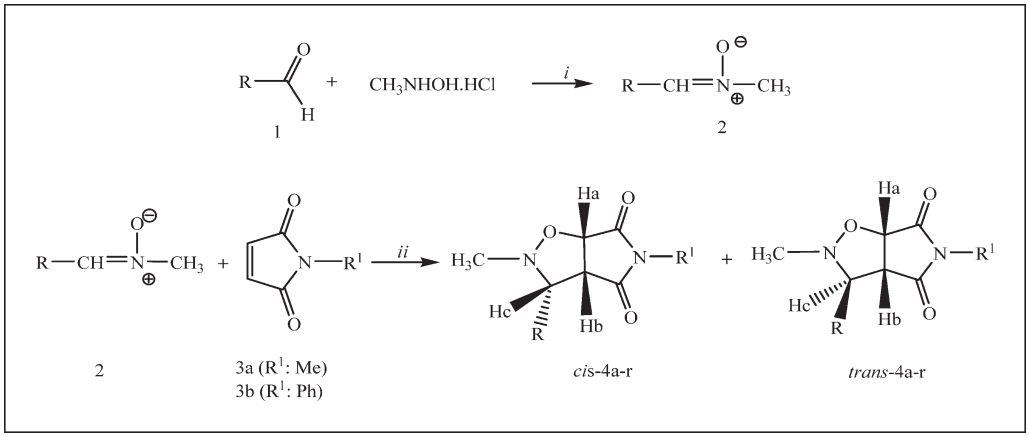
Hamdi Özkan and Yilmaz Yildirir*

Department of Chemistry, Arts and Sciences Faculty, Gazi University, Ankara, Turkey
*E-mail: yildirir@gazi.edu.tr
Received June 22, 2009
DOI 10.1002/jhet.395
Published online 21 June 2010 in Wiley InterScience (www.interscience.wiley.com).



A series of isoxazolidine derivates (isomeric 2,3,5-trisubstitutedperhydropyrrolo[3,4-d]isoxazole-4,6-diones) used as anti-inflammatory, immunosuppressive, antibacterial agent, and inhibitor for some enzymes were synthesized. These compounds were prepared by 1,3-dipolar cycloaddition of *N*-methyl maleimide and *N*-phenyl maleimide with nitrones. Diastereomeric products obtained in this reaction were separated by column chromatography and recrystallized. All compounds synthesized were characterized by elemental analysis and spectroscopic methods (^{1}H NMR, ^{13}C NMR, and FTIR).

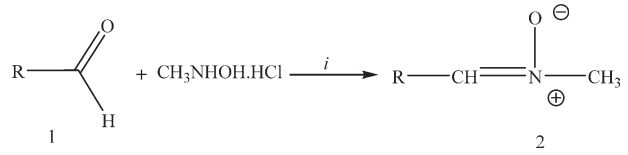
J. Heterocyclic Chem., **47**, 954 (2010).

INTRODUCTION

1,3-Dipolar cycloaddition reactions have been used for the synthesis of heterocyclic compounds [1]. High stereospecificity/stereoselectivity associated with these reactions make them synthetically important [2–5]. It has been found that 1,3-dipolar cycloaddition reactions proceed through a concerted mechanism [6]. The nitrone-olefin 1,3-dipolar cycloaddition reaction is interesting, as it can create as many as three new contiguous stereogenic centers in a single step [7,8]. Both inter and intramolecular nitrone–alkene cycloaddition reactions have received attention because they are useful methods for the formation of heterocycles of biological interest [9–12].

Isoxazolidines, the products of 1,3-dipolar cycloaddition reactions [13–20] between nitrones and alkenes, are saturated, five membered heterocycles containing adjacent nitrogen and oxygen atoms. As a result of the labile nature of the N—O bond under mildly reducing conditions, isoxazolidines have long been regarded as important synthetic intermediates and have been extensively utilized as 1,3-amino alcohol in a similar way to a wide variety of natural products and related molecules, particularly alkaloids [20] amino acids and amino sugars. Among a plethora of functional groups, the nitrone functionality has etched a place of distinction in organic synthesis. Remarkable regio-, stereo-, face-, and chemoselectivity along with efficient incorporation of multiple stereocenters have made nitrone cycloaddition reactions an attractive and efficient key step in the synthesis of a great many natural products of biological interest. In recent years, focus has been shifted toward asymmetric nitrone cycloaddition reactions; enantioselective [21], catalytic enantioselective [22], and diastereoselective [23] synthetic methodologies, as well as metal-assisted stereocontrol [24] have been reported. Isoxazolidines have been found to exhibit antimicrobial activity [25–28] and have been used as enzyme inhibitors [29–31]. Isoxazolidine nucleoside analogues, in which a furanose ring has been replaced by an N,O-heterocyclic system, are a particularly interesting group of compounds due to their potential antiviral activity [32–36]. Isoxazolidines have also been used as useful building blocks in the synthesis of various natural and unnatural compounds, including alkaloids, biologically active β-aminoacids, β-lactams, amino sugars, and simple 1,3-aminoalcohols owing to the facile cleavage of the N—O bond [37–39].

Scheme 1. ***i:*** K_2CO_3, CH_2Cl_2, $MgSO_4$, reflux. **2a:** R = 2-thiophenyl; **2b:** R = 5-methyl-2-thiophenyl; **2c***:* R = 3-methyl-2-thiophenyl; **2d:** R = 4-phenyl-2-thiophenyl; **2e:** 5-phenyl-2-thiophenyl; **2f:** R = 4-methylsulfanylbenzyl; **2g:** R = 2-furanyl; **2h:** R = 5-methyl-2-furanyl; **2i:** 1H-pyrrole-2-yl; **2j:** R = 1-methyl-1-H-indole-3-yl.



