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# Synthesis of New 1*H*-Tetrazoles and 1,2,3-Triazoles *via* Reactions of 3(,5)-(di)chloro-2*H*-1,4-(benz)oxazin-2-ones with Sodium Azide or Diazocompounds.

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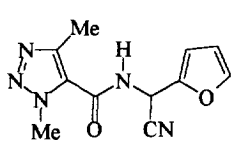
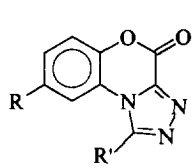
***Abstract:*** 3,5-dichloro-2*H*-1,4-oxazin-2-ones and 3-chloro-2*H*-1,4-benzoxazin-2-ones are reacted with bifunctional reagents as sodium azide and diazocompounds to yield bi(tri)cyclic tetrazolo- or triazolo fused intermediates *via* an intramolecular cyclisation reaction. Conversion of these lactone inter-mediates with various nucleophiles generates new substituted 1*H*-tetrazoles or 1,2,3-triazoles useful for pharmacological screening and for further elaboration *via* the α-chloroketone substituent at N-1. Copyright © 1996 Elsevier Science Ltd

## INTRODUCTION

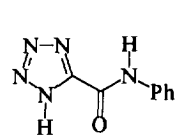
In a previous communication, we reported a novel two-step procedure towards 1,5-substituted tetrazoles and 1,2,3-triazoles.[1] These compounds are readily available *via* reaction of the imidoyl chloride function in 3(,5)-(di)chloro-2*H*-1,4-(benz)oxazin-2-ones **1** and **2** with diazocompounds or sodium azide, followed by cleavage of the intermediate bi(tri)cyclic lactone with nucleophiles. Since tetrazoles and (fused) triazoles have widespread use as fungicides (**I**)[2] and anti-allergic compounds (**II**[3] en **III**[4]), we applied the method to get new tetrazolo- or [1,2,3]triazolo(benz)oxazinones and the corresponding title compounds characterised by a carboxylic group in 5-position and an α-chloroketone substituent or an *ortho*-hydroxyphenyl group at N-1. We intended also to use both electrophilic centers of the α-chloroketone for elaboration into other heterocycles.




**I**



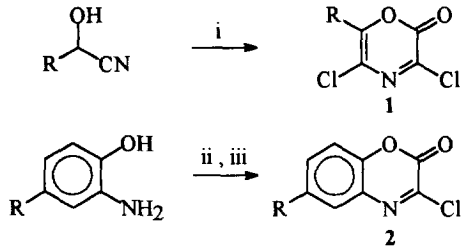

**II**




**III**

## RESULTS AND DISCUSSION

3(,5)-(di)chloro-2*H*-1,4-(benz)oxazin-2-ones **1** and **2** are easily prepared *via* a one-pot synthetic method using oxalyl chloride and the appropriate cyanohydrins[5] or *ortho*-amino phenols.[6]



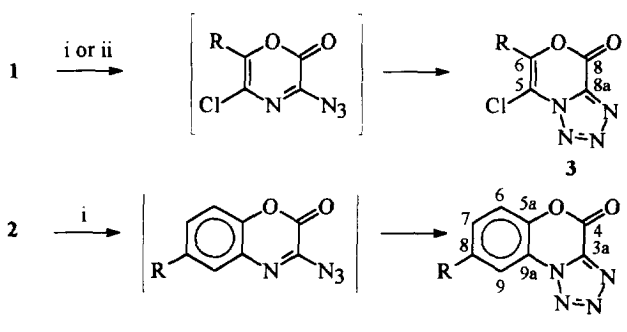
| | R |
|---|---|
| **1a** | Me |
| **1b** | Ph |
| **1c** | 2,6-$Cl_2$-$C_6H_3$ |
| **2a** | H |
| **2b** | Me |
| **2c** | Cl |

*Reagents and conditions*: i, oxalyl chloride (4 equiv.), $NEt_3$.HCl (0.5 equiv.), chlorobenzene, 4 h, 90 °C; ii, oxalyl chloride (1.4 equiv.), chlorobenzene, 3 h, 120 °C; iii, DMF (0.01 equiv.), $SOCl_2$ (1.4 equiv.), 1 h, 120 °C

*Synthesis of tetrazolo[5,1-c][1,4]oxazin-8-ones 3 and the corresponding fused benzoxazin-4-ones 4.*

In a typical procedure, the (benz)oxazinones **1a-c** and **2a-c** were treated with $NaN_3$ in $CH_3CN$ or DMF to yield compounds **3a-c** and **4a-c** after work up. We assume that the latter are generated by substitution of the imidoyl chloride function followed by ring closure *via* the azidoimino-tetrazolo equilibrium.[7] The absence of an IR azido-absorption at 2100 $cm^{-1}$ is a strong indication for the tetrazolo structure. Moreover, the additional ring creates a deshielding effect demonstrated by the appearance of H-9 as a doublet x doublet at 8.30 ppm or as a multiplet at 8.40 ppm in the $^1$H-NMR spectra of the crude compounds **4a** and **4c** respectively.

**Table 1**: tetrazolo[5,1-*c*][1,4]oxazin-8-ones **3** and -benzoxazin-4-ones **4**.



| | R | yield (%) |
|---|---|---|
| **3a** | Me | 81 |
| **3b** | Ph | 80 |
| **3c** | 2,6-$Cl_2$-$C_6H_3$ | 90 |
| **4a** | H | 80 |
| **4b** | Me | * |
| **4c** | Cl | 82 |

* Compound **4b** has not been purified but was used as such in the next step of our procedure.

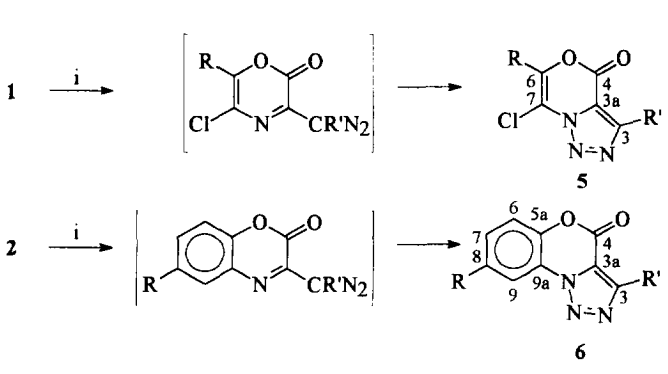
*Reagents and conditions*: i, $NaN_3$ (2 equiv.), $CH_3CN$ or DMF, 10 - 12 h, r.t.; ii, $NaN_3$ (1.1 equiv.), DMF, 2 h, r.t.

Little effect on the resonance values was noticed when changing the substituent in position 6 of the stable compounds **3**: typical $^{13}C$-values are found at 110 (± 3) ppm (C-5), 144 (± 4) ppm (C-6), 146 (± 2) ppm (C-8) and 140.5 (± 1) ppm (C-8a). The IR lactone-carbonyl stretching appears at 1800 (± 20) $cm^{-1}$. The tetrazolobenzoxazinone **4b** is very sensitive to hydrolysis and has been used in the next step without any purification. The IR spectra of the crude compounds **4a** and **4c** show strong absorptions at 1605 (± 5) $cm^{-1}$ (C=N) and at 1770 (± 5) $cm^{-1}$ (lactone). Typical $^{13}C$-absorptions are found at 116.4 (± 0.1) ppm (C-9), 143.0 (± 0.8) ppm (C-3a and C-6) and at 149.6 (± 0.2) ppm (lactone). Mass spectral analyses of compounds **3** and **4** show significant loss of $N_2$.

*Synthesis of [1,2,3]triazolo[5,1-c][1,4]oxazin-4-ones 5 and the corresponding fused benzoxazin-4-ones 6.*

An ethereal solution of **1** and **2** was treated with excess of diazocompound. Selective attack on the imidoyl chloride function followed by ring closure after proton abstraction yielded [1,2,3]triazolo-[5,1-*c*][1,4](benz)oxazin-4-ones **5a**-**e** and **6a**-**e** *via* the diazoimino-triazolo equilibrium.[8] Reaction with diazomethane gave higher yields (68 - 91 %) than reaction with diazoethane or diazopropane (41 - 52 %) presumably due to the unstability or lower reactivity of the diazoalkanes. The absence of an IR-absorption at 2100 $cm^{-1}$ excludes the diazo-structure. With exception of **5d**, **e** all compounds were purified and fully characterised.

**Table 2**: [1,2,3]triazolo[5,1-*c*][1,4]oxazin-4-ones **5** and the corresponding fused benzoxazin-4-ones **6**.




| | R | R' | yield (%) |
|---|---|---|---|
| **5a** | Me | H | 91 |
| **5b** | Ph | H | 81 |
| **5c** | 2,6-$Cl_2$-$C_6H_3$ | H | 72 |
| **5d** | 2,6-$Cl_2$-$C_6H_3$ | Me | * |
| **5e** | Me | Et | * |
| **6a** | H | H | 75 |
| **6b** | Me | H | 71 |
| **6c** | Cl | H | 68 |
| **6d** | H | Me | 52 |
| **6e** | Cl | Et | 41 |

* Compounds **5d**,**e** were obtained as impure oils and were used as such in the next step of our procedure.

