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# A Facile Synthesis of 4-Tetrazolyl-Substituted 4*H*-3,1-Benzoxazines through Sequential Passerini-Azide/Acylation/Catalytic Aza-Wittig Reaction

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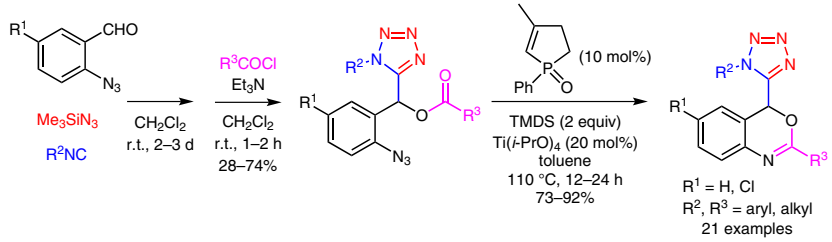


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**Abstract** A facile synthesis of 4-tetrazolyl-4*H*-3,1-benzoxazines by a Passerini-azide/acylation/catalytic aza-Wittig sequence was developed. The Passerini-azide reactions of 2-azidobenzaldehydes, trimethylsilyl azide and isocyanides produced tetrazoles, which were further acylated to give the azides in 28–74% overall yields. The catalytic aza-Wittig reactions of the azides generated 4-tetrazolyl-4*H*-3,1-benzoxazines in good yields, by using a catalytic amount of 3-methyl-1-phenyl phospholene-1-oxide (10 mol%) and TMDS/Ti(*i*-PrO)$_4$ reductant system.

**Key words** tetrazole, 4*H*-3,1-benzoxazine, Passerini-azide reaction, catalytic aza-Wittig reaction, acylation

1,5-Disubstituted tetrazoles may be regarded as bioisosteres of the *cis*-amide bond of peptides, and compounds containing this moiety have shown a range of biological activities.[1] For example (Figure 1), some tetrazoles were recently found to exhibit good antifungal activity against *Candida albicans*,[2] selective antitubercular activities,[3] anticancer activity,[4] reasonable inhibitory activity against DNA methyltransferase 1,[5] and potent Janus kinase 2 inhibitive activity.[6] Benzoxazines are also a class of fused heterocycles that are of interest to organic chemists because of their remarkable biological activities. Some benzoxazine derivatives have been reported to show strong anticancer activity,[7] fungicidal activity,[8] antiplatelet activity,[9,10] promising antiproliferative activity,[11] multifunctional antihyperlipidemic activity,[12] and antiarrhythmics against ischemia-reperfusion injury.[13] The benzoxazine derivative (Etifoxine) was utilized as a nonbenzodiazepine anticonvulsant drug. There are some known methods for the synthesis of 4*H*-3,1-benzoxazines;[14] however, 4-tetrazolyl-substituted 4*H*-3,1-benzoxazines have not yet been prepared, probably because they are not easily accessible by routine synthetic methods.

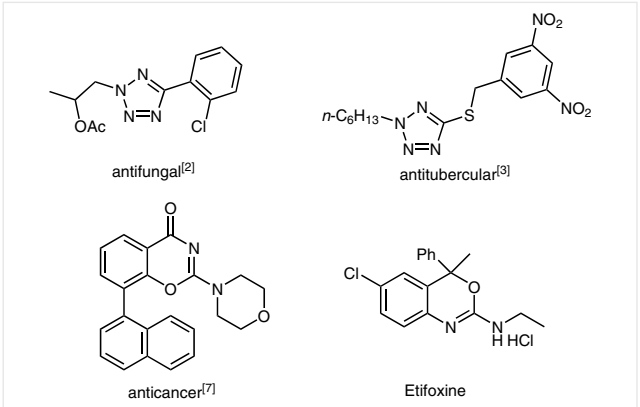
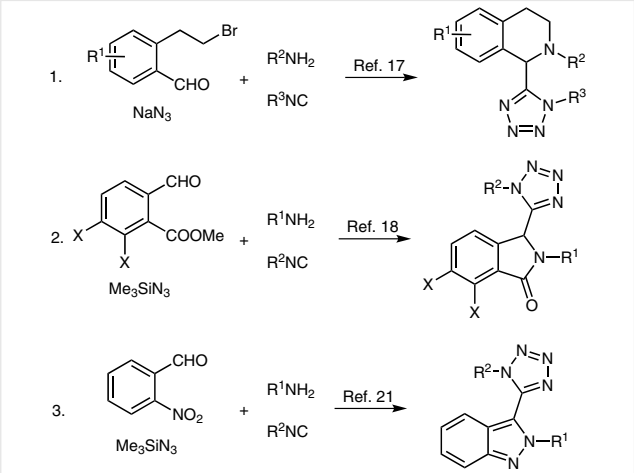



**Figure 1** Representative bioactive tetrazole and benzoxine

Isocyanide-based multicomponent reactions (IMCRs), mainly Passerini and Ugi reactions, have attracted much attention in the synthesis of diverse organic molecules because of their exceptional synthetic efficiency and high atom economy.[15] The so-called Ugi-azide reaction utilized hydrazoic acid (generated in situ from $NaN_3$ or TMS-$N_3$) instead of the carboxylic acid component used in the classical Ugi reaction to prepare 1,5-disubstituted tetrazoles.[16] It has been widely used in the preparation of various classes of heterocyclic compounds (Scheme 1), such as tetrazolyl-tetrahydroisoquinolines,[17] tetrazolyl-isoindolinones,[18] tetrazolyl-hydantoins,[19] tetrazolyl-β-carbolines,[20] tetrazolyl-indazoles,[21] α-amino tetrazoles,[22] tetrazolo-piperazines,[23] and tetrazolobenzodiazepines.[24] However, there were only a few reports on the related Passerini-azide reaction concerning the synthesis of α-hydroxy tetrazoles or the reaction enantioselectivity.[25]

The aza-Wittig reaction has received considerable attention in the synthesis of many heterocycles with complex




**Scheme 1** Reported preparation of tetrazoles through Ugi-azide reaction

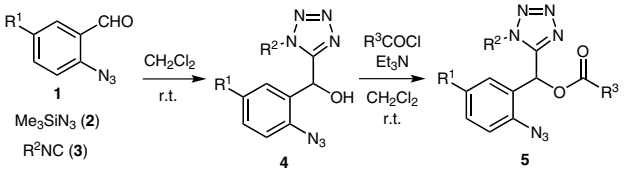
and diverse molecular structures under mild reaction conditions.[26] The development of a catalytic aza-Wittig reaction with recycling of the by-product phosphine oxide to prepare some heterocycles starting from carbonyl azides or isocyanate derivatives was recently reported.[27] The above catalytic aza-Wittig procedure utilized a catalytic amount of organophosphorus reagents compared with the traditional aza-Wittig reaction. Thus, as part of our ongoing investigation into the synthesis of various heterocycles through aza-Wittig reaction and multicomponent reaction,[28] herein we wish to report a new synthetic approach to 4-tetrazolyl-substituted 4*H*-3,1-benzoxazines through a sequential Passerini-azide/acylation/catalytic aza-Wittig reaction, starting from the easily accessible 2-azidobenzaldehydes, trimethylsilyl azide, isocyanides, and acyl chlorides.

