found that these reactions proceed regiospecifically with

the formation of 3,5-disubstituted 4,5-dihydroisoxazoles and 1,2-oxazoles in high yields [24, 25].

In the present work, we studied the reaction of aromatic aldehyde oximes with *N*-allyl-*O*-methyl-*N*-phenylcarbamates in the presence of *N*-chloro-*p*-toluenesulfonamide sodium salt (chloramine T). The reaction was carried out by boiling an equimolar mixture of reagents in ethanol for 5 h. It was found that the 1,3-dipolar cycloaddition of arene carbonitrile-*N*-oxides to compounds **2a**–**2g** also proceeds regiospecifically (Scheme 2) with the formation of the corresponding 3,5-disubstituted 4,5-dihydroisoxazoles **3a**–**3g** in high yields (89–96%).

It was found that the cycloaddition of the obtained *N*-oxides of substituted benzonitriles occurs with regiospecific formation of the corresponding 3,5-disubstituted isoxazoles **3a**–**3g**, the structure of which was confirmed by IR, ^{1}H, ^{13}C NMR spectroscopy and mass spectrometry data.

In the ^{1}H NMR spectra, the protons of the methylene group at the C^4 atom of the isoxazole ring appear as two doublet of doublets signals in the regions of 2.39–3.37 and 3.60–3.67 ppm, and the protons of the CH group appear as a multiplet signal in a weaker field (4.86–5.14 ppm), which does not contradict the literature data [26–28] and our previous studies [23, 24].

Analysis of the mass spectra of compounds **3a**–**3g** allows us to conclude that 2-arylazirines are formed during the fragmentation of molecular ions [29]. Thus, in the mass spectra of isoxazoles, along with signals from other fragments, there are peaks with *m/z* 162 (**3a**, **3f**), 161 (**3b**), 196 (**3c**) and 147 (**3d**, **3e**, **3g**). This fragmentation direction also confirms the formation of 3,5-disubstituted isoxasoles.

EXPERIMENTAL

Commercial reagents from Aldrich and Alfa Aesar (USA) were used in the work.

^{1}H and ^{13}C NMR spectra were registered on a Bruker DRX 500 spectrometer (500, 126 MHz) in DMSO-d_6. IR spectra were measured on an InfraLUMFT-02 IR Fourier spectrophotometer in the range of 4000–400 cm^{-1} from KBr pellets. Purity of the obtained compounds was monitored by TLC on Silufol UV-254 plates (Chemapol, Czech Republic) with visualization in iodine vapor. Mass spectra were recorded on a Finigan MAT INCOS 50 instrument at an ionizing electron energy of 70 eV. Elemental analysis was performed on a PerkinElmer Series II 2400 instrument.

Methyl *N*-allyl-*N*-phenylcarbamate (2a). To 3.02 g (0.02 mol) of methyl *N*-phenylcarbamate **1a** in 25 mL of methylene chloride were added with stirring 0.17 g of TEBAC, 10 g of 50% sodium hydroxide solution and 3.45 mL (0.04 mol) of allyl bromide. The resulting mixture was vigorously stirred at room temperature for 5 h, then poured into 50 mL of water, and acidified with concentrated hydrochloric acid. The organic layer was separated and the aqueous layer was extracted with 25 mL of methylene chloride. The combined organic phases were dried with magnesium sulfate and concentrated to 10 mL. The residue was chromatographed on a silica gel column eluted with benzene. Yield 2.41 g (63%), yellowish oil, n_D^{20} 1.5255. IR spectrum (thin layer), ν, cm^{-1}: 2880–3105 (C–H$_{Ar}$), 1722 (C=O), 1616, 1565 (C=C, C–C$_{Ar}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.78 s (3H, NCO$_2$**Me**), 4.09 t (2H, C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 6.60 d (2H$_{Ar}$, *J* 8.7 Hz), 6.90–6.95 m (1H$_{Ar}$), 7.51–7.55 m (2H$_{Ar}$). Found, %: C 69.45; H 7.01; N 7.22. $C_{11}H_{13}NO_2$. Calculated, %: C 69.11; H 6.81; N 7.33.