*Reagents and conditions*: i, excess of diazocompound, ether, 4 d, 4 °C (when diazoethane or diazopropane was used, the initial temperature was -78 °C)

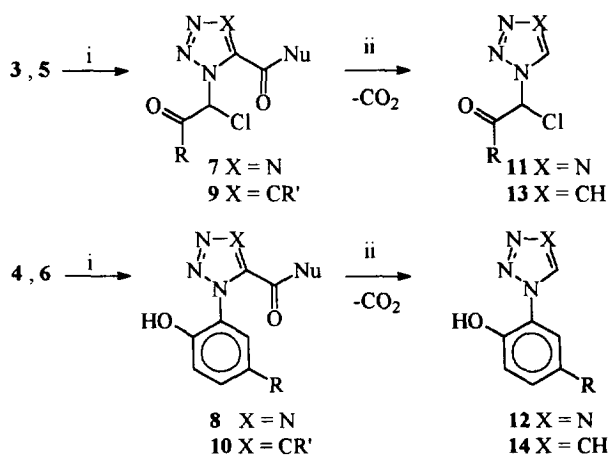
$^1H$-NMR spectra show a singlet at 8.7 (± 0.2) ppm (**5a-c** and **6a**, **c**) or 7.52 ppm (**6b**) assigned to the triazole proton H-3 and a doublet (**6b**, **c**, **e**) or a doublet x doublet (**6a**, **d**) at 8.2 (± 0.2) ppm for the deshielded proton H-9. In the $^{13}C$ NMR-spectra C-3 gives a signal at 136 (± 1) ppm (**5a-c** and **6a-c**), 149.1 ppm (**6d**) and 155.1 ppm (**6e**) whereas the absorption of C-3a is found at 123 (± 1) ppm (**5a-c** and **6a-c**), 121.1 ppm (**6d**) and at 117.9 ppm (**6e**). The lactone carbon atom absorbs at 152 (± 1) ppm and the lactone

IR carbonyl absorption is found at 1775 (± 15) $cm^{-1}$. Mass spectral analyses indicate significant loss of $N_2$ and CO.

*Lactone cleavage of [1,2,3]triazolo- and tetrazolo[5,1-c](benz)oxazin-4-ones 3-6.*

Ring cleavage at the lactone function of compounds **3-6** with nucleophiles such as water, amines and alcohols led to new tetrazoles and 1,2,3-triazoles which are characterised by an α-chloroketone or an *ortho*-hydroxyphenyl substituent at N-1 and a carboxylic group (derivative) at C-5. This method complements the most common generation method for 1,2,3-triazoles using the 1,3-dipolar cycloaddition of azides to unsymmetrical acetylenic compounds. However this procedure gives mainly the C-4 isomer. Other methods providing an electron withdrawing group in 5-position are limited by low yields and/or complicated multistep reactions.[9] Moreover, the direct generation of the α-chloroketone substitution pattern of compounds **7**, **9**, **11** and **13** is rather unusual.

The lactone bridge of the tetrazolo[5,1-*c*](benz)oxazinones **3** and **4** is easily cleaved with ethanol (15 min reflux) and amines (15-30 min at 0 °C) yielding tetrazoles **7** and **8**; for the comparable transformation with [1,2,3]triazolo[5,1-*c*](benz)oxazinones **5** and **6** into 1,2,3-triazoles **9** and **10** larger periods were required: (12 hours reflux in ethanol and one hour at room temperature with amines). On treatment with water, the acids **7** and **8** (Nu = OH) spontaneously decarboxylated yielding the final compounds **11** and **12.** Treatment of **5** and **6** with water yielded new 1,2,3-triazole acids **9** and **10** (Nu = OH) but decarboxylation to the triazoles **13** and **14** required heating at 130 °C. The easy loss of $CO_2$ by the tetrazole-5-carboxylic acids and the relative stability of the analogous 1,2,3-triazole-5-carboxylic acids can be explained by the presence (or absence) of a neighbouring N-atom in 4-position of the heterocyclic ring which can act as a intramolecular base.[10]




*Reagents and conditions*: i, methanol, ethanol or $H_2O/CH_3CN$: 15 min, reflux (**7**, **8**); 12 h, reflux (**9**, **10**); propylamine or diethylamine: 30 min, 0 °C (**7** and **8**); 1 h, r.t. (**9** and **10**); aniline: $AlCl_3$ (0.5 equiv.), 1,2-dichloroethane, 2 h, r.t. (**7d**); 3 h, reflux (**9f** and **10d**); ii, **11** and **12**: spontaneous decarboxylation from **7** and **8** (Nu = OH); **13**, **14**: chlorobenzene, 12 h, reflux: from **9g** and **10f** (Nu = OH).

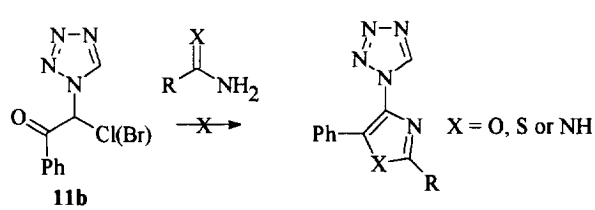
**Table 3**: tetrazoles and 1,2,3-triazoles **7** - **14**.

| | R | Nu | yield (%) | | R | R' | Nu | yield (%) |
|---|---|---|---|---|---|---|---|---|
| **7a** | Me | OEt | 95 | **9a** | Me | H | OMe | 95 |
| **7b** | Ph | OMe | 87 | **9b** | Ph | H | OMe | 80 |
| **7c** | Ph | $NEt_2$ | 78 | **9c** | Me | H | $NEt_2$ | 87 |
| **7d** | Ph | NHPh | 60 | **9d** | Me | Et | OMe | 28* |
| **7e** | 2,6-$Cl_2$-$C_6H_3$ | NHPr | 82 | **9e** | 2,6-$Cl_2$-$C_6H_3$ | Me | OMe | 25* |
| **8a** | H | OEt | 77 | **9f** | 2,6-$Cl_2$-$C_6H_3$ | H | NHPh | 84 |
| **8b** | Cl | $NEt_2$ | 80 | **9g** | Me | H | OH | 55 |
| **11a** | Me | | 85 | **10a** | Cl | H | OMe | 75 |
| **11b** | Ph | | 83 | **10b** | Cl | Et | OMe | 60 |
| **12a** | H | | 60 | **10c** | Cl | Et | NHPr | 76 |
| **12b** | Me | | 63 | **10d** | Me | H | NHPh | 59 |
| **12c** | Cl | | 70 | **10e** | H | H | $NEt_2$ | 60 |
| | | | | **10f** | H | H | OH | 58 |
| | | | | **13** | Me | H | | 76 |
| | | | | **14** | H | H | | 68 |

* overall yields starting from **1c** or **1a**

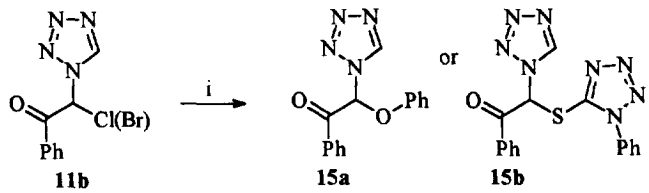
The α-chloroketone substituent on N-1 of compounds **7**, **9**, **11** and **13** shows two $^{13}C$-absorptions at 68.7 (± 2.5) ppm (CHCl) and 190 (± 5) ppm (ketone) whereas the *o*-hydroxyphenyl substituent of compounds **8**, **10**, **12** and **14** is characterised by a typical value of 150 (± 2) ppm ($C_{ar}$-OH). The carbon absorption of the carboxylic group in the tetrazoles and 1,2,3-triazoles **7**-**10** is found around 156 (± 3) ppm. $^1H$-NMR spectra of compounds **7**, **9**, **11** and **13** show a singlet at 8 (± 1) ppm (CHCl) whereas the absorption of the tetrazole proton H-5 of products **11** and **12** appears at 9.5 (± 0.5) ppm. The triazole proton H-4 in compounds **9a-c, f** and **g**, **10a**, **d-f**, **13** and **14** gives a signal at 8 (± 0.5) ppm. The carbonyl stretching of the ketone, ester or amide in the tetrazoles and 1,2,3-triazoles **7**-**11** and **13** is found around 1700 $cm^{-1}$ whereas IR-spectra of products **8**, **10**, **12** and **14** show intensive absorption at >3000 $cm^{-1}$ due to the Ar-OH stretching. Because of the easy loss of CO or $N_2$, mass spectral data show only low intensity peaks for the molecular ions.