A review of the literature revealed that no more reports have been published on the synthesis of sulphur containing isomeric 2,3,5-trisubstitutedperhydropyrrolo[3,4-d] isoxazole-4,6-diones. The aim of this work is to synthesis a new type of isoxazolidine derivatives and characterizes their structures by using spectroscopic techniques such as ^{1}H NMR, ^{13}C NMR.

RESULTS AND DISCUSSION

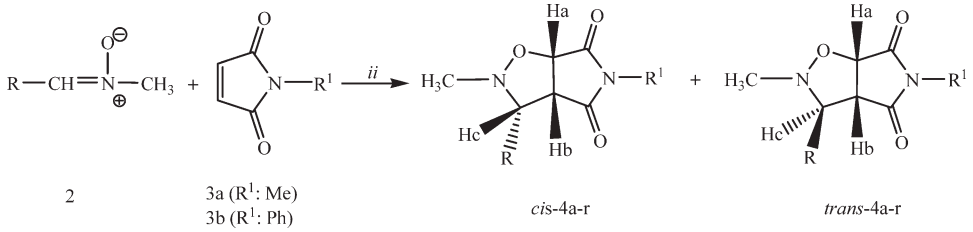
The 1,3-dipolar cycloaddition reactions between nitrones and an alkene is an extremely powerful synthetic method for the creation of complex heterocyclic structures. Best regarded as a concerted but asynchronous [4π + 2 π] suprafacial process, the reaction allows up to three contiguous carbon stereocentres to be created in a single step. In a manner analogous to the famous [4π + 2π] cycloaddition reactions first noted by Diels and Alder [40], nitrone–alkene cycloadditions can occur with the nitrone and alkene approaching each other. The reaction results in two possible products an endo- or exo- fashion; the two possible transition states giving rise to two diastereomeric products [41].

The 1,3-dipolar cycloaddition of nitrones to alkenes has been the most efficient approach used for the construction of isoxazolidines because the stereochemistry of the reaction is predictable, and the mechanism has been established. A wide range of acyclic and cyclic nitrones has been reacted with substituted alkenes leading to the formation of structurally diverse and highly functionalized nitrogen-containing compounds. Studies on both inter- and intramolecular nitrone to alkene dipolar cycloadditions have received much interest from a stereochemical point of view, as up to three new stereogenic centers can be created in the isoxazolidines depending on the structural features of the starting materials. Despite the known existence of acyclic nitrones as mixtures of (*E*)- and (*Z*)-isomers, or as single isomer in the case of cyclic analogues, the diastereoselectivity of cycloaddition depends also on the structures of the alkene dipolarophiles. In most cases, cycloadducts were formed in a predictable stereocontrolled manner due to steric and electronic effects [42].

In this study, a diastereomeric couple of two isoxazolidines was produced by 1,3 dipolar cycloaddition reaction of nitrons to alkenes, and the 1,3 dipolar cycloaddition reactions of substituted-*N*-methyl nitrons with *N*-methyl and *N*-phenyl maleimide were investigated (Schemes 1 and 2).

The evaluation of ^{1}H NMR spectra of *cis*-isomers of isoxazolidines exhibited that Ha protons have chemical shifting between 4 and 5 ppm giving doublet peak with a coupling constant ($J \sim 7$ Hz); chemical shift value of Hb protons 3–4 ppm and doublet's doublet peak J = 8/7 Hz; Hc chemical shifting 3–4 ppm and doublet peak with J = 8.5 Hz.*Cis*-isomers of isoxazolidines have greater coupling constant of Hb-Hc protons (J = 6–8 Hz) than *trans*-isomers (J = 2–5 Hz). Hc proton gives a double peak approximately at 3.8–4.0 ppm for cis- isomers but a broad singlet peak at 4.3–4.5 ppm for *trans* isomers. It was observed that *cis*-isomers were obtained in higher yield than *trans*-isomers in the reaction of *N*-methyl-C-substituted nitrons with *N*-methyl maleimide.The peak multiplicity due to the spin spin coupling of Ha and Hb protons are clearly seen from ^{1}H NMR spectra of the *trans* addition products. On the other hand, the spin spin coupling between Hb and Hc protons could not be seen. The peak belonging to Hc proton, appeared as a wide singlet. This situation is well

Scheme 2. ***ii:*** Benzene, reflux, **4a**: R = 2-thiophenyl, R^1 = Me; **4b**: R = 5-methyl-2-thiophenyl, R^1 = Me; **4c**: R = 3-methyl-2-thiophenyl, R^1 = Me; **4d**: R = 4-phenyl-2-thiophenyl, R^1 = Me; **4e**: R = 5-phenyl-2-thiophenyl, R^1 = Me; **4f**: R = 4-methylsulfanylphenyl, R^1 = Me; **4g**: R = 2-furanyl, R^1 = Me; **4h**: R = 5-methyl-2-furanyl, R^1 = Me; **4i**: R = 1H-pyrrole-2-yl, R^1 = Me; **4j**: R = 1-methyl-1-H-indole-3-yl, R^1 = Me; **4k**: R = 2-thiophenyl, R^1 = Ph; **4l**: R = 5-methyl-2-thiophenyl, R^1 = Ph; **4m**: R = 3-methyl-2-thiophenyl, R^1 = Ph; **4n**: R = 4-phenyl-2-thiophenyl, R^1 = Ph; **4o**: R = 5-phenyl-2-thiophenyl, R^1 = Ph; **4p**: R = 4-methylsulfanylphenyl, R^1 = Ph; **4q**: R = 2-furanyl, R^1 = Ph; **4r**: R = 5-methyl-2-furanyl, R^1 = Ph.



adjusted with the literatures. Because of the free rotation of N—C single bond, the proton in the methyl group and the Hc proton are sterically push each other. The electronic circle of Hc proton is consistently changed. Therefore, the peak due to Hc proton and methyl protons bonded to N atom on the isoxazolidine ring caused to occur a wide peak. The Ortep diagrams obtained from X-Ray analyzes of isoxazolidines (for example, *cis*-4c compound [43] and *cis*-4e compound [44]) it exhibited that Ha, Hb, and Hc protons are at the same side of the plane.The ^{13}C NMR spectra of the *trans* addition products showed that some singlet's carbons did not appear. However, the other data (such as X-Ray analyses of these compounds) confirm the proposed structures.