Methyl *N*-allyl-*N*-(4-methylphenyl)carbamate (2b) was prepared similarly from 3.3 g (0.02 mol) of methyl *N*-(*p*-tolyl)carbamate **1b**, 3.45 mL (0.04 mol) of allyl bromide, 0.17 g of TEBAC and 10 g of 50% sodium hydroxide solution. Yield 2.87 g (70%), yellowish oil, n_D^{20} 1.5240. IR spectrum (thin layer), ν, cm^{-1}: 2880–3105 (C–H$_{Ar}$), 1710 (C=O), 1610, 1566 (C=C, C–C$_{Ar}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.23 s (3H, CH$_3$), 3.78 s (3H, NCO$_2$**Me**), 4.10 t (2H, C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 6.85 d (2H$_{Ar}$, *J* 8.6 Hz), 7.13 d (2H$_{Ar}$, *J* 8.6 Hz). Found, %: C 70.71; H 7.40; N 7.03. $C_{12}H_{15}NO_2$. Calculated, %: C 70.24; H 7.32; N 6.83.

Methyl *N*-allyl-*N*-(4-methoxyphenyl)carbamate (2c) was prepared similarly from 3.62 g (0.02 mol) of methyl *N*-(4-methoxyphenyl)carbamate **1c**, 3.45 mL (0.04 mol) of allyl bromide, 0.17 g of TEBAC and 10 g of 50% sodium hydroxide solution. Yield 3.32 g (75%), yellowish oil, n_D^{20} 1.5280. IR spectrum (thin layer), ν, cm^{-1}: 2880–3100 (C–H$_{Ar}$), 1720 (C=O), 1610, 1565 (C=C, C–C$_{Ar}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.74 s (3H, OCH$_3$), 3.78 s (3H, NCO$_2$**Me**), 4.10 t (2H,

C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis} CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 6.73 d (2H$_{Ar}$, *J* 8.7 Hz), 6.82 d (2H$_{Ar}$, *J* 8.7 Hz). Found, %: C 65.23; H 6.56; N 6.09. $C_{12}H_{15}NO_3$. Calculated, %: C 65.16; H 6.79; N 6.33.

Methyl *N*-allyl-*N*-(4-nitrophenyl)carbamate (2d) was prepared similarly from 3.92 g (0.02 mol) of methyl *N*-(4-nitrophenyl)carbamate **1d**, 3.45 mL (0.04 mol) of allyl bromide, 0.17 g of TEBAC and 10 g of 50% sodium hydroxide solution. Yield 3.82 g (81%), yellow oil, n_D^{20} 1.5725. IR spectrum (thin layer), ν, cm^{-1}: 2880–3100 (C–H$_{Ar}$), 1720 (C=O), 1615, 1570 (C=C, C–C$_{Ar}$), 1534, 1315 (NO$_2$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.78 s (3H, NCO$_2$**Me**), 4.10 t (2H, C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis} CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 7.10 d (2H$_{Ar}$, *J* 8.7 Hz), 8.21 d (2H$_{Ar}$, *J* 8.7 Hz). Found, %: C 56.02; H 4.97; N 11.67. $C_{11}H_{12}N_2O_4$. Calculated, %: C 55.93; H 5.08; N 11.86.

Methyl *N*-allyl-*N*-(4-bromophenyl)carbamate (2e) was prepared similarly from 4.60 g (0.02 mol) of methyl *N*-(4-bromophenyl)carbamate **1e**, 3.45 mL (0.04 mol) of allyl bromide, 0.17 g of TEBAC and 10 g of 50% sodium hydroxide solution. Yield 4.05 g (75%), pale yellow oil, n_D^{20} 1.5550. IR spectrum (thin layer), ν, cm^{-1}: 2885–3100 (C–H$_{Ar}$), 1725 (C=O), 1610, 1575 (C=C, C–C$_{Ar}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.78 s (3H, NCO$_2$**Me**), 4.10 t (2H, C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis} CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 6.76 d (2H$_{Ar}$, *J* 8.4 Hz), 7.28 d (2H$_{Ar}$, *J* 8.4 Hz). Found, %: C 48.74; H 4.32; N 4.97. $C_{11}H_{12}BrNO_2$. Calculated, %: C 48.89; H 4.44; N 5.19.