We explored also the chemistry of these peculiar α-haloketones characterised by two electrophilic centers.[11] However, numerous attempts using bifunctional reagents such as amidines and (thio)amides did not give the expected heterocycles. These reactions failed also when using comparable α-bromoketone derivatives, prepared by alkylation of tetrazole and subsequent bromination.



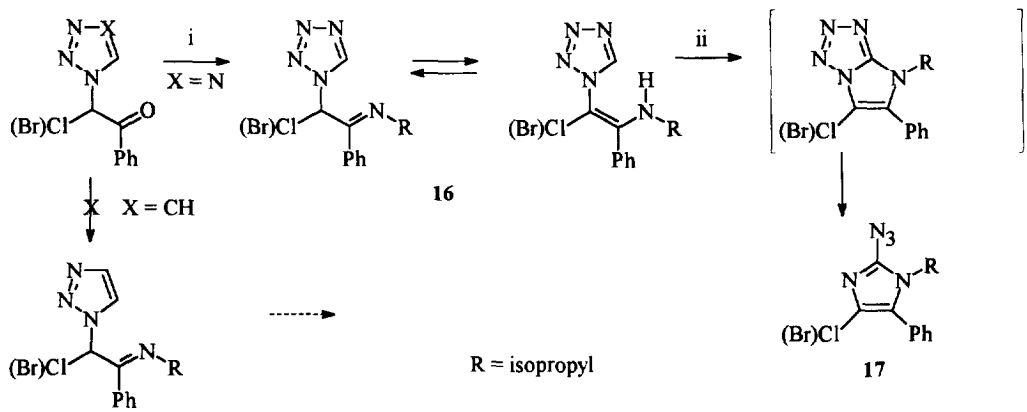

**11b**

Later on, we noticed that a selective halogenide substitution could only be achieved with relatively weak nucleophiles such as phenols and thiocompounds as 1-phenyl-1*H*-tetrazole-5-thiol; in this way tetrazole **11b** was converted into compounds **15a** and **b**. The CHCl $^{13}$C-value shifted from 62.8 ppm (**11b**) to 83.8 ppm (C-OR) or 66.0 ppm (C-SR) in compounds **15a** and **15b**. $^{1}$H-NMR spectra of these tetrazoles show 2 singlets at 7.90 ppm (CHOR) and 9.06 ppm (H-tetrazole) and at 8.75 ppm (CHSR) and 9.06 ppm (H-tetrazole). Reaction with other nucleophiles ($CN^-$, $MeO^-$, $SCN^-$ and $N_3^-$) gave complex reaction mixtures.




*Reagents and conditions*: i, phenol or 1-phenyl-1*H*-tetrazole-5-thiol (1.1 equiv.), NaH (1.3 equiv.), $CH_3CN$, 15 min, r.t.

An α-chlorimine **16** could be generated by selective reaction of the ketone function of compound **11b** with 5 equivalents isopropyl amine and 0.3 equivalents $TiCl_4$ in diethyl ether at 0 °C.[12] Its IR absorption at 1619 cm$^{-1}$ is in agreement with the imine structure but $^{1}$H-NMR spectral data in $CDCl_3$ indicate the imine-enamine equilibrium. Surprisingly this compound could be transformed into the azidoimidazole **17** which was isolated after reaction with 2 equivalents NBS in $CCl_4$ at reflux temperature. The IR-spectrum of compound **17** shows a strong azide absorption at 2141 cm$^{-1}$. Typical $^{13}$C-NMR values are 138.3 ppm (C-2) and 124.3 ppm (C-4). The formation of **17** presumably proceeds *via* an intramolecular attack of an intermediate radical species on the heterocycle. However we did not succeed to create efficiently comparable imines using other amines or a 1,2,3-triazole as heterocycle.




*Reagents and conditions*: i, isopropylamine (5 equiv.), $TiCl_4$ (0.5 equiv.), dry diethyl ether, 24 h, r.t.; ii, NBS (2 equiv.), benzoyl peroxide (cat), $CCl_4$, 5 min, reflux.

## CONCLUSION

The reaction of 3(,5)-(di)chloro-2*H*-1,4-(benz)oxazin-2-ones **1** and **2** with sodium azide or diazoalkanes and the subsequent cleavage of the lactone is shown to be a very general method for the generation of 1*H*-tetrazoles and 1*H*-1,2,3-triazoles with a carboxylic acid group (or derivative) in 5-position. The substituent on N-1 is determined by the oxazinone: using 3,5-dichloro-2*H*-1,4-oxazin-2-ones an α-chloroketone substituent can be introduced whereas 3-chloro-2*H*-1,4-benzoxazin-2-ones yield *o*-hydroxyphenyl substituted tetrazoles or 1,2,3-triazoles. However, the exploration of the chemistry of this peculiar α-chloroketone system shows a limited number of applications.

## EXPERIMENTAL

Infrared spectra were recorded as thin films between NaCl plates or as solids in KBr pellets on a Perkin-Elmer 297 grating IR spectrophotometer and a Perkin-Elmer 1720 Fourier transform spectrometer. The mentioned IR-absorptions were observed as strong bands. $^{1}H$ NMR spectra and $^{13}C$ NMR spectra were recorded on a Bruker WM 250 or on a Bruker AMX 400 instrument. The $^{1}H$ and $^{13}C$ chemical shifts are reported in ppm relative to tetramethylsilane or the deuterated solvent as an internal reference. Mass spectra were run by using a Kratos MS50TC instrument and a DS90 data system. For chromatography analytical TLC plates (Alugram Sil G/$UV_{254}$) and 70-230 mesh silica gel 60 (E.M. Merck) were used. Melting points were taken using a Reichert-Jung Thermovar apparatus and an Electrothermal IA 9000 digital melting point apparatus. Microanalyses were performed by Janssen Pharmaceutica on a Carlo Erba elemental analyser type 1106.

### General procedure for the synthesis of 5-chloro-8*H*-tetrazolo[5,1-*c*][1,4]oxazin-8-ones 3a-c and 4*H*-tetrazolo[5,1-*c*][1,4]-benzoxazin-4-ones 4a-c.

A solution of compounds **1** or **2** (10 mmol) and $NaN_3$ (20 mmol) in $CH_3CN$ (150 ml) was kept at 0 °C for 0.5 hours and then brought to room temperature. When the oxazinone fluorescence (366 nm) had disappeared (10 - 12 hours), the mixture was filtered and the solvent was evaporated to give the crude products **3a-c** and **4a-c**. 5-Chloro-8H-tetrazolo[5,1-*c*][1,4]oxazin-8-ones **3a-c** and **4a**, **c** could be recrystallised from $CHCl_3$/Hexane. The 4*H*-tetrazolo[5,1-*c*][1,4]benzoxazin-4-one **4b** was unstable and could not be purified.

**5-Chloro-6-methyl-8*H*-tetrazolo[5,1-*c*][1,4]oxazin-8-one (3a).** Yield: 81%; m.p.: 209 °C; IR (KBr $cm^{-1}$) 1650, 1790; $^{1}H$-NMR (250 MHz, DMSO-$d_6$): δ 2.38 (s, 3H, 6-$CH_3$); $^{13}C$-NMR (250 MHz, DMSO-$d_6$): δ 149.5, 144.0, 141.6, 108.0, 15.2; MS [m/z (%)]: 186 (100): $M^+$, 158 (4); HRMS calcd. for $C_5H_3ClN_4O_2$: 185.9945; found: 185.9945; anal. calcd. for $C_5H_3ClN_4O_2$: C 32.19, H 1.62, N 30.03; found: C 32.04, H 1.51, N 30.27

**5-Chloro-6-phenyl-8*H*-tetrazolo[5,1-*c*][1,4]oxazin-8-one (3b).** Yield: 80%; m.p.: 158 °C; IR (KBr $cm^{-1}$) 1629, 1788; $^{1}H$-NMR (250 MHz, $CDCl_3$): δ 7.65 (m, 3H, PhH), 8.96 (m, 2H, PhH); $^{13}C$-NMR (250 MHz, $CDCl_3$): δ 147.6, 144.4, 139.6, 132.1, 129.0, 128.7, 126.3, 109.2; MS [m/z (%)]: 248 (9): $M^+$, 220 (4), 105 (100): $PhCO^+$, 77 (81); HRMS calcd. for $C_{10}H_5ClN_4O_2$: 248.0101; found: 248.0096; anal. calcd. for $C_{10}H_5ClN_4O_2$:C 48.31, H 2.03, N 22.53; found: C 48.19, H 1.93, N 22.55