EXPERIMENTAL

All melting points were determined by an Electrothermal 9100 apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 (400 MHz) NMR spectrometer. Samples were prepared in $CDCl_3$ and DMSO-d_6 with TMS as internal standard. Chemical shifts are given in ppm and coupling constant are given in Hz. Microanalyses were performed on a LECO-932 CHNS-O element analyzer. FTIR spectra were recorded on a Mattson 1000 spectrometer as KBr pellets. Column chromatography was carried out on Merck Kieselgel (particle size 0.063–0.200 mm) and solvents were distilled before use. *N*-Methylhydroxylamine hydrochloride, *N*-methylmaleimide, *N*-phenylmaleimide and substituted aldehydes, and other chemicals were obtained from Sigma–Aldrich.

General procedure for the synthesis of substituted nitrones (2a–j). Substituted aldehydes (10 mmol) were added to a solution of *N*-methylhydroxylamine hydrochloride (1.65 g, 20 mmol) in CH_2Cl_2 (50 mL). K_2CO_3 (3.03 g, 22 mmol) and $MgSO_4$ (0.60 g, 5 mmol) were added and the mixture refluxed for 12 h, and the reaction was monitored by TLC. The reaction mixture was filtered and solvent was evaporated. Then, column chromatography of the residue (*n*-hexane/ethyl acetate 1:1) gave nitrone (compound 2). The crude product was recrystallized from CH_2Cl_2/*n*-hexane [45].

General procedure for the synthesis of substituted 2,5-dimethy tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, (exemplified by cis-4a, trans-4a). A mixture of *N*-methyl-*C*-(thiophene-2-yl) nitrone **2a** (3 mmol, 0,429 g) and *N*-methylmaleimide **3a** (3.3 mmol, 0.370 g) was dissolved in 50 mL benzene. The reacting mixture was refluxed for 6–12 h. During this time, the reaction was monitored by TLC. Then, the solvent was evaporated. The products were separated by column chromatography [46]. The mixture of ethylacetate and petroleum ether was used as an eluent. The *cis*- and *trans*-isomers were recrystallized separately from $CHCl_3$/*n*-hexane mixture. Spectroscopic and analytical data of new compounds are given below.

2,5-Dimethyl-3-(thiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4a, trans-4a. *Cis-4a.* Yield: 63%, mp 149–150°C. IR (cm^{-1}): 1714 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.8 (dd, 1H, Hb, $J \approx 8.4/7.5$ Hz), 4.2 (d, 1H, Hc, $J \approx 8.8$ Hz), 5.0 (d, 1H, Ha, $J \approx 7.2$ Hz), 7.0–7.4 (m, 3H, Ar—H), ^{13}C NMR (in *CDCl*$_3$, δ, ppm): 25, 43, 54, 71.35, 77, 127.0–127.9 (3C), 136, 173, 176. Anal. Calcd. For $C_{11}H_{12}N_2O_3S$: C 52.37; H, 4.79; N, 11.10; S, 12.71. Found: C, 51.93; H, 4.73; N, 10.96; S, 12.58.

Trans-4a. Yield: 35%, mp 168–169°C. IR (cm^{-1}): 1700 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.8 (d,1H, Hb, $J \approx 7.2$ Hz), 4.8 (very broad, 1H, Hc), 5.0 (d, 1H, Ha, $J \approx 7$ Hz), 7.0–7.4 (m, 3H, Ar—H); ^{13}C NMR (in *CDCl*$_3$, δ, ppm): 24, 41, 56, 72, 76, 127.0–128.2 (3C), 135, 174, 175. Anal. Calcd. For $C_{11}H_{12}N_2O_3S$: C 52,37; H, 4,79; N, 11,10; S, 12,71. Found: C, 52,06; H, 4,72; N, 11,04; S, 12,30.

2,5-Dimethyl-3-(5-methyl-thiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione cis-4b. *Cis-4b.* Yield: 64%, mp 121–122°C. IR (cm^{-1}): 1707 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.4 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 3.0 (s, 3H, CH_3), 3.7 (dd, 1H, Hb, $J \approx 8.3/7.7$ Hz), 4.1 (d, 1H, Hc, $J \approx 8.8$ Hz), 4.9 (d, 1H, Ha, $J \approx 7.3$ Hz), 6.6–6.9 (dd, 2H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 15, 25, 42, 54, 71.35, 77, 126–142 (4C), 174, 176. Anal. Calcd. For $C_{12}H_{14}N_2O_3S$: C 54.12; H, 5.30; N, 10.52; S, 12.04. Found: C, 54.90; H, 5.33; N, 10.04; S, 11.64.