A mixture of 2-azidobenzaldehydes **1**, trimethylsilyl azide **2**, and isocyanides **3** was stirred in anhydrous dichloromethane at room temperature, and the Passerini-azide reaction occurred smoothly to give α-hydroxy tetrazoles **4** when $R^2$ is an alkyl group ($R^2$ = *t*-Bu, *n*-Bu or cyclohexyl). The products **4** could be acylated with acyl chloride in the presence of triethylamine in the same solvent to produce azides **5** (Table 1). We attempted to perform the above Passerini-azide and acylation reaction in one-pot fashion and found that the reaction also took place successfully to give the products **5a–s**. As indicated in Table 1, the products **5a–s** could be obtained in 58–74% overall yield with various acyl chlorides: $R^3$ could be an alkyl group or an aryl group with substituents ($NO_2$, Cl, Br, F, $CH_3$ and $OCH_3$) on the benzene ring. The reactivity of the acyl chlorides had no obvious effect on the overall yields of the products. However, when arylisocyanide **3** was utilized ($R^2$ = 4-$ClC_6H_4$), products **5t** and **5u** were obtained in low yields (28–30%; Table 1). A by-product 1-(4-chlorophenyl)-1*H*-tetrazole (**5′**) was also isolated from the reaction mixture in 42–45% yield.

The formation of **5′** may be due to the two-component reaction of trimethylsilyl azide **2** with 4-chlorophenylisocyanide **3**, which have been reported previously.[16,29]

Azide **5a** was selected initially to react with triphenylphosphine in toluene at reflux (Table 2). The Staudinger reaction took place quickly but the following intramolecular aza-Wittig reaction occurred slowly. The 4-tetrazolyl-4*H*-3,1-benzoxazine **6a** was obtained in only 10% yield after heating to reflux for 12 hours (entry 1). Further heating the reaction mixture for 72 hours resulted in moderate yield (48%; entry 2). A better yield of product **6a** was produced when methyldiphenylphosphine was used in toluene heated to reflux for 12 hours (76%; entry 3). When the 3-methyl-1-phenyl phospholene, obtained from reduction of the corresponding phospholene-1-oxide, was applied, higher

**Table 1** Preparation of Azides **5** by One-Pot Passerini-Azide/Acylation Reaction




| 5 | $R^1$ | $R^2$ | $R^3$ | Yield (%)[b] |
|---|---|---|---|---|
| **5a** | H | *t*-Bu | Ph | 71 |
| **5b** | H | *t*-Bu | 4-$MeC_6H_4$ | 68 |
| **5c** | H | *t*-Bu | 4-$MeOC_6H_4$ | 66 |
| **5d** | H | *t*-Bu | 2-$MeOC_6H_4$ | 73 |
| **5e** | H | *c*-$C_6H_{11}$[a] | 4-$MeOC_6H_4$ | 63 |
| **5f** | H | *c*-$C_6H_{11}$[a] | 4-$ClC_6H_4$ | 69 |
| **5g** | H | *t*-Bu | 4-$ClC_6H_4$ | 74 |
| **5h** | H | *t*-Bu | 2-$ClC_6H_4$ | 71 |
| **5i** | H | *t*-Bu | 2-$FC_6H_4$ | 67 |
| **5j** | Cl | *t*-Bu | *i*-Pr | 60 |
| **5k** | H | *t*-Bu | Me | 67 |
| **5l** | H | *n*-Bu | Ph | 59 |
| **5m** | Cl | *t*-Bu | 4-$ClC_6H_4$ | 62 |
| **5n** | H | *t*-Bu | 4-$BrC_6H_4$ | 68 |
| **5o** | H | *t*-Bu | 4-$O_2NC_6H_4$ | 66 |
| **5p** | H | *c*-$C_6H_{11}$[a] | 2-$ClC_6H_4$ | 58 |
| **5q** | H | *n*-Bu | 4-$MeC_6H_4$ | 67 |
| **5r** | H | *c*-$C_6H_{11}$[a] | 4-$MeC_6H_4$ | 61 |
| **5s** | H | *t*-Bu | cinnamoyl | 65 |
| **5t** | H | 4-$ClC_6H_4$ | 4-$ClC_6H_4$ | 28 (42[c]) |
| **5u** | H | 4-$ClC_6H_4$ | 4-$MeC_6H_4$ | 30 (45[c]) |

[a] Cyclohexyl.
[b] Isolated yields based on azides **1**.
[c] Isolated yield of the by-product **5′** [1-(4-chlorophenyl)-1*H*-tetrazole].

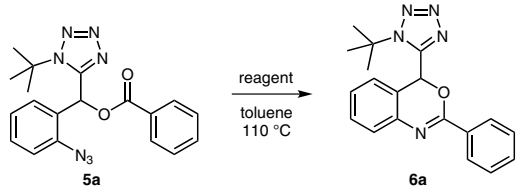
yield of the product **6a** was generated (93%; entry 4) upon heating the reaction mixture to reflux for only 6 hours.

The catalytic aza-Wittig reaction of **5a** was then investigated. In the presence of a catalytic amount of 3-methyl-1-phenyl phospholene-1-oxide (10 mol%), the product **6a** was obtained in 91% yield after heating to reflux for 12 hours with the tetramethyldisiloxane (TMDS) and Ti(*i*-PrO)$_4$ (20 mol%) reductant system (Table 2, entry 5). Reducing the amount of either 3-methyl-1-phenyl phospholene-1-oxide to 5 mol% or Ti(*i*-PrO)$_4$ to 10 mol% resulted in lower yields of the product (72–83%; Table 2, entries 6 and 7).

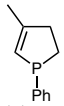
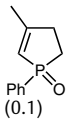
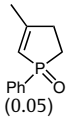
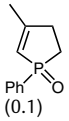
The catalytic aza-Wittig reaction conditions (Table 2, entry 5) were then used further for the preparation of other 4-tetrazolyl-4*H*-3,1-benzoxazines **6** (Table 3). The reaction proceeded smoothly to afford 4-tetrazolyl-4*H*-3,1-benzoxazines **6** in 73–92% yields with various substituents on the reactants (Table 3). The investigated functional groups ($NO_2$, Cl, Br, F, Me, OMe, alkenyl) were all tolerated in the one-pot method because of the mild reaction conditions and the reaction selectivity. The reaction yields were related to the electronic effect of the $R^3$ group: good to high yields (81–92%) were reached when $R^3$ are phenyl groups substituted by H, methyl or electron-withdrawing $NO_2$, Cl, Br and F groups (compounds **6a**,**b**,**f**–**i**,**l**–**r**,**t**,**u**). Lower yields (73–79%) were obtained when $R^3$ are alkyl, alkenyl or phenyl groups substituted by strong electron-donating $OCH_3$ groups (compounds **6c**–**e**,**j**,**k**,**s**).