**5-Chloro-6-(2,6-dichlorophenyl)-8*H*-tetrazolo[5,1-*c*][1,4]oxazin-8-one (3c).** Yield: 90%; m.p.: 150 °C; IR (KBr $cm^{-1}$) 1650, 1807; $^{1}H$-NMR (250 MHz, $CDCl_3$): δ 7.60 (m, 3H, ArH); $^{13}C$-NMR (250 MHz, $CDCl_3$): δ 147.4, 140.0, 139.9, 136.3, 133.7, 128.6, 125.6, 113.5; MS [m/z (%)]: 316 (4): $M^+$, 173 (100): $Cl_2PhCO^+$; HRMS calcd. for $C_{10}H_3Cl_3N_4O_2$: 315.9322; found: 315.9326; anal. calcd. for $C_{10}H_3Cl_3N_4O_2$: C 37.83, H 0.95, N 17.65; found: C 37.80, H 0.87, N 17.51

**4*H*-tetrazolo[5,1-*c*][1,4]benzoxazin-4-one (4a).** Yield: 80 %; m.p.: 244 °C; IR (KBr $cm^{-1}$): 1610, 1773; $^1$H-NMR (400 MHz, DMSO-$d_6$): δ 7.57 (m, 1H, H-6), 7.70 (m, 2H, H-7, 8), 8.28 (dxd, 1H, H-9); $^{13}$C-NMR (400 MHz, DMSO-$d_6$): 149.8, 143.5, 142.2, 130.8, 126.1, 120.2, 117.8, 116.5; MS [m/z (%)]: 188 (26): $M^+$, 160 (83), 116 (100): $M^+$-$N_2$, -$CO_2$; HRMS calcd. for $C_8H_4N_4O_2$: 188.0334; found: 188.0340; anal. calcd. for $C_8H_4N_4O_2$: C 51.07, H 2.14, N 29.78; found: C 51.17, H 2.02, N 29.61

**8-Chloro-4*H*-tetrazolo[5,1-*c*][1,4]benzoxazin-4-one (4c).** Yield: 82 %; m.p.: 180 °C; IR (KBr $cm^{-1}$): 1605, 1768; $^1$H-NMR (400 MHz, DMSO-$d_6$): δ 7.80 (m, 2H, H-6, 7), 8.40 (m, 1H, H-9); $^{13}$C-NMR (400 MHz, DMSO-$d_6$): 149.5, 142.4, 142.3, 130.7, 130.0, 121.0, 119.6, 116.4; MS [m/z (%)]: 222 (10): $M^+$, 194 (32), 194 (53); HRMS calcd. for $C_8H_3ClN_4O_2$: 221.9945; found: 221.9951

**General procedure for the synthesis of 7-chloro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazin-4-ones 5a-e and 4*H*-[1,2,3]triazolo-[5,1-*c*][1,4]benzoxazin-4-ones 6a-e.**

Diazomethane, diazoethane and diazopropane were obtained *via* reaction of KOH with *N*-alkyl-*N*-nitrosourea derivatives using the procedure of F. Arndt in *Organic Synthesis*, John Wiley and Sons Inc., New York, **1945** Coll. Vol II, 161.

Compounds **1** and **2** (10 mmol) were slowly added to a diisopropyl ether solution of a 4-fold excess of diazoethane or diazopropane at -78 °C to avoid violent reaction. In the case of diazomethane, diethyl ether was used as solvent (0° C). Afterwards the temperature was brought to 4 °C. After stirring for 3 days the excess of diazocompound and the solvent was evaporated. Then the residue was recrystallised from a mixture of $CHCl_3$/hexane (except for compounds **5d** and **5e**).

**7-Chloro-6-methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazin-4-one (5a).** Yield: 91%; m.p.: 136 °C; IR (KBr $cm^{-1}$) 1655, 1780; $^1$H-NMR (250 MHz, $CDCl_3$): δ 2.46 (s, 3H, 6-$CH_3$), 8.50 (s, 1H, H-3); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 151.2, 142.1, 136.9, 122.4, 110.5, 15.6; MS [m/z (%)]: 185 (10): $M^+$, 129 (16), 43 (100): $CH_3CO^+$; HRMS calcd. for $C_6H_4ClN_3O_2$: 184.9992; found: 184.9991; anal. calcd. for $C_6H_4ClN_3O_2$: C 38.83, H 2.17, N 22.64; found: C 38.79, H 2.18, N 22.39

**7-Chloro-6-phenyl-4*H*-[1,2,3]triazolo[5,1-c][1,4]oxazin-4-one (5b).** Yield: 81%; m.p.: 112 °C; IR (KBr $cm^{-1}$): 1630, 1760; $^1$H-NMR (250 MHz, $CDCl_3$): δ 7.55 (m, 3H, PhH), 7.85 (m, 2H, PhH), 8.57 (s, 1H, H-3); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 151.0, 142.2, 136.9, 131.4, 129.1, 128.9, 127.9, 122.5, 110.7; MS [m/z (%)]: 247 (22): $M^+$, 219 (5), 105 (100): $PhCO^+$; HRMS calcd. for $C_{11}H_6ClN_3O_2$: 247.0148; found: 247.0147; anal. calcd. for $C_{11}H_6ClN_3O_2$: C 53.35, H 2.44, N 16.97; found: C 52.96, H 2.38, N 16.85

**7-Chloro-6-(2,6-dichlorophenyl)-4*H*-[1,2,3]triazolo[5,1-c][1,4]oxazin-4-one (5c).** Yield: 72%; m.p.: 135 °C; IR (KBr $cm^{-1}$): 1654, 1770; $^1$H-NMR (250 MHz, $CDCl_3$): δ 7.50 (s, 3H, ArH), 8.60 (s, 1H, H-3); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 150.8, 137.8, 137.2, 136.4, 133.5, 128.5, 126.5, 122.7, 114.6; MS [m/z (%)]: 315 (11): $M^+$, 259 (6): $M^+$ , 173 (100): $Cl_2PhCO^+$; HRMS calcd. for $C_{11}H_4Cl_3N_3O_2$: 314.9369; found: 314.9379; anal. calcd. for $C_{11}H_4Cl_3N_3O_2$: C 41.74, H 1.27, N 13.28; found: C 41.59, H 1.22, N 13.21

**4*H*-[1,2,3]triazolo[5,1-c][1,4]benzoxazin-4-one (6a).** Yield: 75%; m.p.: 197 °C; IR (KBr $cm^{-1}$): 1630, 1760; $^1$H-NMR (250 MHz, $CD_3CN$): δ 7.58 (m, 3H, H-6, 7, 8), 8.34 (dxd, 1H, H-9), 8.58 (s, 1H, H-3); $^{13}$C-NMR (250 MHz, $CD_3CN$): δ 152.8, 143.8, 137.0, 131.0, 126.8, 124.1, 122.0, 118.6, 116.8; MS [m/z (%)]: 187 (37): $M^+$, 159 (42), 131 (27), 103 (100): $M^+$-$N_2$, -CO, -CO; HRMS calcd. for $C_9H_5N_3O_2$: 187.0382; found: 187.0383; anal. calcd. for $C_9H_5N_3O_2$: C 57.76, H 2.69, N 22.45; found: C 57.82, H 2.60, N 22.67

**8-Methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]benzoxazin-4-one (6b).** Yield: 71%; m.p.: 180 °C; IR (KBr $cm^{-1}$): 1645, 1763; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 2.45 (s, 3H, 8-$CH_3$), 7.42 (dxd, 1H, H-7), 7.50 (d, 1H, H-6), 7.52 (s, 1H, H-3), 8.11 (d, 1H, H-9); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 152.1, 140.9, 136.1, 135.6, 130.5, 123.8, 120.5, 117.4, 115.5, 20.3, MS [m/z (%)]: 201 (35): $M^+$, 173 (28), 145 (17), 117 (100): $M^+$-$N_2$, -CO, -CO; HRMS calcd. for $C_{10}H_7N_3O_2$: 201.0538; found: 201.0549; anal. calcd. for $C_{10}H_7N_3O_2$: C 59.70, H 3.51, N 20.89; found: C 59.68, H 3.40, N 20.87

**8-Chloro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]benzoxazin-4-one (6c).** Yield: 68%; m.p.: 221°C; IR (KBr $cm^{-1}$): 1616, 1751. $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 7.70 (m, 2H, H-6, 7), 8.36 (d, 1H, H-9), 8.87 (s, 1H, H-3); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 151.7, 141.9, 141.9, 136.2, 129.7, 129.4, 121.7, 119.6, 115.4; MS [m/z (%)]: 221 (31): $M^+$, 193 (26), 165 (23), 137 (100): $M^+$-$N_2$, -CO, -CO; HRMS calcd. for $C_9H_4ClN_3O_2$: 220.9992; found: 220.9996; anal. calcd. for $C_9H_4ClN_3O_2$: C 48.78, H 1.82, N 18.96; found: C 48.43, H 1.66, N 18.85