2,5-Dimethyl-3-(3-methyl-thiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4c, trans-4c. *Cis-4c.* Yield: 61%, mp 130–132°C IR (cm^{-1}): 1704 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.3 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 3.0 (s, 3H, CH_3), 3.6–3.8 (dd, 1H, Hb, $J \approx 8.7/7.5$ Hz), 4.2 (t, 1H, Hc, $J \approx 8.8$ Hz), 4.9–5.0 (d, 1H, Ha, $J \approx 7.3$ Hz), 6.8–7.2 (dd, 2H, Ar—H, $J \approx 5.05$); ^{13}C NMR (in $CDCl_3$, δ, ppm): 14, 25, 43, 53, 70, 77, 126–137 (4C), 174, 176. Anal. Calcd. For $C_{12}H_{14}N_2O_3S$: C 54.12; H, 5.30; N, 10.52; S, 12.04. Found: C, 53.71; H, 5.21; N, 10.39; S, 12.03.

Trans-4c. Yield: 30%, mp 137–138°C IR (cm^{-1}): 1714 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.3 (s, 3H, CH_3), 2.4 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.6–3.8 (dd,1H, Hb $J \approx 7.2$ Hz), 4.5–4.8 (very broad, 1H, Hc), 4.8–5.0 (d, 1H, Ha, $J \approx 6$ Hz),, 6.5–6.9(dd, 2H, Ar—H, $J \approx 5.05$); ^{13}C NMR (in $CDCl_3$, δ, ppm): 15, 25, 39, 57, 67, 72, 75, 125–142 (4C), 173, 176. Anal. Calcd. For $C_{12}H_{14}N_2O_3S$: C 54.12; H, 5.30; N, 10.52; S, 12.04. Found: C, 53.81; H, 5.38; N, 10.78; S, 12.02.

2,5-Dimethyl-3-(4-phenyl-thiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4d, trans-4d. *Cis-4d.* Yield: 65%, mp 146–148°C IR (cm^{-1}): 1716 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.7 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7–3.8 (dd, 1H, Hb, $J \approx 8.4/7.7$ Hz), 4.2 (d, 1H, Hc, $J \approx 8.8$ Hz), 4.9–5.0 (d, 1H, Ha, $J \approx 7.3$ Hz), 7.3–7.6 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 43, 54, 71, 77, 122–143 (8C), 173, 176.15. Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 62.75; H, 4.88; N, 8.24; S, 10.01.

Trans-4d. Yield: 32%, mp 158–160°C IR (cm^{-1}): 1700 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7–3.8 (d, 1H, Hb, $J \approx 7.2$ Hz), 4.8 (very broad, 1H, Hc), 4.9–5.0 (d, 1H, Ha, $J \approx 7.1$ Hz), 7.3–7.7 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 39, 57, 67, 75, 119–142 (8C), 175, 176. Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 39.17; H, 3.05; N, 5.32; S, 5.68.

2,5-Dimethyl-3-(5-phenyl-thiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4e, trans-4e. *Cis-*

4e. Yield: 60%, mp 180–181°C IR (cm^{-1}): 1704 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.8 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7–3.8 (dd, 1H, Hb, $J \approx 8.4/7.7$ Hz), 4.1– 4.2 (d, 1H, Hc, $J \approx 8.8$ Hz), 4.9–5.0 (d, 1H, Ha, $J \approx 7.3$ Hz), 7.2–7.6 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 43, 54, 71, 77, 123–128 (4C),134–135 (3C), 172, 175. Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 60.94; H, 5.22; N, 8.59; S, 9.17.

Trans-4e. Yield: 33%, mp 126–128°C IR (cm^{-1}): 1700 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.8 (d, 1H, Hb, $J \approx 7.2$ Hz), 4.6–4.8 (very broad, 1H, Hc), 4.9.5.0 (d, 1H, Ha, $J \approx 7.2$ Hz), 6.8–7.7 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 75, 122–133 (5C). Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 62.52; H, 5.06; N, 8.56; S, 9.55.

2,5-Dimethyl-3-(4-methylsulfanyl-phenyl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4f, trans-4f. *Cis-4f*. Yield: 62%, mp 140–141°C IR (cm^{-1}): 1718 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7–3.8 (dd, 1H, Hb, $J \approx 8.4/7.4$ Hz), 3.8 (d, 1H, Hc, $J \approx 8.6$ Hz), 4.9 (d, 1H, Ha, $J \approx 7.2$ Hz), 7.1–7.3 (dd, 4H, Ar—H, $J \approx 8$ Hz); ^{13}C NMR (in $CDCl_3$, δ, ppm): 15, 25, 42.8, 54.6, 75, 76.75, 127–128 (2C), 134–135 (3C), 174, 176. Anal. Calcd. For $C_{14}H_{16}N_2O_3S$: C 57.52; H, 5.52; N, 9.58; S, 10.97. Found: C, 60.79; H, 7.26; N, 8.15; S, 9.29.

Trans-4f. Yield: 32%, mp 148–150°C IR (cm^{-1}): 1696 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.4–2.8 (6H, $2CH_3$), 3.1 (s, 3H, CH_3), 3.6–3.8 (d, 1H, Hb, $J \approx 7.2$ Hz), 4.6–4.8 (very broad, 1H, Hc), 4.9.5.0 (d, 1H, Ha, $J \approx 7.2$ Hz), 7.2–7.7.4 (m, 4H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 17, 26, 43, 54, 71, 77, 122–143 (5C), 161, 176. Anal. Calcd. For $C_{14}H_{16}N_2O_3S$: C 57.52; H, 5.52; N, 9.58; S, 10.97. Found: C, 57.91; H, 6.63; N, 9.43; S, 10.73

2,5-Dimethyl-3-(furan-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4g, trans-4g. *Cis-4g*. Yield: 52%, mp 143–144°C IR (cm^{-1}): 1717 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.7 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7–3.8 (dd, 1H, Hb, $J \approx 8.1/7.8$ Hz), 3.9 (d, 1H, Hc, $J \approx 8.5$ Hz), 4.9 (d, 1H, Ha, $J \approx 7.3$ Hz), 6.2–7.5 (m, 3H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 40, 44, 50, 69, 76, 110–147 (4C), 174, 176. Anal. Calcd. For $C_{11}H_{12}N_2O_4$: C 55.93; H, 5.12; N, 11.86. Found: C, 58.02; H, 5.47; N, 12.03.