The structure of compounds **6a**–**u** was confirmed based on their spectral data. For example, the $^1$H NMR spectrum of **6a** shows signals attributable to CH and Ar-H atoms at δ = 8.06–6.71 ppm as multiplets. The signal of *tert*-butyl appears at δ = 1.79 ppm as a singlet. The $^{13}$C NMR spectrum of **6a** shows the signals of tetrazole-5-C and benzoxazine-2-C at δ = 154.0 and 152.1 ppm. The signals of benzoxazine-4-C and *tert*-butyl carbon appear at δ = 68.5, 62.6 and 30.2

**Table 2** Preparation of the 4-Tetrazolyl-4*H*-3,1-benzoxazine **6a**; Optimization of the Reaction Conditions

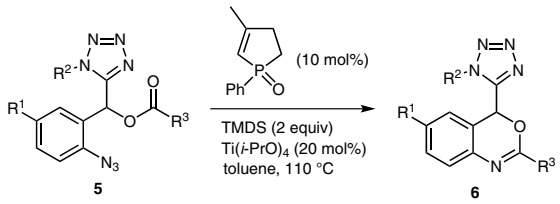



**5a** **6a**

| Entry | Reagent (equiv) | Reductant (equiv) | Ti(*i*-PrO)$_4$ (equiv) | Time (h) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | $Ph_3P$ (1) | 0 | 0 | 12 | 10 |
| 2 | $Ph_3P$ (1) | 0 | 0 | 72 | 48 |
| 3 | $Ph_2MeP$ (1) | 0 | 0 | 12 | 76 |
| 4 |  (1) | 0 | 0 | 6 | 93 |
| 5 |  (0.1) | TMDS (2) | 0.2 | 12 | 91 |
| 6 |  (0.05) | TMDS (2) | 0.2 | 24 | 83 |
| 7 |  (0.1) | TMDS (2) | 0.1 | 24 | 72 |

[a] Isolated yield based on azide **5a**.

**Table 3** Preparation of **6** through Catalytic Aza-Wittig Reaction




**5** **6**

| 6 | $R^1$ | $R^2$ | $R^3$ | Yield (%)[b] |
|---|---|---|---|---|
| **6a** | H | *t*-Bu | Ph | 91 |
| **6b** | H | *t*-Bu | 4-Me$C_6H_4$ | 85 |
| **6c** | H | *t*-Bu | 4-MeO$C_6H_4$ | 79 |
| **6d** | H | *t*-Bu | 2-MeO$C_6H_4$ | 73 |
| **6e** | H | *c*-$C_6H_{11}$[a] | 4-MeO$C_6H_4$ | 76 |
| **6f** | H | *c*-$C_6H_{11}$[a] | 4-Cl$C_6H_4$ | 88 |
| **6g** | H | *t*-Bu | 4-Cl$C_6H_4$ | 87 |
| **6h** | H | *t*-Bu | 2-Cl$C_6H_4$ | 81 |
| **6i** | H | *t*-Bu | 2-F$C_6H_4$ | 87 |
| **6j** | Cl | *t*-Bu | *i*-Pr | 74 |
| **6k** | H | *t*-Bu | Me | 75 |
| **6l** | H | *n*-Bu | Ph | 90 |
| **6m** | Cl | *t*-Bu | 4-Cl$C_6H_4$ | 92 |
| **6n** | H | *t*-Bu | 4-Br$C_6H_4$ | 91 |
| **6o** | H | *t*-Bu | 4-$O_2$N$C_6H_4$ | 82 |
| **6p** | H | *c*-$C_6H_{11}$[a] | 2-Cl$C_6H_4$ | 84 |
| **6q** | H | *n*-Bu | 4-Me$C_6H_4$ | 89 |
| **6r** | H | *c*-$C_6H_{11}$[a] | 4-Me$C_6H_4$ | 86 |
| **6s** | H | *t*-Bu | cinnamoyl | 73 |
| **6t** | H | 4-Cl$C_6H_4$ | 4-Cl$C_6H_4$ | 90 |
| **6u** | H | 4-Cl$C_6H_4$ | 4-Me$C_6H_4$ | 85 |

[a] Cyclohexyl.
[b] Isolated yield based on azides **5**.

ppm. The mass spectrum of **6a** shows a molecular ion peak at *m*/*z* 333 with 12% abundance.

In summary, we have developed a facile synthesis of 4-tetrazolyl-4*H*-3,1-benzoxazines through sequential Passerini-azide/acylation/catalytic aza-Wittig reaction. The mild reaction conditions, good yields and easily accessible starting materials make this method a valuable tool for generating multisubstituted 4-tetrazolyl-4*H*-1,3-benzoxazines, which are of considerable interest as potential biologically active compounds or pharmaceuticals.

Melting points were determined with an X-4 model apparatus and are uncorrected. MS were measured with a Finnigan Trace mass spectrometer. HRMS were measured with an Agilent 6224 TOF LC/MS spectrometer. NMR spectra were recorded in $CDCl_3$ or DMSO-$d_6$ with a Varian Mercury 600 or 400 spectrometer and resonances are reported relative to TMS. Elemental analyses were taken with a Vario EL III elementary analysis instrument.

### Preparation of Azides 5a–s; General Procedure

To a solution of 2-azidobenzaldehyde **1** (1 mmol) in anhydrous $CH_2Cl_2$ (5 mL) was added sequentially trimethylsilyl azide **2** (0.115 g, 1 mmol) and isocyanide **3** (1 mmol) at r.t. After stirring the reaction mixture for 2–3 days at ambient temperature, $Et_3N$ (0.121 g, 1.2 mmol) was added to the reaction system followed by the dropwise addition of acyl chloride (1.2 mmol). The reaction mixture was stirred at r.t. for 1–2 h. The solvent was evaporated under reduced pressure and the residue was purified by silica gel chromatography (EtOAc/petroleum ether, 1:6) to afford **5a–s** or 1-(4-chlorophenyl)-1*H*-tetrazole (**5′**).

### (2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl Benzoate (5a)

Yield: 0.268 g (71%); white solid; mp 128–129 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.06 (d, *J* = 7.2 Hz, 2 H, Ar-H), 7.69 (s, 1 H, CH), 7.61–7.19 (m, 7 H, Ar-H), 1.79 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 165.1, 152.2, 137.4, 133.7, 130.7, 129.8, 129.1, 128.4, 128.3, 126.0, 125.2, 118.0, 63.0, 62.0, 29.7.

Anal. Calcd for $C_{19}H_{19}N_7O_2$: C, 60.47; H, 5.07; N, 25.98. Found: C, 60.57; H, 5.18; N, 25.75.