2-Furylmethyl *N*-allyl-*N*-phenylcarbamate (2f) was prepared similarly from 4.34 g (0.02 mol) of 2-furylmethyl *N*-phenylcarbamate **1f**, 3.45 mL (0.04 mol) of allyl bromide, 0.17 g of TEBAC and 10 g of 50% sodium hydroxide solution. Yield 3.19 g (62%), yellowish oil, n_D^{20} 1.5410. IR spectrum (thin layer), ν, cm^{-1}: 2880–3105 (C–H$_{Ar}$), 1720 (C=O), 1635, 1530 (C=C, C–C$_{Ar}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.25 t (2H, C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 4.91 s (2H, OCH$_2$), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 6.45 t (1H$_{Fur}$, *J* 3.5 Hz), 6.54 d (1H$_{Fur}$, *J* 3.5 Hz), 6.60 d (2H$_{Ar}$, *J* 8.7 Hz), 6.92 t (1H$_{Ar}$, *J* 8.7 Hz), 7.53–7.56 m (2H$_{Ar}$), 7.65 d (1H$_{Fur}$, 3.5 Hz). Found, %: C 69.87; H 5.60; N 5.39. $C_{15}H_{15}NO_3$. Calculated, %: C 70.04; H 5.84; N 5.45.

2-Morpholinoethyl *N*-allyl-*N*-phenylcarbamate (2g) was prepared similarly from 5.0 g (0.02 mol) of 2-morpholinoethyl *N*-phenylcarbamate **1g**, 3.45 mL (0.04 mol) of allyl bromide, 0.17 g of TEBAC and 10 g of 50% sodium hydroxide solution. Yield 3.65 g (63%), yellowish oil, n_D^{20} 1.5300. IR spectrum (thin layer), ν, cm^{-1}: 2880–3110 (C–H$_{Ar}$), 1715 (C=O), 1635, 1530 (C=C, C–C$_{Ar}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.32–2.36 m (4H, CH$_2$NCH$_2$, morpholine), 2.94–3.01 m (2H, OCH$_2$C**H**$_2$), 3.52–3.67 m (4H, CH$_2$OCH$_2$, morpholine), 4.10–4.16 m (2H, OC**H**$_2$CH$_2$), 4.81 t (2H, C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 6.57 d (2H$_{Ar}$, *J* 8.7 Hz), 6.95 t (1H$_{Ar}$, *J* 8.7 Hz), 7.51–7.56 m (2H$_{Ar}$). Found, %: C 66.18; H 7.37; N 9.51. $C_{16}H_{22}N_2O_3$. Calculated, %: C 66.21; H 7.59; N 9.66.

2-(2-Pyridinyl)ethyl *N*-allyl-*N*-phenylcarbamate (2h) was prepared similarly from 4.84 g (0.02 mol) of 2-(2-pyridinyl)ethyl *N*-phenylcarbamate **1h**, 3.45 mL (0.04 mol) of allyl bromide, 0.17 g of TEBAC and 10 g of 50% sodium hydroxide solution. Yield 3.44 g (61%), yellowish oil, n_D^{20} 1.5515. IR spectrum (thin layer), ν, cm^{-1}: 2880–3105 (C–H$_{Ar}$), 1720 (C=O), 1635, 1565 (C=C, C–C$_{Ar}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.08–3.12 m (2H, OCH$_2$C**H**$_2$), 4.32–4.36 m (2H, OC**H**$_2$CH$_2$), 4.28 t (2H, C**H**$_2$CH=CH$_2$, *J* 5.8 Hz), 4.85 d. d (1H^{cis} CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.17 d. d (1H^{trans}, CH$_2$CH=C**H**$_2$, *J* 10.0, 17.0 Hz), 5.77–5.85 m (1H, CH$_2$C**H**=CH$_2$), 6.61 d (2H$_{Ar}$, *J* 8.7 Hz), 6.91–6.95 m (1H$_{Ar}$), 7.03 t (1H$_{Ar}$, *J* 5.0 Hz), 7.20 d (1H$_{Ar}$, *J* 5.0 Hz), 7.47–7.56 m (3H$_{Ar}$), 8.42 d (1H$_{Ar}$, *J* 5.0 Hz). Found, %: C 72.07; H 6.19; N 10.01. $C_{17}H_{18}N_2O_2$. Calculated, %: C 72.34; H 6.38; N 9.93.