Trans-4g. Yield: 40%, mp 150–152°C IR (cm^{-1}): 1704 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.4 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7 (d, 1H, Hb, $J \approx 7.3$ Hz), 4.6 (very broad, 1H, Hc), 4.9 (d, 1H, Ha, $J \approx 7.4$ Hz), 6.3–7.5 (m, 3H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 40, 54, 71, 77, 135–150 (4C), 173, 176. Anal. Calcd. For $C_{11}H_{12}N_2O_4$: C 55.93; H, 5.12; N, 11.86. Found: C, 55.77; H, 4.75; N, 11.65.

2,5-Dimethyl-3-(5-methylfuran-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4h, trans-3h. *Cis-4h*. Yield: 64%, mp 150–151°C IR (cm^{-1}): 1702 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.3 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7–3.8 (dd, 1H, Hb, $J \approx 8.2/7.7$ Hz), 3.9 (d, 1H, Hc, $J \approx 8.6$ Hz), 4.9 (d, 1H, Ha, $J \approx 7.3$ Hz), 5.9–6.2 (dd, 2H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 13, 25, 39, 54, 69, 76, 110–153 (4C), 175, 176. Anal. Calcd. For $C_{12}H_{14}N_2O_4$: C 57.59; H, 5.64; N, 11.19. Found: C, 57.37; H, 5.59; N, 11.25.

Trans-4h. Yield: 33%, mp 154–155°C IR (cm^{-1}): 1701 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.3 (s, 3H, CH_3), 2.4 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.8 (d, 1H, Hb, $J \approx 7$ Hz), 4.5 (very broad, 1H, Hc), 4.9–5.0 (d, 1H, Ha, $J \approx 7.4$ Hz), 5.98–6.25 (m, 2H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 13, 25, 53, 75, 106, 111. Anal. Calcd. For $C_{12}H_{14}N_2O_4$: C 57.59; H, 5.64; N, 11.19. Found: C, 58.08; H, 5.46; N, 11.21.

2,5-Dimethyl-3-(1-methyl-1H-pyrrol-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4i, trans-4i. *Cis-4i*. Yield: 62%, mp 179–180°C IR (cm^{-1}): 1703 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.7 (s, 3H, CH_3), 2.9–3.0 (s, 3H, CH_3), 3.7 (s, 3H, CH_3), 3.7–3.8 (dd, 1H, Hb, $J \approx 7.8$ Hz), 3.9 (d, 1H, Hc, $J \approx 8.6$ Hz), 4.9 (d, 1H, Ha, $J \approx 7.3$ Hz), 6.2–7.5 (m, 3H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 34, 43, 53, 69, 76, 110–125 (4C), 174, 176. Anal. Calcd. For $C_{12}H_{15}N_3O_3$: C 57.82; H, 6.07; N, 16.86. Found: C, 58.28; H, 5.96; N, 17.01.

Trans-4i. Yield: 29%, mp 145–146°C IR (cm^{-1}): 1705 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.7 (s, 3H, CH_3), 3.7–3.8 (d, 1H, Hb, $J \approx 7$ Hz), 4.6 (very broad, 1H, Hc), 4.9–5.0 (d, 1H, Ha, $J \approx 7.5$ Hz), 6.0–6.7 (m, 3H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 37 43, 54, 71, 77, 135–150 (4C), 175, 176. Anal. Calcd. For $C_{12}H_{15}N_3O_3$: C 57.82; H, 6.07; N, 16.86. Found: C, 57.72; H, 6.09; N, 17.09.

2,5-Dimethyl-3-(1-methyl-1H-indol-3-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4j, trans-4j. *Cis-4j*. Yield: 60%, mp 198–200°C IR (cm^{-1}): 1703 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.7 (s, 3H, CH_3), 3.0 (s, 3H, CH_3), 3.8 (s, 3H, CH_3), 3.6–3.7 (dd, 1H, Hb, $J \approx 8.0/7.7$ Hz), 4.1–4.2 (d, 1H, Hc, $J \approx$ 8.6 Hz), 4.9–5.0 (d, 1H, Ha, $J \approx 7.3$ Hz), 6.9–7.0 (s,1H), 7.1–7.6 (m, 4H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 25, 33, 43, 54, 70, 76, 106, 109–127 (6C), 173, 176. Anal. Calcd. For $C_{16}H_{17}N_3O_3$: C 64.20; H, 5.72; N, 14.04. Found: C, 63.67; H, 5.79; N, 14.17.

Trans-4j. Yield: 32%, mp 131–133°C IR (cm^{-1}): 1704 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 3.1 (s, 3H, CH_3), 3.9 (s, 3H, CH_3), 3.7–3.8 (d, 1H, Hb, $J \approx 7$ Hz), 4.8 (very broad, 1H, Hc), 4.9–5.0 (d, 1H, Ha, $J \approx 7.1$ Hz), 6.9–7.0 (s,1H), 7.1–7.8 (m, 4H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 24, 25, 30, 32, 56, 76, 108, 109–128 (6C). Anal. Calcd. For $C_{16}H_{17}N_3O_3$: C 64.20; H, 5.72; N, 14.04. Found: C, 65.21; H, 5.34; N, 14.50.