### (2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 4-Methylbenzoate (5b)

Yield: 0.265 g (68%); white solid; mp 172–173 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.95 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.67 (s, 1 H, CH), 7.59–7.19 (m, 6 H, Ar-H), 2.41 (s, 3 H, $CH_3$), 1.79 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 165.0, 152.2, 144.6, 137.2, 130.5, 129.8, 129.1, 128.9, 126.1, 125.5, 125.1, 117.9, 62.8, 61.9, 29.6, 21.5.

Anal. Calcd for $C_{20}H_{21}N_7O_2$: C, 61.37; H, 5.41; N, 25.05. Found: C, 61.59; H, 5.47; N, 25.01.

### (2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 4-Methoxybenzoate (5c)

Yield: 0.269 g (66%); white solid; mp 168–169 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.02 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.66 (s, 1 H, CH), 7.59–7.19 (m, 4 H, Ar-H), 6.92 (d, *J* = 9.0 Hz, 2 H, Ar-H), 3.86 (s, 3 H, $OCH_3$), 1.79 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.7, 163.9, 152.4, 137.3, 132.6, 132.0, 130.5, 128.9, 126.3, 125.2, 120.6, 118.0, 114.0, 113.7, 62.7, 62.0, 55.4, 29.7.

Anal. Calcd for $C_{20}H_{21}N_7O_3$: C, 58.96; H, 5.20; N, 24.06. Found: C, 58.92; H, 5.03; N, 24.29.

### (2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 2-Methoxybenzoate (5d)

Yield: 0.296 g (73%); white solid; mp 118–119 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.94 (t, *J* = 8.4 Hz, 1 H, Ar-H), 7.68 (s, 1 H, CH), 7.61–6.97 (m, 7 H, Ar-H), 3.89 (s, 3 H, $OCH_3$), 1.78 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.0, 159.8, 152.4, 137.4, 134.6, 132.2, 130.6, 129.3, 126.2, 125.2, 120.1, 118.0, 117.5, 111.9, 62.7, 62.0, 55.8, 29.7.

Anal. Calcd for $C_{20}H_{21}N_7O_3$: C, 58.96; H, 5.20; N, 24.06. Found: C, 58.89; H, 5.10; N, 24.27.

### (2-Azidophenyl)(1-cyclohexyl-1*H*-tetrazol-5-yl)methyl 4-Methoxybenzoate (5e)

Yield: 0.271 g (63%); white solid; mp 128–129 °C.

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 8.05 (d, *J* = 8.8 Hz, 2 H, Ar-H), 7.83 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.48 (s, 1 H, CH), 7.46–7.19 (m, 3 H, Ar-H), 6.93 (d, *J* = 8.8 Hz, 2 H, Ar-H), 4.63–4.57 (m, 1 H, NCH), 3.86 (s, 3 H, $OCH_3$), 2.10–1.31 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.6, 164.0, 152.2, 136.9, 131.9, 130.5, 128.6, 126.1, 125.4, 120.5, 118.0, 113.8, 61.3, 58.4, 55.4, 32.9, 32.8, 25.2, 25.1, 24.7.

Anal. Calcd for $C_{22}H_{23}N_7O_3$: C, 60.96; H, 5.35; N, 22.62. Found: C, 60.85; H, 5.27; N, 22.73.

### (2-Azidophenyl)(1-cyclohexyl-1*H*-tetrazol-5-yl)methyl 4-Chlorobenzoate (5f)

Yield: 0.303 g (69%); white solid; mp 135–136 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.03 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.83 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.47–7.21 (m, 6 H, Ar-H and CH), 4.60–4.55 (m, 1 H, NCH), 2.13–1.33 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.2, 151.9, 140.2, 136.9, 131.7, 131.1, 130.7, 129.1, 128.8, 126.7, 125.5, 118.0, 61.8, 58.4, 32.9, 32.6, 25.1, 24.6.

Anal. Calcd for $C_{21}H_{20}ClN_7O_2$: C, 57.60; H, 4.60; N, 22.39. Found: C, 57.84; H, 4.65; N, 22.14.

### (2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 4-Chlorobenzoate (5g)

Yield: 0.304 g (74%); white solid; mp 157–158 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.99 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.67 (s, 1 H, CH), 7.54–7.20 (m, 6 H, Ar-H), 1.77 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.3, 152.1, 140.2, 137.5, 131.2, 130.9, 129.4, 128.8, 126.9, 125.6, 125.3, 118.1, 63.3, 62.0, 29.6.

Anal. Calcd for $C_{19}H_{18}ClN_7O_2$: C, 55.41; H, 4.41; N, 23.81. Found: C, 55.26; H, 4.55; N, 22.91.

**(2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 2-Chlorobenzoate (5h)**

Yield: 0.291 g (71%); white solid; mp 136–137 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.99 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.71 (s, 1 H, CH), 7.54–7.19 (m, 7 H, Ar-H), 1.77 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 163.8, 152.1, 137.7, 134.2, 133.3, 132.0, 131.1, 131.0, 129.7, 127.9, 126.7, 125.5, 125.3, 118.2, 63.5, 62.1, 29.7.

Anal. Calcd for $C_{19}H_{18}ClN_7O_2$: C, 55.41; H, 4.41; N, 23.81. Found: C, 55.59; H, 4.51; N, 22.58.

**(2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 2-Fluorobenzoate (5i)**

Yield: 0.265 g (67%); white solid; mp 148–149 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.98 (t, *J* = 7.2 Hz, 1 H, Ar-H), 7.69 (s, 1 H, CH), 7.59–7.13 (m, 7 H, Ar-H), 1.78 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 163.5, 162.7, 160.9, 152.2, 137.6, 135.5, 135.4, 132.2, 130.9, 129.6, 125.7, 125.4, 124.1, 118.1, 117.2, 116.9, 63.3, 62.1, 29.8.

Anal. Calcd for $C_{19}H_{18}FN_7O_2$: C, 57.72; H, 4.59; N, 24.80. Found: C, 57.59; H, 4.51; N, 22.96.

**(2-Azido-5-chlorophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl Isobutyrate (5j)**

Yield: 0.225 g (60%); white solid; mp 120–121 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.48–7.39 (m, 2 H, Ar-H), 7.35 (s, 1 H, CH), 7.13 (d, *J* = 8.4 Hz, 1 H, Ar-H), 2.69–2.65 (m, 1 H, CH), 1.76 (s, 9 H, $3CH_3$), 1.20 (d, *J* = 6.6 Hz, 6 H, $2CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 175.5, 151.7, 135.9, 130.6, 130.5, 129.0, 127.7, 119.3, 62.0, 61.9, 33.5, 29.6, 18.5.

Anal. Calcd for $C_{16}H_{20}ClN_7O_2$: C, 50.86; H, 5.34; N, 25.95. Found: C, 50.69; H, 5.41; N, 25.87.

**(2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl Acetate (5k)**

Yield: 0.212 g (67%); white solid; mp 133–134 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.47–7.17 (m, 5 H, Ar-H and CH), 2.16 (s, 3 H, $CH_3$), 1.72 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 169.8, 152.3, 137.6, 130.9, 129.6, 125.7, 125.3, 118.1, 62.8, 61.9, 29.7, 20.6.