**3-Methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]benzoxazin-4-one (6d).** Yield: 52%; m.p.: 161 °C; IR (KBr $cm^{-1}$): 1616, 1764; $^1$H-NMR (250 MHz, $CDCl_3$): δ 2.70 (s, 3H, 3-$CH_3$), 7.45 (m, 3H, H-6, 7, 8), 8.28 (dxd, 1H, H-9); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 152.3, 149.1, 142.7, 129.8, 125.8, 121.1, 118.5, 117.8, 116.1, 11.2; MS [m/z (%)]: 201 (4): $M^+$, 173 (3), 145 (100): $M^+$-$N_2$, -CO; HRMS calcd. for $C_{10}H_7N_3O_2$: 201.0538; found: 201.0536; anal. calcd. for $C_{10}H_7N_3O_2$: C 20.89, H 59.70, N 3.51; found: 20.96, H 59.75, N 3.40

**8-Chloro-3-ethyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]benzoxazin-4-one (6e).** Yield: 41%; m.p.: 125 °C; IR (KBr $cm^{-1}$): 1613, 1760; $^1$H-NMR (250 MHz, $CDCl_3$): δ 1.40 (t, 3H, $CH_3$), 3.15 (q, 2H, $CH_2$), 7.42 (d, 1H, H-6), 7.50 (dxd, 1H, H-7), 8.32 (d, 1H, H-9); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 155.1, 151.8, 141.3, 131.6, 130.0, 121.7, 119.3, 117.9, 116.4, 19.3, 13.1; MS [m/z (%)]: 249 (2): $M^+$, 221 (9), 193 (88), 63 (100): $C_5H_3$; HRMS calcd. for $C_{11}H_8ClN_3O_2$: 249.0305; found: 249.0303; anal. calcd. for $C_{11}H_8ClN_3O_2$: C 52.92, H 3.23, N 16.83; found: 52.97, H 3.15, N 16.84

**General procedure for the lactone cleavage of compounds 3 - 6 with alcohols, amines and water.**

Compounds **3** - **6** (10 mmol) were dissolved in 50 ml of the appropriate alcohol, amine or a 50/50 mixture of $H_2O$ and $CH_3CN$. When alcohols or water was used, the solution was brought to reflux temperature and the solvent was evaporated after 15 minutes (**3** and **4**) or 12 hours (**5** and **6**). In the case of diethyl amine and propylamine, the solvent was evaporated after 10 minutes (**3** and **4**) while compounds **5** and **6** were reacted for one hour at room temperature. Reactions with aniline were carried out in presence of 0.5 equivalents $AlCl_3$ in 50 ml 1,2-dichloroethane (**3**: 2 hours, room temperature; **5** and **6**: 3 hours, reflux). Further purification was performed by recrystallisation from a mixture of $CHCl_3$/hexane. Compounds **7d**, **7e**, **9c** and **9d** were additionally subjected to chromatographic purification ($SiO_2$, $CH_2Cl_2$/EtOAc).

**(±)-Ethyl 1-(1-chloro-2-oxopropyl)-1*H*-tetrazole-5-carboxylate (7a).** Yield: 95%; m.p.: 55 °C; IR (KBr $cm^{-1}$): 1750; $^1$H-NMR (250 MHz, $CDCl_3$): δ 1.47 (t, 3H, $CH_3$), 2.60 (s, 3H, $CH_3$), 4.53 (q, 2H, $CH_2$), 7.30 (s, 1H, CHCl); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 193.6, 156.1, 145.7, 68.9, 64.3, 26.1, 13.9; MS [m/z (%)]: 233 (11): $MH^+$, 89 (100); anal. calcd. for $C_7H_9ClN_4O_3$: C 36.14, H 3.90, N 24.08; found: 36.16, H 3.79, N 24.30

**(±)-Methyl 1-(1-chloro-2-phenyl-2-oxoethyl)-1*H*-tetrazole-5-carboxylate (7b).** Yield: 87%; m.p.: 92 °C; IR (KBr $cm^{-1}$): 1737; $^1$H-NMR (250 MHz, $CDCl_3$): δ 4.00 (s, 3H, $CH_3$), 7.50 (dxd, 2H, PhH-3, 5), 7.65 (dxd, 1H, PhH-4), 8.00 (d, 2H, PhH-2, 6), 8.32 (s, 1H, CHCl); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 184.7, 156.5, 145.5, 134.9, 131.5, 129.0, 66.2, 54.1; MS [m/z (%)]: 281 (45): $MH^+$, 105 (100): $PhCO^+$; HRMS calcd. for $C_9H_5ClN_4O$ (M-$CH_3OCO$): 220.0109; found: 220.0105

**(±)-1-(1-Chloro-2-phenyl-2-oxoethyl)-*N,N*-diethyl-1*H*-tetrazole-5-carboxamide (7c).** Yield: 78%; m.p.: 107 °C; IR (KBr $cm^{-1}$): 1708; $^1$H-NMR (250 MHz, $CDCl_3$): δ 1.20 and 1.30 [2xt, 6H, $N(CH_2CH_3)_2$], 3.50 and 3.90 [2xq, 4H, $N(CH_2CH_3)_2$], 7.55 (m, 3H, PhH-3, 4, 5), 8.00 (d, 2H, PhH-2, 6), 8.30 (s, 1H, CHCl); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 184.6, 155.7, 148.0, 134.8, 132.4, 129.3, 129.2, 67, 41.7, 44.1, 14.5, 12.5; MS [m/z (%)]: 322 (1): $MH^+$, 105 (100): $PhCO^+$; HRMS calcd. for $C_{14}H_{17}ClN_5O_2$ ($MH^+$): 322.1070; found: 322.1062; anal. calcd. for $C_{14}H_{16}ClN_5O_2$: C 52.26, H 5.01, N 21.77; found: C 51.84, H 5.12, N 21.77

**(±)-1-(1-Chloro-2-phenyl-2-oxoethyl)-*N*-phenyl-1*H*-tetrazole-5-carboxamide (7d).** Yield: 60%; m.p.: oil; IR (NaCl $cm^{-1}$): 1600, 1693, 3377; $^1$H-NMR (250 MHz, $CDCl_3$): 7.15 (dxd, 1H, NPh), 7.30 (dxd, 2H, NPh), 7.50 (dxd, 2H, NPh), 7.60 (m, 3H, COPhH-3, 4, 5), 8.00 (d, 2H, COPhH-2, 6), 8.60 (s, 1H, CHCl), 9.38 (s, 1H, CONH); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 185.0, 152.3, 135.5, 134.7, 131.8, 129.0, 128.9, 126.0, 120.4, 66.2; MS [m/z (%)]: 341 (1): $M^+$, 105 (100): $PhCO^+$; HRMS calcd. for $C_{16}H_{12}ClN_5O_2$: 341.0680; found: 341.0680

**(±)-1-[1-Chloro-2-(2,6-dichlorophenyl)-2-oxoethyl)-*N*-propyl-1*H*-tetrazole-5-carboxamide (7e).** Yield: 82%; m.p.: oil; IR (NaCl $cm^{-1}$): 1734, 3388; $^1$H-NMR (250 MHz, $CDCl_3$): δ 1.00 (t, 3H, $NHCH_2CH_2CH_3$), 1.70 (txq, 2H, $NHCH_2CH_2CH_3$), 3.50 (dxt, 2H, $NHCH_2CH_2CH_3$), 7.40 (s, 3H, ArH), 8.32 (t, 1H, NH), 8.80 (s, 1H, CHCl); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 187.6, 154.1, 146.9, 134.1, 132.2, 131.6, 128.1, 67.7, 41.5, 22.2, 11.1; MS [m/z (%)]: 376 (6): $MH^+$, 347 (2): $M^+$, 173 (100): $Cl_2PhCO^+$; HRMS calcd. for $C_{13}H_{12}Cl_3N_3O_2$ ($M-N_2$): 346.9995; found: 346.9982; anal. calcd. for $C_{13}H_{12}Cl_3N_5O_2$: C 41.46, H 3.21, N 18.59; found: C 41.40, H 3.14, N 18.73

**Ethyl 1-(2-hydroxyphenyl)-1*H*-tetrazole-5-carboxylate (8a).** Yield: 77%; m.p.: 110 °C; IR (KBr $cm^{-1}$): 1752 , >3000; $^1$H-NMR (250 MHz, $CD_3CN$): δ 1.20 (t, 3H, $CH_2CH_3$), 4.30 (q, 2H, $CH_2CH_3$), 7.12 (m, 2H, ArH-4, 6), 7.50 (m, 2H, ArH-3, 5), 7.90 (s, 1H, OH); $^{13}$C-NMR (250 MHz, $CD_3CN$): 156.8, 151.8, 148.8, 133.2, 127.9, 123.2, 121.5, 117.6, 64.1, 14.0; MS [m/z (%)]: 234 (1): $M^+$, 160 (59); HRMS calcd. for $C_{10}H_{10}N_4O_3$: 234.0753; found: 234.0743; anal. calcd. for $C_{10}H_{10}N_4O_3$: C 51.28, H 4.30, N 23.92; found: 51.08, H 4.08, N 24.30