2-Methyl-5-phenyl-3-(thiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4k. *Cis-4k*. Yield: 43%, mp 154–156°C IR (cm^{-1}): 1711 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.8 (s, 3H, CH_3), 3.8–3.9 (dd, 1H, Hb, $J \approx 8.3/8.0$ Hz), 4.4 (d, 1H, Hc, $J \approx 8.8$ Hz), 5.0–5.1 (d, 1H, Ha, $J \approx 7.5$ Hz), 7.0–7.5 (m, 8H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 43, 55, 72, 77, 112–136 (8C), 173, 176. Anal. Calcd. For $C_{16}H_{14}N_2O_3S$: C 61.13; H, 4.49; N, 8.91; S, 10.20. Found: C, 62.42; H, 4.49; N, 8.92; S, 10.17.

2-Methyl-5-phenyl-3-(5-methylthiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4l, trans-4l. *Cis-4l*. Yield: 41%, mp 139–141°C IR (cm^{-1}): 1722 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 2.7 (s, 3H, CH_3) 3.7–3.8 (dd, 1H, Hb, $J \approx 8.5/7.7$ Hz), 4.2 (d, 1H, Hc, $J \approx 8.8$ Hz), 5.0–5.1 (d, 1H, Ha, $J \approx 7.5$ Hz), 6.6–7.5 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 16, 43, 54, 72, 77, 126–142 (8C), 173, 176. Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 61.96; H, 4.86; N, 8.72; S, 9.55.

Trans-4l. Yield: 47%, mp 152–155°C IR (cm^{-1}): 1718 s (C=O); ^1H NMR: (in $CDCl_3$, δ, ppm): 2.4 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 3.8–3.9 (d, 1H, Hb, $J \approx 7,2$ Hz), 4.8–4.9 (very broad, 1H, Hc), 5.0–5.1 (d, 1H, Ha, J ≈ 7.1 Hz), 6.6–7.6 (m,

8H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 15, 39, 53, 71, 77, 125–142 (8C), 175.0, 175.46. Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 61.91; H, 4.90; N, 8.41; S, 10.16.

2-Methyl-5-phenyl-3-(3-methylthiophen-2-yl)-tetrahydro-pyrrolo [3,4-d]isoxazole-4,6-dione, cis-4m, trans-4m. *Cis-4m.* Yield: 40%, mp 108–109°C IR (cm^{-1}): 1722 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 2.8 (s, 3H, CH_3) 3.8–3.9 (dd, 1H, Hb, $J \approx 8.5/7.9$ Hz), 4.2–4.4 (d, 1H, Hc, $J \approx 8.9$ Hz), 5.0–5.1 (d, 1H, Ha, $J \approx 7.5$ Hz), 6.8–7.6 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 14, 43, 53, 70, 77, 125–137 (8C), 171, 175. Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 62.63; H, 5.15; N, 8.65; S, 9.46.

Trans-4m. Yield: 46%, mp 144–145°C IR (cm^{-1}): 1718 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.4 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 3.8–3.9 (d, 1H, Hb $J \approx 7$ Hz), 5.0–5.1 (very broad, 1H, Hc), 5.1–5.2 (d, 1H, Ha, J ≈ 7.1 Hz), 6.8–7.6 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 14, 44, 54, 67, 77, 126–144 (8C), 175, 177. Anal. Calcd. For $C_{17}H_{16}N_2O_3S$: C 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 61.91; H, 4.90; N, 8.41; S, 10.16

2-Methyl-5-phenyl-3-(4-phenylthiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4n, trans-4n. *Cis-4n.* Yield: 41%, mp 145–146°C IR (cm^{-1}): 1723 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.8–2.9 (s, 3H, CH_3) 3.7–3.8 (dd, 1H, Hb, $J \approx 8.7/7.7$ Hz), 4.3 (d, 1H, Hc, $J \approx 8.8$ Hz), 5.0–5.1 (d, 1H, Ha, $J \approx 7.5$ Hz), 7.2–7.6 (m, 12H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 43, 55, 72, 77, 122–143 (12C), 173, 176. Anal. Calcd. For $C_{22}H_{18}N_2O_3S$: C 67.67; H, 4.65; N, 7.17; S, 8.21. Found: C, 67.83; H, 4.68; N, 7.11; S, 7.92.

Trans-4n. Yield: 44%, mp 134–138°C IR (cm^{-1}): 1710 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.6 (s, 3H, CH_3), 3.8–3.9 (d, 1H, Hb $J \approx 7.3$ Hz), 4.9–5.0 (very broad, 1H, Hc), 5.1–5.2 (d, 1H, Ha, J ≈ 7.1 Hz), 6.8–7.6 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 49, 76, 120–142 (11C), 175. Anal. Calcd. For $C_{22}H_{18}N_2O_3S$: C 67.67; H, 4.65; N, 7.17; S, 8.21. Found: C, 67.23; H, 4.67; N, 6.99; S, 7.36.

2-Methyl-5-phenyl-3-(5-phenylthiophen-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4o, trans-4o. *Cis-4o.* Yield: 43%, mp 166–167°C IR (cm^{-1}): 1717 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.9 (s, 3H, CH_3), 3.9 (dd, 1H, Hb, $J \approx 8.5/7.8$ Hz), 4.3 (d, 1H, Hc, $J \approx 8.8$ Hz), 5.1–5.2 (d, 1H, Ha, $J \approx 7.5$ Hz), 7.2–7.6 (m, 12H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm):. 43, 55, 72, 77, 122–135 (12C), 173, 175. Anal. Calcd. For $C_{22}H_{18}N_2O_3S$: C 67.67; H, 4.65; N, 7.17; S, 8.21. Found: C, 67.64; H, 4.59; N, 7.27; S, 8.08.