Anal. Calcd for $C_{14}H_{17}N_7O_2$: C, 53.32; H, 5.43; N, 31.09. Found: C, 53.55; H, 5.51; N, 31.01.

**(2-Azidophenyl)(1-butyl-1*H*-tetrazol-5-yl)methyl Benzoate (5l)**

Yield: 0.222 g (59%); white solid; mp 88–89 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.09 (d, *J* = 7.2 Hz, 2 H, Ar-H), 7.84 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.62–7.21 (m, 7 H, Ar-H and CH), 4.52–4.49 (m, 2 H, $NCH_2$), 1.96–1.92 (m, 2 H, $CH_2$), 1.42–1.38 (m, 2 H, $CH_2$), 0.94 (t, *J* = 7.2 Hz, 3 H, $CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.9, 152.7, 137.0, 133.8, 130.6, 129.7, 128.6, 128.4, 128.2, 125.5, 125.4, 118.0, 61.5, 47.5, 31.3, 19.4, 13.2.

Anal. Calcd for $C_{19}H_{19}N_7O_2$: C, 60.47; H, 5.07; N, 25.98. Found: C, 60.75; H, 5.17; N, 25.79.

**(2-Azido-5-chlorophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 4-Chlorobenzoate (5m)**

Yield: 0.321 g (62%); white solid; mp 170–171 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.00 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.62 (s, 1 H, CH), 7.57–7.15 (m, 5 H, Ar-H), 1.79 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.1, 151.6, 140.5, 136.0, 131.7, 131.3, 130.8, 129.1, 128.9, 127.4, 126.6, 119.4, 62.7, 62.2, 29.7.

Anal. Calcd for $C_{19}H_{17}Cl_2N_7O_2$: C, 51.13; H, 3.84; N, 21.97. Found: C, 51.25; H, 3.67; N, 21.88.

**(2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 4-Bromobenzoate (5n)**

Yield: 0.311 g (68%); white solid; mp 161–162 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.92 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.67 (s, 1 H, CH), 7.59–7.19 (m, 6 H, Ar-H), 1.77 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 164.5, 152.1, 137.5, 131.8, 131.4, 130.9, 129.4, 129.0, 127.3, 125.6, 125.3, 118.1, 63.4, 62.0, 29.7.

Anal. Calcd for $C_{19}H_{18}BrN_7O_2$: C, 50.01; H, 3.98; N, 21.49. Found: C, 50.15; H, 4.07; N, 21.24.

**(2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl 4-Nitrobenzoate (5o)**

Yield: 0.277 g (66%); white solid; mp 180–181 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.28 (d, *J* = 8.4 Hz, 2 H, Ar-H), 8.23 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.71 (s, 1 H, CH), 7.52–7.20 (m, 4 H, Ar-H), 1.76 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 163.5, 151.9, 150.6, 137.8, 133.8, 131.3, 131.0, 129.8, 125.3, 124.9, 123.5, 118.2, 64.0, 62.0, 29.6.

Anal. Calcd for $C_{19}H_{18}N_8O_4$: C, 54.03; H, 4.30; N, 26.53. Found: C, 54.25; H, 4.39; N, 26.37.

**(2-Azidophenyl)(1-cyclohexyl-1*H*-tetrazol-5-yl)methyl 2-Chlorobenzoate (5p)**

Yield: 0.255 g (58%); white solid; mp 144–145 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.98 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.85 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.51–7.21 (m, 7 H, Ar-H and CH), 4.63–4.59 (m, 1 H, NCH), 2.15–1.33 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 163.7, 151.8, 136.9, 134.0, 133.4, 131.8, 131.1, 130.7, 128.9, 127.8, 126.6, 125.4, 125.2, 117.9, 62.1, 58.4, 32.9, 32.6, 25.1, 25.0, 24.6.

Anal. Calcd for $C_{21}H_{20}ClN_7O_2$: C, 57.60; H, 4.60; N, 22.39. Found: C, 57.51; H, 4.49; N, 22.56.

**(2-Azidophenyl)(1-butyl-1*H*-tetrazol-5-yl)methyl 4-Methylbenzoate (5q)**

Yield: 0.262 g (67%); light-yellow oil.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.98 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.83 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.48 (s, 1 H, CH), 7.47–7.20 (m, 5 H, Ar-H), 4.52–4.49 (m, 2 H, $NCH_2$), 2.42 (s, 3 H, $CH_3$), 1.96–1.92 (m, 2 H, $CH_2$), 1.42–1.38 (m, 2 H, $CH_2$), 0.94 (t, *J* = 7.2 Hz, 3 H, $CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 165.0, 152.8, 144.8, 137.1, 130.6, 129.9, 129.2, 128.6, 125.8, 125.5, 125.4, 118.0, 61.3, 47.6, 31.4, 21.6, 19.5, 13.3.

Anal. Calcd for $C_{20}H_{21}N_7O_2$: C, 61.37; H, 5.41; N, 25.05. Found: C, 61.51; H, 5.53; N, 24.82.

**(2-Azidophenyl)(1-cyclohexyl-1*H*-tetrazol-5-yl)methyl 4-Methylbenzoate (5r)**

Yield: 0.256 g (61%); white solid; mp 140–141 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.98 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.84 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.49 (s, 1 H, CH), 7.46–7.20 (m, 5 H, Ar-H), 4.62–4.58 (m, 1 H, NCH), 2.42 (s, 3 H, $CH_3$), 2.13–1.32 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 165.0, 152.1, 144.8, 136.9, 130.5, 129.8, 129.2, 128.6, 126.0, 125.5, 125.4, 118.0, 61.5, 58.5, 32.9, 32.8, 25.2, 25.1, 24.7, 21.6.

Anal. Calcd for $C_{22}H_{23}N_7O_2$: C, 63.30; H, 5.55; N, 23.49. Found: C, 63.13; H, 5.65; N, 23.35.

**(2-Azidophenyl)[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]methyl Cinnamate (5s)**

Yield: 0.263 g (65%); white solid; mp 131–132 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.76 (d, *J* = 16.2 Hz, 1 H, =CH), 7.58 (s, 1 H, CH), 7.54–7.20 (m, 9 H, Ar-H), 6.51 (d, *J* = 16.2 Hz, 1 H, =CH), 1.78 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 165.4, 152.4, 147.0, 137.4, 133.7, 130.7, 129.3, 128.8, 128.5, 128.2, 126.0, 125.3, 118.1, 116.0, 62.7, 62.0, 29.7.

Anal. Calcd for $C_{21}H_{21}N_7O_2$: C, 62.52; H, 5.25; N, 24.30. Found: C, 62.63; H, 5.15; N, 24.37.