**1-(5-Chloro-2-hydroxyphenyl)-*N,N*-diethyl-1*H*-tetrazole-5-carboxamide (8b).** Yield: 80%; m.p.: 157 °C; IR (KBr $cm^{-1}$): 1650, >3000; $^1$H-NMR (250 MHz, $CD_3CN$): δ 1.10 and 1.30 [2xt, 6H, $N(CH_2CH_3)_2$], 3.45 [m, 4H, $N(CH_2CH_3)_2$], 7.05 (d, 1H, ArH-3), 7.41 (dxd, 1H, ArH-4), 7.52 (d, 1H, ArH-6), 8.10-8.80 (br, 1H, OH); $^{13}$C-NMR (250 MHz, $CD_3CN$): δ 155.8, 149.4, 148.9, 131.0, 125.8, 123.6, 122.0, 117.5, 42.6, 39.2, 12.8, 10.8; MS [m/z (%)]: 253 (11): [$M^+$-NEt]H, 72 (100): $NEt_2^+$; anal. calcd. for $C_{12}H_{14}ClN_5O_2$: C 48.74, H 4.77, N 23.68; found: C 49.15, H 4.77, N 23.92

**(±)-Methyl 1-(1-chloro-2-oxopropyl)-1*H*-1,2,3-triazole-5-carboxylate (9a).** Yield: 95%; m.p.: 70 °C; IR (KBr $cm^{-1}$): 1740; $^1$H-NMR (250 MHz, $CDCl_3$): δ 2.55 (s, 3H, $COCH_3$), 3.95 (s, 3H, $OCH_3$), 7.48 (s, 1H, CHCl), 8.17 (s, 1H, H-4); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 194.2, 185.1, 138.0, 127.6, 70.3, 52.8, 26.3; MS [m/z (%)]: 218 (27): $MH^+$, 175 (43), 43 (100): $CH_3CO^+$; HRMS calcd. for $C_7H_9ClN_3O_3$: 218.0332; found: 218.0350; anal. calcd. for $C_7H_8ClN_3O_3$: C 38.64, H 3.71, N 19.31; found: C 38.30, H 3.55, N 19.17

**(±)-Methyl 1-(1-chloro-2-phenyl-2-oxoethyl)-1*H*-1,2,3-triazole-5-carboxylate (9b).** Yield: 80%; m.p.: 80 °C; IR (KBr $cm^{-1}$): 1723; $^1$H-NMR ($CDCl_3$): δ 3.90 (s, 3H, $OCH_3$), 7.35 (m, 2H, PhH-3, 5), 7.50 (m, 1H, PhH-4), 7.86 (m, 2H, PhH-2, 6), 8.11 (s, 1H, H-4), 8.31 (s, 1H, CHCl); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 184.7, 158.4, 137.9, 134.1, 132.5, 128.8, 128.6, 127.6, 68.2, 52.8; MS [m/z (%)]: 279 (1): $M^+$, 105 (100): $PhCO^+$; HRMS calcd. for $C_{12}H_{10}ClN_3O_3$: 279.0411; found: 279.0406; anal. calcd. for $C_{12}H_{10}ClN_3O_3$: C 51.53, H 3.60, N 15.02; found: C 51.11, H 3.47, N 14.76

**(±)-1-(1-Chloro-2-oxopropyl)-*N,N*-diethyl-1*H*-1,2,3-triazole-5-carboxamide (9c).** Yield: 87%; m.p.: oil; IR (KCl $cm^{-1}$): 1750; $^1$H-NMR (250 MHz, $CDCl_3$): δ 1.28 (m, 6H, 2x$CH_3$), 2.41 (m, 3H, $CH_3CO$), 3.52 (m, 4H, 2x$CH_2$), 7.18 (s, 1H, CHCl), 7.89 (s, 1H, H-4); $^{13}$C-NMR (250 MHz, $CHCl_3$): δ 193.6, 157.9, 132.3, 130.7, 70.8, 43.2, 40.2, 25.9, 14.2, 12.1; MS [m/z (%)]: 258 (1): $M^+$, 100 (100): $Et_2NCO^+$; HRMS calcd. for $C_{10}H_{15}ClN_4O_2$: 258.0884; found: 258.0887

**(±)-Methyl 1-(1-chloro-2-oxopropyl)-4-ethyl-1*H*-1,2,3-triazole-5-carboxylate (9d).** Yield: 28%; m.p.: oil; IR (KCl $cm^{-1}$): 1729; $^1$H-NMR ($CDCl_3$): δ 1.35 (t, 3H, $CH_2CH_3$), 2.50 (s, 3H, $COCH_3$), 3.00 (q, 2H, $CH_2CH_3$), 3.95 (s, 3H, $OCH_3$), 7.19 (s, 1H, CHCl); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 194.4, 159.1, 154.2, 123.4, 71.2, 52.6, 26.4, 19.9, 13.3 MS [m/z (%)]: 246 (25): $MH^+$, 43 (100): $CH_3CO^+$; HRMS calcd. for $C_9H_{12}ClN_3O_3$-$CH_3CO$: 202.0271; found: 202.0384

**(±)-Methyl 1-[1-chloro-2-(2,6-dichlorophenyl)-2-oxoethyl]-4-methyl-1*H*-1,2,3-triazole-5-carboxylate (9e).** Yield: 25%; m.p.: 139-141°C; IR (KBr $cm^{-1}$); 1740; $^1$H-NMR (250 MHz, $CDCl_3$): δ 2.60 (s, 3H, $CH_3$), 4.00 (s, 3H, $OCH_3$), 7.45 (s, 3H, ArH), 8.40 (s, 1H, CHCl); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 188.2, 159.3, 148.2, 134.8, 132.0, 131.8, 128.3, 124.9, 69.2, 52.8, 12.4; MS [m/z (%)]: 361 (1): $M^+$, 173 (100): $Cl_2PhCO^+$; HRMS calcd. for $C_{13}H_{10}Cl_3N_3O_3$: 360.9788; found: 360.9799; anal. calcd. for $C_{13}H_{10}Cl_3N_3O_3$: C 43.06, H 2.78, N 11.59; found: C 43.01, H 2.69, N 11.48

**(±)-1-[1-Chloro-2-(2,6-dichlorophenyl)-2-oxoethyl]-*N*-phenyl-1*H*-1,2,3-triazole-5-carboxamide (9f).** Yield: 84%; m.p.: 135 °C; IR (KBr $cm^{-1}$): 1730; $^1$H-NMR (250 MHz, $CDCl_3$): δ 7.15 (m, 6H, ArH, NPhH-3, 4, 5), 7.75 (m, 2H, NPhH-2, 6), 8.25 (s, 1H, H-4), 8.75 (s, 1H, CHCl), 9.50 (s, 1H, NH); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 188.8, 155.4, 136.3, 134.4, 133.5, 132.1, 132.0, 131.5, 128.1, 125.5, 121.2, 68.5; MS [m/z (%)]: 408 (1): $M^+$, 173 (100): $Cl_2PhCO^+$; HRMS calcd. for $C_{17}H_{11}Cl_3N_4O_2$: 407.9948; found: 407.9948; anal. calcd. for $C_{17}H_{11}Cl_3N_4O_2$: C 49.84, H 2.71, N 13.68; found: C 49.74, H 2.66, N 13.69

**(±) 1-(1-Chloro-2-oxopropyl)-1*H*-1,2,3-triazole-5-carboxylic acid (9g).** Yield: 55%; IR (KCl $cm^{-1}$): 1740, >3000; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 2.30 (s, 3H, $CH_3$), 7.80 (s, 1H, CHCl), 8.40 (s, 1H, H-4); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 194.4, 158.7, 138.2, 129.2, 71.2, 26.2; MS [m/z (%)]: 204 (1): $MH^+$, 161 (1), 43 (100): $CH_3CO^+$; HRMS calcd. for $C_4H_4ClN_3O_2$ ($M^+$·-$CH_3CO$)H: 160.9992; found: 160.9984

**Methyl 1-(5-chloro-2-hydroxyphenyl)-1*H*-1,2,3-triazole-5-carboxylate (10a).** Yield: 75%; m.p.: 204 °C; IR (KBr $cm^{-1}$): 1760, >3000; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 3.75 (s, 3H, $OCH_3$), 7.05 (d, 1H, ArH-3), 7.47 (dxd, 1H, ArH-4), 7.58 (d, 1H, ArH-6), 8.43 (s, 1H, H-4), 10.6 (s, 1H, OH); $^{13}$C NMR (250 MHz, DMSO-$d_6$): 157.7, 150.9, 136.6, 131.0, 130.1, 126.9, 125.0, 122.1, 117.7, 52.4; MS [m/z (%)]: 253 (7): $M^+$·, 221 (15), 193 (26), 165 (31), 137 (91); HRMS calcd. for $C_{10}H_8ClN_3O_3$: 253.0254; found: 253.0254; anal. calcd. for $C_{10}H_8ClN_3O_3$: C 47.35, H 3.18, N 16.57; found: C 47.02, H 3.15, N 16.41