Trans-4o. Yield: 48%, mp 175–176°C IR (cm^{-1}): 1718 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.7 (s, 3H, CH_3), 3.9 (d, 1H, Hb $J \approx 7.3$ Hz), 4.3 (very broad, 1H, Hc), 5.1–5.2 (d, 1H, Ha, J ≈ 7.3 Hz), 7.0–7.7 (m, 12H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 122–135 (9C). Anal. Calcd. For $C_{22}H_{18}N_2O_3S$: C 67.67; H, 4.65; N, 7.17; S, 8.21. Found: C, 67.82; H, 4.64; N, 7.11; S, 8.00.

2-Methyl-5-phenyl-3-(4-methylsulfanyl-phenyl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4p, trans-4p. *Cis-4p.* Yield: 40%, mp 172–174°C IR (cm^{-1}): 1714 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.5 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 3.8–3.9 (dd, 1H, Hb, $J \approx 7.3/7.4$ Hz), 3.9–4.0 (d, 1H, Hc, $J \approx 8.7$ Hz), 5.0–5.1 (d, 1H, Ha, $J \approx 7.3$ Hz), 7.2–7.5 (m, 9H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 16, 43, 55, 76, 77, 127–140 (8C), 174, 176. Anal. Calcd. For $C_{19}H_{18}N_2O_3S$: C 64.39; H, 5.12; N, 7.90; S, 9.05. Found: C, 64.43; H, 5.14; N, 7.75; S, 8.87.

Trans-4p. Yield: 42%, mp 184–185°C IR (cm^{-1}): 1718 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.0–3.0 (6H, $2CH_3$), 3.8–3.9 (d, 1H, Hb, $J \approx 7.5$ Hz), 4.8 (broad, 1H, Hc), 5.0–5.1 (d, 1H, Ha, $J \approx 7.4$ Hz), 7.2–7.6 (m, 9H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 15, 75, 126–139 (6C). Anal. Calcd. For $C_{19}H_{18}N_2O_3S$: C 64.39; H, 5.12; N, 7.90; S, 9.05. Found: C, 64.43; H, 5.50; N, 8.07; S, 7.67.

2-Methyl-5-phenyl-3-(furan-2-yl)-tetrahydro-pyrrolo[3,4-d]isoxazole-4,6-dione, cis-4q. *Cis-4q.* Yield: 40%, mp 101–103°C IR (cm^{-1}): 1710 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.7 (s, 3H, CH_3), 3.8–3.9 (dd, 1H, Hb, $J \approx 8.5/7.7$ Hz), 4.0–4.1 (d, 1H, Hc, $J \approx 8.7$ Hz), 5.0–5.1 (d, 1H, Ha, $J \approx 7.5$ Hz), 6.3–7.6 (m, 8H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 43, 53, 71, 77, 110–147 (7C), 172, 175. Anal. Calcd. For $C_{16}H_{14}N_2O_4$: C 64.42; H, 4.73; N, 9.39 Found: C, 56.33; H, 5.02; N, 12.10.

2-Methyl-5-phenyl-3-(5-methylfuran-2-yl)-tetrahydro-pyrrolo [3,4-d]isoxazole-4,6-dione, cis-4r. *Cis-4r.* Yield: 42%, mp 137–140°C IR (cm^{-1}): 1701 s (C=O); ^{1}H NMR: (in $CDCl_3$, δ, ppm): 2.4 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 3.8–3.9 (dd, 1H, Hb, $J \approx 8.5/7.7$ Hz), 3.9–4.0 (d, 1H, Hc, $J \approx 8.7$ Hz), 5.1–5.2 (d, 1H, Ha, $J \approx 7.5$ Hz), 6.3–7.6 (m, 7H, Ar—H); ^{13}C NMR (in $CDCl_3$, δ, ppm): 14, 43, 50, 53, 77, 111–147 (8C), 155, 176. Anal. Calcd. For $C_{17}H_{16}N_2O_4$: C 65.38; H, 5.16; N, 8.97. Found: C, 68.07; H, 5.19; N, 9.14.

Acknowledgment. The authors are grateful to Gazi University (BAP Project Number: FEF 05/2006-46).

REFERENCES AND NOTES

[1] Padwa, A. 1,3-Dipolar Cycloaddition Chemistry; Wiley-Interscience: New York, 1984; pp 83–87.

[2] Pandey, G.; Sahoo, A. K.; Gadre, S. R.; Bagul, T. D.; Phalgune, U. D. J Org Chem 1999, 64, 4990.

[3] Werner, K. M.; de los Santos, J. M.; Weinreb, S. M. J Org Chem 1999, 64, 4865.

[4] Young, D. G.; Gomez-Bengoa, E.; Hoveyda, A. H. J Org Chem 1999, 64, 692.

[5] Snider, B. B.; Lin, H. J Am Chem Soc 1999, 121, 7778.

[6] Huisgen, R. In 1,3-Dipolar-Cycloaddition Chemistry; Padwa, A., Ed.; Wiley-Interscience: New York, 1984; pp 1–167.

[7] Dondas, H. A.; Cummins, J. E.; Grigg, R.; Thornton-Pett, M. Tetrahedron 2001, 57, 7951.

[8] Alibes, R.; Blanco, P.; de March, P.; Figueredo, M.; Font, J.; Alvarez-Larena, A.; Piniella, J. F. Tetrahedron Lett 2003, 44, 523.

[9] Kumar, K. R. R.; Mallesha, H.; Rangappa, K. S. Eur J Med Chem 2003, 38, 613.