**(2-Azidophenyl)[1-(4-chlorophenyl)-1*H*-tetrazol-5-yl]methyl 4-Chlorobenzoate (5t)**

Yield: 0.131 g (28%); white solid; mp 126–127 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.95 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.73 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.56–7.41 (m, 7 H, Ar-H), 7.35 (s, 1 H, CH), 7.24–7.14 (m, 2 H, Ar-H).

$^{13}$C NMR ($CDCl_3$, 150 MHz): δ = 164.3, 153.6, 140.5, 137.5, 137.2, 131.9, 131.3, 131.1, 130.0, 129.2, 129.0, 126.8, 126.7, 125.5, 125.1, 118.2, 62.6.

HRMS: *m*/*z* calcd for $[C_{21}H_{13}Cl_2N_7O_2 + H]^+$: 466.0581; found: 466.0575.

**(2-Azidophenyl)[1-(4-chlorophenyl)-1*H*-tetrazol-5-yl]methyl 4-Methylbenzoate (5u)**

Yield: 0.132 g (30%); white solid; mp 98–99 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.90 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.75 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.55–7.42 (m, 5 H, Ar-H), 7.36 (s, 1 H, CH), 7.26–7.13 (m, 4 H, Ar-H), 2.42 (s, 3 H, $CH_3$).

$^{13}$C NMR ($CDCl_3$, 150 MHz): δ = 165.1, 153.8, 144.9, 137.4, 137.1, 132.0, 130.9, 130.0, 129.6, 129.3, 129.1, 129.0, 126.8, 126.7, 125.5, 118.2, 62.2, 21.8.

HRMS: *m*/*z* calcd for $[C_{22}H_{16}ClN_7O_2 + Na]^+$: 468.0946; found: 468.0938.

**1-(4-Chlorophenyl)-1*H*-tetrazole (5')**

Yield: 0.076 or 0.081 g (42% or 45%); white solid; mp 155–156 °C (Lit.[30] 152–153 °C).

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 9.08 (s, 1 H, tetrazol-5-H), 7.71 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.58 (d, *J* = 8.4 Hz, 2 H, Ar-H).

$^{13}$C NMR ($CDCl_3$, 150 MHz): δ = 140.4, 136.0, 132.2, 130.4, 122.4.

HRMS: *m*/*z* calcd for $[C_7H_5ClN_4 + H]^+$: 181.0276; found: 181.0271.

**Preparation of 4-Tetrazolyl-4*H*-3,1-benzoxazines 6 through Catalytic Aza-Wittig Reaction; General Procedure**

To a solution of azide **5** (1 mmol) in toluene (5 mL) was added 3-methyl-1-phenyl phospholene-1-oxide (0.019 g, 0.1 mmol), Ti(*i*-PrO)$_4$ (0.053 g, 0.2 mmol) and TMDS (0.27 g, 2 mmol). The reaction mixture was then stirred at 110 °C and monitored by TLC. When the reaction was complete (12–24 h), the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (EtOAc–petroleum ether, 1:4) to give 4-tetrazolyl-4*H*-3,1-benzoxazines **6a–s**.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-phenyl-4*H*-1,3-benzoxazine (6a)**

Yield: 0.304 g (91%); white solid; mp 145–146 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.06 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.51–7.18 (m, 7 H, Ar-H and CH), 6.71 (d, *J* = 7.8 Hz, 1 H, Ar-H), 1.79 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 154.0, 152.1, 138.4, 131.7, 131.3, 130.1, 128.2, 127.6, 127.1, 125.6, 124.2, 120.6, 68.5, 62.6, 30.2.

MS (EI, 70 eV): *m*/*z* (%) = 333 (12) $[M]^+$, 208 (100), 172 (3), 105 (14), 77 (11).

Anal. Calcd for $C_{19}H_{19}N_5O$: C, 68.45; H, 5.74; N, 21.01. Found: C, 68.57; H, 5.84; N, 20.87.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-(*p*-tolyl)-4*H*-1,3-benzoxazine (6b)**

Yield: 0.294 g (85%); white solid; mp 187–188 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.95 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.40–7.16 (m, 6 H, Ar-H and CH), 6.69 (d, *J* = 7.8 Hz, 1 H, Ar-H), 2.40 (s, 3 H, $CH_3$), 1.77 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 154.0, 152.0, 142.1, 138.5, 129.9, 128.9, 128.4, 127.5, 126.7, 125.3, 124.1, 120.5, 68.3, 62.5, 30.1, 21.3.

MS (EI, 70 eV): *m*/*z* (%) = 347 (18) $[M]^+$, 222 (100), 119 (18), 91 (15).

Anal. Calcd for $C_{20}H_{21}N_5O$: C, 69.14; H, 6.09; N, 20.16. Found: C, 69.35; H, 6.17; N, 20.02.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-(4-methoxyphenyl)-4*H*-1,3-benzoxazine (6c)**

Yield: 0.285 g (79%); white solid; mp 168–169 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.02 (d, *J* = 9.0 Hz, 2 H, Ar-H), 7.39–6.91 (m, 6 H, Ar-H and CH), 6.67 (d, *J* = 7.8 Hz, 1 H, Ar-H), 3.86 (s, 3 H, $OCH_3$), 1.77 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 162.5, 154.2, 152.1, 138.8, 130.2, 129.6, 126.7, 125.4, 124.1, 123.6, 120.7, 113.7, 68.9, 62.7, 55.3, 30.3.

MS (EI, 70 eV): *m*/*z* (%) = 363 (23) $[M]^+$, 238 (100), 135 (21), 92 (5).

Anal. Calcd for $C_{20}H_{21}N_5O_2$: C, 66.10; H, 5.82; N, 19.27. Found: C, 66.19; H, 5.63; N, 19.01.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-(2-methoxyphenyl)-4*H*-1,3-benzoxazine (6d)**

Yield: 0.266 g (73%); white solid; mp 136–137 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.61 (d, *J* = 7.2 Hz, 1 H, Ar-H), 7.42–7.21 (m, 4 H, Ar-H), 7.13 (s, 1 H, CH), 6.99–6.77 (m, 3 H, Ar-H), 3.67 (s, 3 H, $OCH_3$), 1.80 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 158.0, 155.8, 152.1, 138.6, 132.1, 130.5, 130.1, 127.2, 125.5, 124.4, 122.1, 120.4, 120.3, 111.3, 68.1, 62.4, 55.5, 30.1.

MS (EI, 70 eV): *m*/*z* (%) = 363 (8) [M]$^+$, 238 (100), 135 (58), 132 (9).

Anal. Calcd for $C_{20}H_{21}N_5O_2$: C, 66.10; H, 5.82; N, 19.27. Found: C, 66.34; H, 5.71; N, 19.42.