**Methyl 1-(5-chloro-2-hydroxyphenyl)-4-ethyl-1*H*-1,2,3-triazole-5-carboxylate (10b).** Yield: 60%; m.p.: 150 °C; IR (KBr $cm^{-1}$): 1752, >3000; $^1$H-NMR δ (250 MHz, DMSO-$d_6$): δ 1.30 (t, 3H, $CH_2CH_3$), 2.90 (q, 2H, $CH_2CH_3$), 3.75 (s, 3H, $COOCH_3$), 7.05 (d, 1H, ArH-3), 7.43 (dxd, 1H, ArH-4), 7.52 (d, 1H, ArH-6), 10.60 (s, 1H, OH); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 158.6, 151.2, 150.7, 130.7, 126.7, 126.1, 125.7, 122.1, 117.7, 52.2, 18.9, 13.2; MS [m/z (%)]: 281 (1): $M^+$, 221 (12), 193 (100): $M^+$-$CH_3OH$, -$N_2$, -CO; HRMS calcd. for $C_{12}H_{12}ClN_3O_3$: 281.0567; found: 281.0549

**1-(5-Chloro-2-hydroxyphenyl)-4-ethyl-*N*-propyl-1*H*-1,2,3-triazole-5-carboxamide (10c).** Yield: 76%; m.p.: 145 °C; IR (KBr $cm^{-1}$): 1741, >3000; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 0.75 (t, 3H, $NHCH_2CH_2CH_3$), 1.30 (t, 3H, $CH_2CH_3$), 1.45 (txq, 2H, $NHCH_2CH_2CH_3$), 2.80 (q, 2H,

$CH_2CH_3$), 3.10 (dxt, 2H, $NHCH_2CH_2CH_3$), 7.00 (d, 1H, ArH-3), 7.38 (dxd, 1H, ArH-4), 7.45 (d, 1H, ArH-6), 8.41 (t, 1H, NH); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 158.5, 151.1, 146.2, 131.4, 130.3, 127.0, 125.3, 121.5, 117.8, 40.6, 22.0, 18.3, 13.2, 11.2; MS [m/z (%)]: 265 (2): $M^+$, 237 (1), 43 (100): $CH_3CH_2CH_2^+$; HRMS calcd. for $C_{14}H_{17}ClN_4O_2$: 308.1040; found: 308.1046

**1-(2-Hydroxyphenyl)-*N*-phenyl-1*H*-1,2,3-triazole-5-carboxamide (10d).** Yield: 59%, m.p.: 207 °C; IR (KBr cm$^{-1}$): 1666, >3000; $^1$H-NMR (250 MHz, $CDCl_3$): δ 2.25 (s, 3H, $CH_3$), 6.85 (d, 1H, ArH-3), 7.10 (dxd, 1H, NPhH-4), 7.15 (dxd, 1H, ArH-4), 7.25 (d, 1H, ArH-6), 7.33 (dxd, 2H, NPhH-3, 5), 7.65 (d, 2H, NPhH-2, 6), 8.35 (s, 1H, H-4), 10.0 (s, 1H, OH or NH), 10.60 (1H, OH or NH); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 156.1, 148.9, 138.4, 133.8, 133.6, 131.0, 128.7, 128.0, 127.9, 124.3, 124.1, 120.0, 116.1, 19.8; MS [m/z (%)]: 294 (7): $M^+$, 266 (18), 93 (100): $C_6H_7N^+$; HRMS calcd. for $C_{16}H_{14}N_4O_2$: 294.1117; found: 294.1110

**1-(2-Hydroxyphenyl)-*N,N*-diethyl-1*H*-1,2,3-triazole-5-carboxamide (10e).** Yield: 60%; m.p.: 155 °C; IR (KBr cm$^{-1}$): 1637, >3000; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 1.10 and 1.21 [2xt, 6H, $N(CH_2CH_3)_2$], 3.30 [m, 4H, $N(CH_2CH_3)_2$], 6.95 (dxdxd, 1H, ArH-5), 7.10 (dxd, 1H, ArH-3), 7.35 (m, 2H, ArH-4, 6), 8.10 (s, 1H, H-4), 10.30 (s, 1H, OH); $^{13}$C-NMR (250 MHz, $CHCl_3$): δ 158.9, 151.0, 133.7, 131.1, 130.7, 127.0, 123.9, 119.0, 116.3, 42.6, 39.5, 13.8, 12.0; MS [m/z (%)]: 260 (1): $M^+$, 232 (1), 72 (100): $NEt_2^+$; HRMS calcd. for $C_{13}H_{16}N_4O_2$: 260.1273; found: 260.1268; anal. calcd. for $C_{13}H_{16}N_4O_2$: C 59.99, H 6.20, N 21.52; found: 59.83, H 6.23, N 21.63

**1-(2-Hydroxyphenyl)-1*H*-1,2,3-triazole-5-carboxylic acid (10f).** Yield: 58%; IR (KCl cm$^{-1}$): >2500, 1713; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 6.60 (s, 1H, OH), 7.00 (m, 2H, ArH-3, 5), 7.35 (m, 2H, ArH-4, 6), 8.30 (s, 1H, H-4), 10-13 (br s, 1H, COOH); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 158.8, 151.9, 136.5, 131.7, 127.3, 124.8, 118.9, 116.4; MS [m/z (%)]: 205 (2): $M^+$, 187 (72), 103 (100); HRMS calcd. for $C_9H_7N_3O_3$: 205.0487; found: 205.0479

**(±)-1-Chloro-1-(1*H*-tetrazol-1-yl)-2-propanone (11a).** Yield: 85%; m.p.: 70 °C; IR (KBr cm$^{-1}$): 1750; $^1$H-NMR (250 MHz, $CDCl_3$): δ 2.63 (s, 3H, $CH_3$), 7.05 (s, 1H, CHCl), 9.05 (s, 1H, H-5); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 192.5, 142.9, 66.6, 25.9; MS [m/z (%)]: 161 (6): $MH^+$, 118 (100): $[M^+-CH_3CO]H$; HRMS calcd. for $C_4H_6ClN_4O$ (MH): 161.0230; found: 161.0320; anal. calcd. for $C_4H_5ClN_4O$: C 29.92, H 3.14, N 34.89; found: C 29.83, H 3.00, N 34.88

**(±)-2-Chloro-1-phenyl-2-(1*H*-tetrazol-1-yl)ethanone (11b).** Yield: 83%; m.p.: 86 °C; IR (KBr cm$^{-1}$): 1703; $^1$H-NMR (250 MHz, $CDCl_3$): δ 7.60 (m, 2H, PhH-3, 5), 7.75 (m, 1H, PhH-4), 7.88 (s, 1H, CHCl), 8.10 (dxd, 2H, PhH-2, 6), 9.28 (s, 1H, H-5); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 184.8, 143.6, 135.7, 131.0, 129.5, 129.4, 62.8; MS [m/z (%)]: 223 (1): $MH^+$, 105 (100): $PhCO^+$, 77 (51), 51 (17); HRMS calcd. for $C_9H_8ClN_4O$ (MH): 223.0389; found: 223.0392; anal. calcd. for $C_9H_7ClN_4O$: C 48.56, H 3.17, N 25.17; found: 48.22, H 3.14, N 25.08

**2-(1*H*-tetrazol-1-yl)phenol (12a).** Yield: 60%; m.p.: 135 °C; IR (KBr cm$^{-1}$): >3000; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 6.97 (dxdxd, 1H, H-4), 7.14 (dxd, 1H, H-6), 7.37 (dxdxd, 1H, H-5), 7.60 (dxd, 1H, H-3), 7.75 (s, 1H, H-tetrazole), 8.50-11.50 (s, 1H, OH); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 150.7, 144.4, 131.1, 125.3, 121.5, 119.2, 117.2; MS [m/z (%)]: 162 (8): $M^+$, 134 (48); anal. calcd. for $C_7H_6N_4O$: C 51.85, H 3.73, N 34.55; found: 51.90, H 4.12, N 34.13

**4-Chloro-2-(1*H*-tetrazol-1-yl)phenol (12b).** Yield: 63%; m.p.: 195 °C; IR (KBr cm$^{-1}$): >3000;; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 6.19 (d, 1H, H-6), 7.48 (dxd, 1H, H-5), 7.78 (d, 1H, H-3), 9.85 (s, 1H, H-tetrazole), 10.20-12.30 (br, 1H, OH); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 149.4, 144.5, 130.9, 125.1, 122.7, 122.2, 118.6; MS [m/z (%)]: 196 (4): $M^+$, 128 (30); anal. calcd. for $C_8H_8N_4O$: C 54.54, H 4.58, N 31.80; found: 54.56, H 4.49, N 31.83