Methyl *N*-{[3-(3-nitrophenyl)-4,5-dihydro-5-isoxazolyl]methyl}-*N*-phenylcarbamate (3a). A mixture of 0.26 g (1.35 mmol) of methyl *N*-allyl-*N*-phenylcarbamate **2a**, 0.22 g (1.35 mmol) of 3-nitrobenzaldehyde oxime, 0.38 g (1.35 mmol) of chloramine T in 25 mL ethanol was refluxed for 5 h. After the solvent was removed, the residue was treated (2×25 mL) with methylene chloride, the extract was washed with water (2×30 mL), 1 N sodium hydroxide solution, and dried over anhydrous sodium sulfate. The solution was concentrated and then 5 mL of diethyl ether was added to the residue,

the formed precipitate was filtered off. Yield 0.46 g (96%), colorless crystals, mp 154–156°C ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1710 (C=O), 1610, 1565 (C=C, C–C_{Ar}), 1532, 1295 (NO_2). ^1H NMR spectrum, δ, ppm: 3.23 d. d (1H, H^4, *J* 5.0, 13.2 Hz), 3.55 d. d (1H, H^4, *J* 5.0, 13.2 Hz), 3.63 s (3H, NCO_2Me), 3.85 d (2H, OCH_2, *J* 4.4 Hz), 4.86–4.95 m (1H, H^5), 7.25–7.55 m ($5H_{Ar}$), 7.75 t ($1H_{Ar}$, *J* 7.7 Hz), 8.08 t ($1H_{Ar}$, *J* 7.7 Hz), 8.32 d ($1H_{Ar}$, *J* 7.7 Hz), 8.37 s ($1H_{Ar}$). ^{13}C NMR spectrum, δ_C, ppm: 43.28 (C^4), 49.21 (CH_2), 54.07 (OCH_3), 74.38 (C^5), 121.89, 125.72, 126.89, 127.84, 130.49, 133.20, 134.51, 143.48, 148.77 (C_{Ar}), 155.28 (C=O), 161.82 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 355 (20) $[M]^+$, 236 (5), 205 (100), 191 (30), 162 (24), 148 (25), 123 (20), 119 (95), 77 (15). Found, %: C 60.79; H 4.54; N 11.67. $C_{18}H_{17}N_3O_5$. Calculated, %: C 60.85; H 4.79; N 11.83. *M* 355.