[10] Gothelf, K. V.; Jorgenson, K. A. Chem Rev 1998, 98, 863.

[11] Broggini, G.; Zecchi, G. Synthesis 1999, 6, 905.

[12] Mulzer, J. Organic Synthesis Highlights; Verlag Chemie: Weinheim, 1991, 77.

[13] Tufariello, J. J. In 1,3-Dipolar Cycloaddition Chemistry; Padwa, A. Ed.; John Wiley: New York, 1984; pp 83–87.

[14] Torsell, K. B. G. Nitrile oxides, Nitrones and Nitronates in Organic Synthesis; VCH: New York, 1988.

[15] Confalone, P. N.; Huie, E. M. Org React 1988, 36, 1.

[16] Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L. Gazz Chim Ital 1989, 119, 253.

[17] Padwa, A. In Comprehensive Organic Synthesis 4; Trost, B.M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; pp 1069–1109.

[18] Wade, P. A. In Comprehensive Organic Synthesis 4; Trost, B.M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; pp 1113–1124.

[19] (a) Breuer, E. In Nitrones, Nitronates and Nitroxides, Breuer, E., Aurich, H. G., Nielsen, A., Eds.; John Wiley: Chichester, 1989; (b) Breuer, E. In Nitrones, Nitronates and Nitroxides; Breuer, E., Aurich, H. G., Nielsen, A., Eds.; John Wiley: Chichester, 1989; pp 248–312.

[20] Tufariello, J. J. Acc Chem Res 1979, 12, 396.

[21] (a) Ding, S.; Tangiguchi, K.; Ukaji, Y.; Inomata, K. Chem Lett 2001,468; (b) Jen, W. S.; Weiner, J. J. M.; McMillan, D. W. C. J Am Chem Soc 2000, 122, 9874.

[22] Goethelf, K. V.; Jorgensen, K. A. Chem Commun 2000,1449.

[23] Karlsson, S.; Högberg, H. Org Prep Proced Int 2001, 33, 103.

[24] Kanemasa, S. Synlett 2002,1371.

[25] Sadashiva, M. P.; Mallesha, H.; Hitesh, N. A.; Rangappa, K. S. Bioorg Med Chem 2004, 12, 6389.

[26] Ravi Kumar, K. R.; Mallesha, H.; Rangappa, K. S. Synth Commun 2003, 33, 1545.

[27] Vishu Kumar, B. K.; Dhananjaya, K.; Rangappa, K. S. Synth Commun 2002, 32, 1887.

[28] Vallance, P.; Bush, H. D.; Mok, B. J.; Hurtado-Guerrero, R.; Gill, H.; Rossiter, S.; Wilden, J. D.; Caddick, S. Chem Commun 2005,5563.

[29] Ding, P.; Miller, M. J.; Chen, Y.; Helquist, P.; Oliver, A. J.; Wiest, O. Org Lett 2004, 6, 1805.

[30] Rescifina, A.; Chiacchio, M. A.; Corsaro, A.; De Clercq, E.; Iannazzo, D.; Mastino, A.; Piperno, A.; Romeo, G.; Romeo, R.; Valveri, V. J Med Chem 2006, 49, 709.

[31] Procopio, A.; Alcaro, S.; De Nino, A.; Maiuolo, L.; Ortuso, F.; Sindona, G. Bioorg Med Chem Lett 2005, 15, 545.

[32] Chiacchio, U.; Genovese, F.; Iannazzo, D.; Piperno, A.; Quadrelli, P.; Antonino, C.; Romeo, R.; Valveri, V.; Mastino, A. Bioorg Med Chem 2004, 12, 3903.

[33] Merino, P.; Tejero, T.; Unzurrunzaga, F. J.; Franco, S.; Chiacchio, U.; Saita, M. G.; Iannazzo, D.; Piperno, A.; Romeo, G. Tetrahedron Asymmetry 2005, 16, 3865.

[34] Richichi, B.; Cicchi, S.; Chiacchio, U.; Romeo, G.; Brandi, A. Tetrahedron 2003, 59, 5231.

[35] Merino, P.; Franco, S.; Merchan, F. L.; Tejero, T. J Org Chem 2000, 65, 5575.

[36] Chiacchio, U.; Saita, M. G.; Crispino, L.; Gumina, G.; Mangiafico, S.; Pistara, V.; Romeo, G.; Piperno, A.; De Clercq, E. Tetrahedron 2006, 62, 1171.

[37] Padwa, A.; Pearson, W. H. Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products; Wiley: New York, NY, 2003; pp 1–81.

[38] Osborn, H. M. I.; Gemmell, N.; Harwood, L. M. J Chem Soc Perkin Trans 1 2002, **22**, 2419.

[39] Kobayashi, S.; Jorgensen, K. A. Cycloaddition Reactions in Organic Synthesis; Wiley-VCH: Weinheim, 2001; pp 3737–3740.

[40] Diels, O.; Alder, K. Liebigs Ann Chem 1928, 460, 98.

[41] Frederickson, M. Tetrahedron 1997, 53, 403.

[42] Piotrowska, D. G. Tetrahedron 2006, 62, 12306.

[43] Odabasoglu, M.; Ozkan, H.; Yildirir, Y.; Buyukgungor, O. Acta Cryst 2008, E64, 1102.

[44] Odabasoglu, M.; Ozkan, H.; Yildirir, Y.; Buyukgungor, O. Acta Cryst 2008, E64, 1423.

[45] Heaney, F.; Rooney, O.; Cunningham, D. J Chem Soc Perkin Trans 2, 2001, 3, 373.

[46] Fisera, L.; Altimari, U. A. R.; Ertl, P.; Pronayova, N. Monatsh Chem 1993, 124, 1019.