**4-Methyl-2-(1*H*-tetrazol-1-yl)phenol (12c).** Yield: 70%; m.p.: 155 °C; IR (KBr $cm^{-1}$): >3000; $^1$H-NMR (250 MHz, DMSO-$d_6$): δ 2.27 (s, 3H, 4-$CH_3$), 7.03 (d, 1H, H-6), 7.21 (dxd, 1H, H-5), 7.41 (d, 1H, H-3), 9.73 (s, 1H, H-tetrazole), 10.54 (s, 1H, OH); $^{13}$C-NMR (250 MHz, DMSO-$d_6$): δ 147.8, 144.4, 128.7, 131.6, 125.5, 121.0, 116.9, 19.8; MS [m/z (%)]: 176 (5): $M^+$, 148 (100): $M^+$-$N_2$; anal. calcd. for $C_5H_7ClN_4O$: C 42.77, H 2.56, N 28.50; found: C 42.64, H 2.47, N 28.49

**Decarboxylation of the acids 9g and 10f: synthesis of compounds 13 and 14.**

Compounds **9g** or **10f** (10 mmol) were dissolved in chlorobenzene (100 ml) and refluxed for 12 hours. Then, the solvent was evaporated and the residue was recrystallised from a mixture of $CHCl_3$/hexane to yield **13** and **14** respectively.

**(±) 1-(1-Chloro-2-oxopropyl)-1*H*-1,2,3triazole (13).** Yield: 76%; m.p.: 55 °C; IR (KBr $cm^{-1}$) 1747; $^1$H-NMR (250 MHz, $CDCl_3$): δ 2.50 (s, 3H, $CH_3$), 7.05 (s, 1H, CHCl), 7.80 (s, 1H, H-4), 7.95 (s, 1H, H-5); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 193.7, 134.6, 124.1, 69.1, 25.8; anal. calcd. for $C_5H_6ClN_3O$: C 37.64, H 3.79, N 26.33; found: C 37.51, H 3.74, N 26.22

**2-[1*H*-1,2,3-triazol-1-yl]phenol (14).** Yield: 68%; m.p.: 154 °C; IR (KBr $cm^{-1}$) >2500; 7.03 (dxdxd, 1H, H-4), 7.20 (dxd, 1H, H-6), 7.30 (dxdxd, 1H, H-5), 7.43 (dxd, 1H, H-3), 7.90 (d, 1H, triazole-H-4), 8.50 (d, 1H, H-triazole-5); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 149.8, 133.0, 132.9, 129.9, 126.3, 119.4, 117.0; MS [m/z (%)]: 161 (54): $M^+$, 133 (45), 78 (100): $C_6H_4$; HRMS calcd. for $C_8H_7N_3O$: 161.0589; found: 161.0583;

**Preparation of compounds 15a and 15b.**

To a stirred mixture of phenol or 1-phenyl-1*H*-tetrazole-5-thiol (3 mmol) and NaH (3 mmol) in $CH_3CN$ (50 ml) compound **11b** (3 mmol) was added. After 15 minutes, the solvent was evaporated and the residue was subjected to chromatography ($SiO_2$, $CH_2Cl_2$/ hexane) and crystallised from a mixture of $CHCl_3$/hexane.

**(±)-2-Phenoxy-1-phenyl-2-(1*H*-tetrazol-1-yl)ethanone (15a).** Yield: 83%; m.p.: 150 °C; IR (KBr $cm^{-1}$): 1714; $^1$H-NMR (250 MHz, $CDCl_3$): δ 7.05 (d, 1H, OPhH-2), 7.13 (dxd, 1H, OPhH-4), 7.31 (dxd, 2H, OPhH-3, 5), 7.52 (dxdxd, 2H, COPhH-3, 5), 7.68 (dxdxd, 1H, COPhH-4), 7.90 (s, 1H, CHOPh), 8.03 (dxd, 2H, COPhH-2, 6), 9.06 (s, 1H, H-5) 13C-NMR (250 MHz, $CDCl_3$): δ 186.4, 154.8, 143.1, 135.3, 132.3, 130.3, 129.4, 129.3, 124.6, 83.8; MS [m/z (%)]: 281 (49): $M^+$, 239 (1), 211 (100): $M^+$-$N_3$, -CO; anal. calcd. for: $C_{15}H_{12}N_4O_2$: C 64.28, H 4.34, N 19.99; found: C 63.99, H 4.18, N 20.08

**(±)-1-Phenyl-2-[(1-phenyl-1*H*-tetrazol-5-yl)thio]-2-(1*H*-tetrazol-1-yl)ethanone (15b).** Yield: 80%; m.p.: 156 °C; IR (KBr $cm^{-1}$): 1694; $^1$H-NMR (250 MHz, $CDCl_3$): δ 7.48 (m, 7H, NPhH, COPhH-3, 5), 7.61 (dxd, 1H, COPhH-4), 8.00 (d, 2H, COPhH-2, 6), 8.75 (s, 1H, CHS), 9.06 (s, 1H, H-5); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 186.1, 150.2, 144.1, 135.6, 132.6, 131.7, 131.0, 130.2, 129.5, 129.3, 124.0, 66.0 MS [m/z (%)] (CI): 365 (100): $MH^+$, 189 (92), 105 (76); anal. calcd. for $C_{16}H_{12}N_8OS$: C 52.74, H 3.32, N 30.75; found: C 52.33, H 3.10, N 30.47

**Synthesis of (±)-*N*-(isopropyl)-2-chloro-1-(2,6-dichlorophenyl)-2-(1*H*-tetrazol-1-yl)ethanimine (16).**

Isopropyl amine (14 mmol) was added to a mixture of compound **11b** (3 mmol) in dry diethyl ether (50 ml) at 0 °C followed by dropwise addition of $TiCl_4$ (1 mmol). After addition, the reaction mixture was stirred for 24 hours at room temperature. Then, the reaction mixture was poored into 50 ml of an aqueous 0.5 - 1 N NaOH solution. After removal of the diethyl ether layer and extraction of the aqueous phase with

diethyl ether, the combined ether fractions were dried with $CaCO_3$ and evaporated. The residue was kept at low temperature to avoid decomposition.

**(±)-*N*-(isopropyl)-2-Chloro-1-(2,6-dichlorophenyl)-2-(1*H*-tetrazol-1-yl)ethanimine (16).** Yield: 82 %; m.p.: 104 - 105 °C; IR (KBr $cm^{-1}$): 1619, 3400; $^1$H-NMR (250 MHz, $CDCl_3$): imine: δ 0.95 and 1.25 (2xd, 6H, $CH(CH_3)_2$), 3.50 (m, 1H, $CH(CH_3)_2$), 9.20 (s, 1H, H-5); enamine: 1.15 (d, 6H, $CH(CH_3)_2$), 3.17 (m, 1H, $CH(CH_3)_2$, 4.38 (d, 1H, NH), 8.25 (s, 1H, H-5); enamine and imine: 7.0 - 7.6 (m, 10H, PhH); $^{13}$C-NMR (250 MHz, $CDCl_3$): imine: 159.0, 143.6, 132.2, 129.9, 129.0, 127.1, 69.3, 53.0, 23.2, 23.1; enamine: 147.4, 145.1, 130.5, 129.7, 128.7, 128.4, 90.1, 46.0, 24.1; MS [m/z (%)]: 264 (57): $MH^+$, 104 (100): Ph-$CN^+$; HRMS calcd. for $C_{12}H_{14}ClN_5$: 263.0938; found: 263.0941

**Synthesis of 2-azido-4-chloro-1-isopropyl-5-phenyl-imidazole (17).**

Compound **16** (3 mmol), NBS (6 mmol) and a catalytic amount of benzoyl peroxide were dissolved in $CCl_4$ (50 ml) and brought to reflux temperature. After 5 minutes, the reaction mixture was cooled and the precipitate was removed. After evaporation of the solvent, the residue was subjected to chromatographic purification ($SiO_2$, $CH_2Cl_2$/ hexane) and crystallised from a mixture of $CHCl_3$/hexane.

**2-Azido-4-chloro-1-isoproyl-5-phenyl-imidazole (17).** Yield: 60 %; m.p.: 102 °C; IR (KBr $cm^{-1}$): 2141; $^1$H-NMR (250 MHz, $CDCl_3$): δ 1.41 (d, 6H, $CH(CH_3)_2$), 4.17 (m, 1H, $CH(CH_3)_2$), 7.39 (m, 5H, PhH); $^{13}$C-NMR (250 MHz, $CDCl_3$): δ 138.3, 130.3, 128.8, 128.7, 127.9, 126.1, 124.3, 48.6, 21.3; MS [m/z (%)]: 261 (57): $M^+$, 104 (100); HRMS calcd. for $C_{12}H_{12}ClN_5$: 261.0781; found: 261.0780

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