Methyl *N*-{[3-(1,3-benzodioxol-5-yl)-4,5-dihydro-5-isoxazolyl]methyl}-*N*-phenylcarbamate (3b) was prepared similarly from 0.26 g (1.35 mmol) of methyl *N*-allyl-*N*-phenylcarbamate **2a**, 0.223 g (1.35 mmol) of piperonal oxime, 0.38 g (1.35 mmol) of chloramine T. Yield 0.44 g (92%), colorless crystals, mp 152–154°C ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1715 (C=O), 1610, 1575, 1565 (C=C, C–C_{Ar}). ^1H NMR spectrum, δ, ppm: 3.37 d. d (1H, H^4, *J* 5.1, 13.1 Hz), 3.60 d. d (1H, H^4, *J* 5.1, 13.1 Hz), 3.65 s (3H, NCO_2Me), 3.89 d (2H, OCH_2, *J* 4.3 Hz), 5.07–5.13 m (1H, H^5), 5.87 s (2H, OCH_2O), 6.35 s ($1H_{Ar}$), 6.59–6.64 m ($3H_{Ar}$), 6.85 t ($1H_{Ar}$, *J* 7.8 Hz), 7.46–7.52 m ($2H_{Ar}$), 7.65 d ($1H_{Ar}$, *J* 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 43.49 (C4), 49.20 (CH_2), 54.07 (OCH_3), 74.40 (C5), 101.01 (OCH_2O), 107.95, 111.62, 122.93, 125.38, 126.68, 127.82, 128.79, 143.48, 148.89, 151.08 (C_{Ar}), 155.28 (C=O), 161.13 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 354 (18) $[M]^+$, 235 (7), 204 (199), 190 (30), 161 (25), 147 (27), 121 (23), 119 (96), 77 (10). Found, %: C 64.29; H 4.84; N 7.64. $C_{19}H_{18}N_2O_5$. Calculated, %: C 64.41; H 5.08; N 7.91. *M* 354.

Methyl *N*-{[3-(4-bromophenyl)-4,5-dihydro-5-isoxazolyl]methyl}-*N*-(4-methylphenyl)carbamate (3c) was prepared similarly from 0.26 g (1.35 mmol) of methyl *N*-allyl-*N*-(4-methylphenyl)carbamate **2b**, 0.27 g (1.35 mmol) of 4-bromobenzaldehyde oxime, 0.38 g (1.35 mmol) of chloramine T. Yield 0.51 g (94%), colorless crystals, mp 130–133°C ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1713 (C=O), 1620, 1575 (C=C, C–C_{Ar}). ^1H NMR spectrum, δ, ppm: 2.23 s (3H, Me), 2.39 d. d (1H, H^4, *J* 4.9, 12.8 Hz), 3.60 d. d (1H, H^4, *J* 4.9, 12.8 Hz), 3.65 s (3H, NCO_2Me), 3.89 d (2H, OCH_2, *J* 4.4 Hz), 5.08–5.13 m (1H, H^5), 6.88 d ($2H_{Ar}$, *J* 8.6 Hz), 7.10 d ($2H_{Ar}$, *J* 8.6 Hz), 7.80 d ($2H_{Ar}$, *J* 8.3 Hz), 7.87 d ($2H_{Ar}$, *J* 8.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.79 (Me), 43.39 (C^4), 48.12 (CH_2), 54.09 (NCO_2**Me**), 74.28 (C^5), 119.26, 123.8, 127.87, 128.48, 129.54, 131.80, 135.85, 144.81 (C_{Ar}), 155.13 (C=O), 159.31 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 404 (5) $[M+1]^+$, 403 (5) $[M]^+$, 270 (4), 239 (100), 225 (32), 196 (30), 182 (25), 156 (20), 133 (84), 77 (10). Found, %: C 56.43; H 4.35; N 6.68. $C_{19}H_{19}BrN_2O_3$. Calculated, %: C 56.58; H 4.71; N 6.95. *M* 403.

Methyl *N*-(4-methoxyphenyl)-*N*-{[3-(4-methoxyphenyl)-4,5-dihydro-5-isoxazolyl]methyl}carbamate (3d) was prepared similarly from 0.298 g (1.35 mmol) of methyl *N*-allyl-*N*-(4-methoxyphenyl)carbamate **2c**, 0.204 g (1.35 mmol) of 4-methoxybenzaldehyde oxime, 0.38 g (1.35 mmol) of chloramine T. Yield 0.44 g (89%), colorless crystals, mp 97–99°C ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1715 (C=O), 1620, 1575 (C=C, C–C_{Ar}). ^1H NMR spectrum, δ, ppm: 3.36 d. d (1H, H^4, *J* 4.5, 12 Hz), 3.58 d. d (1H, H^4, *J* 4.5, 12 Hz), 3.65 s (3H, NCO_2**Me**), 3.71 s (3H, OMe), 3.74 s (3H, OMe), 3.91 d (2H, OCH_2, *J* 4.4 Hz), 5.09–5.14 m (1H, H^5), 6.65–6.74 m ($4H_{Ar}$), 6.81 d ($2H_{Ar}$, *J* 8.5 Hz), 7.83 d ($2H_{Ar}$, *J* 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 37.28 (OMe), 43.32 (C^4), 49.18 (CH_2), 54.18 (NCO_2**Me**), 55.45 (OMe), 114.78, 115.72, 122.21, 124.01, 127.87, 137.62, 160.85 (C_{Ar}), 154.03 (C=O), 158.23 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 370 (10) $[M]^+$, 221 (7), 190 (100), 176 (30), 149 (78), 147 (27), 133 (27), 107 (5), 77 (10). Found, %: C 64.72; H 6.03; N 7.35. $C_{20}H_{22}N_2O_5$. Calculated, %: C 64.86; H 5.95; N 7.57. *M* 370.