**4-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-2-(4-methoxyphenyl)-4*H*-1,3-benzoxazine (6e)**

Yield: 0.297 g (76%); white solid; mp 154–155 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.05 (d, *J* = 9.0 Hz, 2 H, Ar-H), 7.41–7.14 (m, 4 H, Ar-H and CH), 6.94 (d, *J* = 9.0 Hz, 2 H, Ar-H), 6.69 (d, *J* = 7.2 Hz, 1 H, Ar-H), 4.26–4.21 (m, 1 H, NCH), 3.87 (s, 3 H, $OCH_3$), 1.91–1.00 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 162.4, 154.2, 151.9, 138.0, 130.1, 129.3, 126.6, 125.1, 123.9, 123.0, 119.0, 113.4, 68.4, 58.7, 55.0, 32.9, 32.1, 24.8, 24.7, 24.2.

MS (EI, 70 eV): *m*/*z* (%) = 389 (26) [M]$^+$, 238 (100), 135 (20), 107 (2), 77 (9).

Anal. Calcd for $C_{22}H_{23}N_5O_2$: C, 67.85; H, 5.95; N, 17.98. Found: C, 67.68; H, 5.84; N, 17.91.

**2-(4-Chlorophenyl)-4-(1-cyclohexyl-1*H*-tetrazol-5-yl)-4*H*-1,3-benzoxazine (6f)**

Yield: 0.346 g (88%); white solid; mp 138–139 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.04 (d, *J* = 9.0 Hz, 2 H, Ar-H), 7.43–7.19 (m, 5 H, Ar-H), 7.18 (s, 1 H, CH), 6.72 (d, *J* = 7.2 Hz, 1 H, Ar-H), 4.22–4.17 (m, 1 H, NCH), 1.92–1.02 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 153.5, 151.8, 138.0, 137.6, 130.4, 129.4, 128.9, 128.5, 127.5, 125.7, 124.1, 119.1, 68.8, 58.9, 33.0, 32.2, 24.9, 24.8, 24.3.

MS (EI, 70 eV): *m*/*z* (%) = 393 (19) [M]$^+$, 242 (100), 139 (14), 111 (8), 77 (9).

Anal. Calcd for $C_{21}H_{20}ClN_5O$: C, 64.04; H, 5.12; N, 17.78. Found: C, 64.15; H, 5.25; N, 17.60.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-(4-chlorophenyl)-4*H*-1,3-benzoxazine (6g)**

Yield: 0.321 g (87%); white solid; mp 207–208 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.00 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.42–7.19 (m, 6 H, Ar-H and CH), 6.72 (d, *J* = 7.2 Hz, 1 H, Ar-H), 1.79 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 153.2, 152.0, 138.2, 137.9, 130.3, 129.9, 129.0, 128.6, 127.4, 125.8, 124.3, 120.6, 68.8, 62.6, 30.3.

MS (EI, 70 eV): *m*/*z* (%) = 367 (14) [M]$^+$, 242 (100), 139 (17), 111 (10), 77 (8).

Anal. Calcd for $C_{19}H_{18}ClN_5O$: C, 62.04; H, 4.93; N, 19.04. Found: C, 62.07; H, 4.80; N, 19.28.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-(2-chlorophenyl)-4*H*-1,3-benzoxazine (6h)**

Yield: 0.296 g (81%); white solid; mp 110–111 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.67 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.43–7.21 (m, 7 H, Ar-H and CH), 6.76 (d, *J* = 7.2 Hz, 1 H, Ar-H), 1.71 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 154.6, 152.1, 138.0, 132.7, 131.8, 131.6, 131.0, 130.2, 127.7, 126.7, 125.8, 124.5, 120.2, 68.4, 62.5, 30.2.

MS (EI, 70 eV): *m*/*z* (%) = 367 (14) [M]$^+$, 242 (100), 139 (26), 111 (11), 77 (9).

Anal. Calcd for $C_{19}H_{18}ClN_5O$: C, 62.04; H, 4.93; N, 19.04. Found: C, 62.23; H, 4.99; N, 18.96.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-(2-fluorophenyl)-4*H*-1,3-benzoxazine (6i)**

Yield: 0.305 g (87%); white solid; mp 141–142 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.96 (t, *J* = 7.8 Hz, 1 H, Ar-H), 7.45–7.06 (m, 7 H, Ar-H and CH), 6.78 (d, *J* = 7.8 Hz, 1 H, Ar-H), 1.82 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 162.2, 159.6, 152.7, 152.1, 138.1, 133.0, 132.9, 131.0, 130.1, 127.4, 125.6, 124.4, 123.9, 120.2, 116.6, 116.4, 67.9, 62.5, 30.0.

MS (EI, 70 eV): *m*/*z* (%) = 351 (13) [M]$^+$, 226 (100), 172 (4), 123 (29).

Anal. Calcd for $C_{19}H_{18}FN_5O$: C, 64.95; H, 5.16; N, 19.93. Found: C, 64.73; H, 5.08; N, 20.12.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-6-chloro-2-isopropyl-4*H*-1,3-benzoxazine (6j)**

Yield: 0.248 g (74%); white solid; mp 100–101 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.31 (d, *J* = 9.0 Hz, 1 H, Ar-H), 7.22 (d, *J* = 8.4 Hz, 1 H, Ar-H), 6.91 (s, 1 H, CH), 6.74 (s, 1 H, Ar-H), 2.57–2.53 (m, 1 H, CH), 1.83 (s, 9 H, $3CH_3$), 1.12 (d, *J* = 6.6 Hz, 6 H, $2CH_3$).

$^{13}$C NMR ($CDCl_3$, 150 MHz): δ = 163.5, 151.8, 136.7, 131.7, 130.1, 126.5, 124.4, 121.6, 67.1, 62.5, 33.9, 30.2, 19.3, 19.1.

MS (EI, 70 eV): *m*/*z* (%) = 333 (12) [M]$^+$, 208 (100), 179 (12), 151 (8).

Anal. Calcd for $C_{16}H_{20}ClN_5O$: C, 57.57; H, 6.04; N, 20.98. Found: C, 57.69; H, 6.21; N, 20.86.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-methyl-4*H*-1,3-benzoxazine (6k)**

Yield: 0.203 g (75%); white solid; mp 157–158 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.38–7.16 (m, 3 H, Ar-H), 6.98 (s, 1 H, CH), 6.73 (d, *J* = 7.8 Hz, 1 H, Ar-H), 2.12 (s, 3 H, $CH_3$), 1.80 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 157.0, 152.3, 137.7, 130.1, 126.9, 124.8, 124.4, 119.6, 67.9, 62.5, 30.1, 21.3.

MS (EI, 70 eV): *m*/*z* (%) = 271 (16) [M]$^+$, 146 (100), 117 (17), 89 (9), 77 (12).

Anal. Calcd for $C_{14}H_{17}N_5O$: C, 61.98; H, 6.32; N, 25.81. Found: C, 61.82; H, 6.23; N, 25.60.