2-Furylmethyl *N*-{[3-(4-methoxyphenyl)-4,5-dihydro-5-isoxazolyl]methyl}-*N*-phenylcarbamate (3e) was prepared similarly from 0.347 g (1.35 mmol) of 2-furylmethyl *N*-allyl-*N*-phenylcarbamate **2f**, 0.204 g (1.35 mmol) of 4-methoxybenzaldehyde oxime, 0.38 g (1.35 mmol) of chloramine T. Yield 0.47 g (93%), colorless crystals, mp 97–99°C ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1710 (C=O), 1615, 1565 (C=C, C–C_{Ar}). ^1H NMR spectrum, δ, ppm: 3.34 d. d (1H, H^4, *J* 4.5, 12.1 Hz), 3.60 d. d (1H, H^4, *J* 4.5, 12.1 Hz), 3.70 s (3H, OMe), 3.89 d (2H, OCH_2, *J* 4.4 Hz), 4.92 s (2H, OCH_2), 5.09–5.14 m (1H, H^5), 6.45 d ($1H_{Ar}$, *J* 3.2 Hz), 6.54 d ($1H_{Ar}$, *J* 3.2 Hz), 6.60 d ($2H_{Ar}$, *J* 8.7 Hz), 6.68 d ($2H_{Ar}$, *J* 8.4 Hz), 6.86–6.92 m ($1H_{Ar}$), 7.46–7.52 m ($2H_{Ar}$), 7.65 d ($1H_{Ar}$, *J* 3.2 Hz), 7.84 d ($2H_{Ar}$, *J* 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 37.14 (OMe), 43.34 (C^4), 49.18 (CH_2), 66.14 (OCH_2), 74.41 (C^5), 109.28, 112.74,

114.84, 124.51, 126.64, 127.84, 128.18, 128.89, 143.47, 144.27, 160.74 (C_{Ar}), 155.14 (C=O), 159.92 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 406 (3) $[M]^+$, 287 (2), 190 (100), 176 (25), 147 (30), 133 (26), 119 (90) 107 (20), 77 (14). Found, %: C 68.02; H 5.12; N 6.67. $C_{23}H_{22}N_2O_5$. Calculated, %: C 67.98; H 5.42; N 6.90. *M* 406.

2-Furylmethyl *N*-{[3-(3-nitrophenyl)-4,5-dihydro-5-isoxazolyl]methyl}-*N*-phenylcarbamate (3f) was prepared similarly from 0.347 g (1.35 mmol) of 2-furylmethyl *N*-allyl-*N*-phenylcarbamate **2f**, 0.224 g (1.35 mmol) of 3-nitrobenzaldehyde oxime, 0.38 g (1.35 mmol) of chloramine T. Yield 0.54 g (95%), pale yellow crysrtals, mp 100–103°C ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1715 (C=O), 1615, 1570 (C=C, C–C_{Ar}), 1538, 1295 (NO_2). ^{1}H NMR spectrum, δ, ppm: 3.35 d. d (1H, H^4, *J* 4.5, 12.2 Hz), 3.67 d. d (1H, H^4, *J* 4.5, 12.2 Hz), 3.90 d (2H, OCH_2, *J* 4.4 Hz), 4.91 s (2H, OCH_2), 5.07–5.14 m (1H, H^5), 6.44 d (1H_{Ar}, *J* 3.1 Hz), 6.55 d (1H_{Ar}, *J* 3.1 Hz), 6.64 d (2H_{Ar}, *J* 8.8 Hz), 6.86–6.89 m (1H_{Ar}), 7.50 t (2H_{Ar}, *J* 8.8 Hz), 7.65 d (1H_{Ar}, *J* 3.1 Hz), 7.84 s (1H_{Ar}), 7.86–7.96 m (2H_{Ar}), 8.09 d (1H_{Ar}, *J* 7.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 43.55 (C^4), 48.42 (CH_2), 66.12 (OCH_2), 109.38, 113.54, 122.14, 125.68, 126.74, 127.94, 128.84, 130.51, 133.36, 135.32, 143.34, 144.20, 144.69, 148.76 (C_{Ar}), 154.11 (C=O), 161.87 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 421 (5) $[M]^+$, 302 (15), 205 (100), 191 (20), 162 (30), 148 (10), 122 (7), 119 (87), 77 (12). Found, %: C 62.54; H 4.48; N 9.72. $C_{22}H_{19}N_3O_6$. Calculated, %: C 62.71; H 4.51; N 9.98. *M* 421.

Methyl *N*-[3-(4-methoxyphenyl)-4,5-dihydro-5-isoxazolyl]methyl-*N*-(4-nitrophenyl)carbamate (3g) was prepared similarly from 0.319 g (1.35 mmol) of methyl *N*-allyl-*N*-(4-nitrophenyl)carbamate **2d**, 0.204 g (1.35 mmol) of 4-methoxybenzaldehyde oxime, 0.38 g (1.35 mmol) of chloramine T. Yield 0.50 g (96%), pale yellow crystals, mp 115–118°C ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1710 (C=O), 1615, 1565 (C=C, C–C_{Ar}). ^{1}H NMR spectrum, δ, ppm: 3.40 d. d (1H, H^4, *J* 4.4, 12.1 Hz), 3.60 d. d (1H, H^4, *J* 4.4, 12.1 Hz), 3.64 s (3H, NCO_2Me), 3.70 s (3H, OMe), 3.91 d (2H, OCH_2, *J* 4.3 Hz), 5.08–5.13 m (1H, H^5), 6.68 d (2H_{Ar}, *J* 8.4 Hz), 7.12 d (2H_{Ar}, *J* 8.7 Hz), 7.83 d (2H_{Ar}, *J* 8.4 Hz), 8.18 d (2H_{Ar}, *J* 8.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 37.43 (OMe), 43.41 (C^4), 48.35 (CH_2), 54.17 (NCO_2**Me**), 74.32 (C^5), 114.72, 120.28, 122.98, 127.54, 128.12, 144.84, 148.03, 160.84 (C_{Ar}), 155.24 (C=O), 159.20 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 385 (7) $[M]^+$, 221 (14), 190 (100), 176 (12), 164 (53), 147 (30), 133 (20), 107 (12), 77 (10). Found, %: C 59.04; H 5.06; N 10.56. $C_{19}H_{19}N_3O_6$. Calculated, %: C 59.22; H 4.94; N 10.91. *M* 385.

CONCLUSIONS

Alkylation of methyl (hetarylalkyl) *N*-phenylcarbamates with allyl bromides in methylene chloride in the presence of 50% sodium hydroxide solution and triethylbenzylammonium chloride as a phase-transfer catalyst afforded the corresponding *N*-allyl derivatives. 1,3-Dipolar cycloaddition of arene carbonitrile *N*-oxides, generated *in situ* from the corresponding aromatic aldehyde oximes under the action of chloramine T, to methyl (hetarylalkyl) *N*-allyl-*N*-phenylcarbamates proceeds regiospecifically with the formation of new 3,5-disubstituted 4,5-dihydroisoxazole derivatives.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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