**4-(1-Butyl-1*H*-tetrazol-5-yl)-2-phenyl-4*H*-1,3-benzoxazine (6l)**

Yield: 0.300 g (90%); white solid; mp 108–109 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.11 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.55–7.18 (m, 7 H, Ar-H and CH), 6.69 (d, *J* = 7.2 Hz, 1 H, Ar-H), 4.24–4.20 (m, 2 H, $NCH_2$), 1.69–1.61 (m, 2 H, $CH_2$), 1.16–1.08 (m, 2 H, $CH_2$), 0.68 (t, *J* = 7.2 Hz, 3 H, $CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 154.6, 152.4, 138.0, 132.0, 130.9, 130.5, 128.4, 127.8, 127.5, 125.9, 124.1, 119.2, 69.2, 48.3, 31.3, 19.4, 13.1.

MS (EI, 70 eV): *m*/*z* (%) = 333 (19) [M]$^+$, 208 (100), 152 (5), 105 (13), 77 (24).

Anal. Calcd for $C_{19}H_{19}N_5O$: C, 68.45; H, 5.74; N, 21.01. Found: C, 68.55; H, 5.83; N, 20.82.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-6-chloro-2-(4-chlorophenyl)-4*H*-1,3-benzoxazine (6m)**

Yield: 0.369 g (92%); white solid; mp 235–236 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.96 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.40–7.35 (m, 4 H, Ar-H), 7.11 (s, 1 H, CH), 6.76 (s, 1 H, Ar-H), 1.83 (s, 9 H, $3CH_3$).

$^{13}$C NMR (DMSO-$d_6$, 150 MHz): δ = 152.5, 151.7, 136.6, 130.5, 130.3, 129.4, 129.3, 128.6, 128.5, 126.1, 125.4, 122.5,65.4, 62.3, 29.2.

MS (EI, 70 eV): *m*/*z* (%) = 401 (14) [M]$^+$, 276 (100), 139 (31), 125 (14), 75 (15).

Anal. Calcd for $C_{19}H_{17}Cl_2N_5O$: C, 56.73; H, 4.26; N, 17.41. Found: C, 56.99; H, 4.35; N, 17.28.

**2-(4-Bromophenyl)-4-[1-(*tert*-butyl)-1*H*-tetrazol-5-yl]-4*H*-1,3-benzoxazine (6n)**

Yield: 0.376 g (91%); white solid; mp 191–192 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.92 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.56–7.19 (m, 6 H, Ar-H and CH), 6.72 (d, *J* = 7.2 Hz, 1 H, Ar-H), 1.79 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 150 MHz): δ = 153.1, 152.0, 138.1, 131.5, 130.3, 130.2, 129.1, 127.3, 126.4, 125.7, 124.2, 120.5, 68.6, 62.6, 30.3.

MS (EI, 70 eV): *m*/*z* (%) = 411 (16) [M]$^+$, 286 (100), 182 (17), 154 (13), 77 (13).

Anal. Calcd for $C_{19}H_{18}BrN_5O$: C, 55.35; H, 4.40; N, 16.99. Found: C, 55.53; H, 4.47; N, 16.87.

**4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-(4-nitrophenyl)-4*H*-1,3-benzoxazine (6o)**

Yield: 0.309 g (82%); white solid; mp 233–234 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 8.26 (d, *J* = 9.0 Hz, 2 H, Ar-H), 8.22 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.48–7.24 (m, 4 H, Ar-H and CH), 6.78 (d, *J* = 7.8 Hz, 1 H, Ar-H), 1.84 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 152.0, 151.9, 149.5, 137.8, 137.3, 130.5, 128.6, 128.3, 126.4, 124.4, 123.5, 120.4, 68.8, 62.6, 30.4.

MS (EI, 70 eV): *m*/*z* (%) = 378 (13) [M]$^+$, 253 (100), 207 (15), 172 (8), 125 (11).

Anal. Calcd for $C_{19}H_{18}N_6O_3$: C, 60.31; H, 4.79; N, 22.21. Found: C, 60.23; H, 4.59; N, 22.35.

**2-(2-Chlorophenyl)-4-(1-cyclohexyl-1*H*-tetrazol-5-yl)-4*H*-1,3-benzoxazine (6p)**

Yield: 0.332 g (84%); white solid; mp 125–126 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.75 (d, *J* = 7.2 Hz, 1 H, Ar-H), 7.46–7.20 (m, 7 H, Ar-H and CH), 6.74 (d, *J* = 7.8 Hz, 1 H, Ar-H), 4.34–4.30 (m, 1 H, NCH), 2.01–1.04 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 155.1, 151.4, 137.6, 132.6, 131.7, 131.3, 130.8, 130.4, 130.3, 127.9, 126.7, 125.7, 124.2, 119.1, 68.7, 58.9, 32.7, 32.4, 24.9, 24.8, 24.4.

MS (EI, 70 eV): *m*/*z* (%) = 393 (14) [M]$^+$, 242 (100), 139 (21), 111 (8), 77 (8).

Anal. Calcd for $C_{21}H_{20}ClN_5O$: C, 64.04; H, 5.12; N, 17.78. Found: C, 64.22; H, 5.23; N, 17.53.

**4-(1-Butyl-1*H*-tetrazol-5-yl)-2-(*p*-tolyl)-4*H*-1,3-benzoxazine (6q)**

Yield: 0.308 g (89%); white solid; mp 125–126 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.99 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.41–7.17 (m, 6 H, Ar-H and CH), 6.68 (d, *J* = 7.2 Hz, 1 H, Ar-H), 4.24–4.18 (m, 2 H, $NCH_2$), 2.42 (s, 3 H, $CH_3$), 1.69–1.60 (m, 2 H, $CH_2$), 1.16–1.07 (m, 2 H, $CH_2$), 0.68 (t, *J* = 7.2 Hz, 3 H, $CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 154.8, 152.4, 142.6, 138.1, 130.4, 129.1, 128.1, 127.8, 127.2, 125.7, 124.0, 119.2, 69.1, 48.2, 31.2, 21.5, 19.3, 13.0.

MS (EI, 70 eV): *m*/*z* (%) = 347 (19) [M]$^+$, 222 (100), 119 (17), 91 (15).

Anal. Calcd for $C_{20}H_{21}N_5O$: C, 69.14; H, 6.09; N, 20.16. Found: C, 69.26; H, 6.27; N, 20.03.

**4-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-2-(*p*-tolyl)-4*H*-1,3-benzoxazine (6r)**

Yield: 0.321 g (86%); white solid; mp 130–131 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.98 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.41–7.16 (m, 6 H, Ar-H and CH), 6.70 (d, *J* = 7.8 Hz, 1 H, Ar-H), 4.25–4.22 (m, 1 H, NCH), 2.42 (s, 3 H, $CH_3$), 1.91–1.00 (m, 10 H, $5CH_2$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 154.6, 151.9, 142.4, 138.0, 130.3, 129.0, 128.1, 127.6, 127.1, 125.5, 124.0, 119.2, 68.7, 58.9, 33.0, 32.1, 24.9, 24.8, 24.4, 21.4.

MS (EI, 70 eV): *m*/*z* (%) = 373 (22) [M]$^+$, 222 (100), 119 (14), 91 (11).

Anal. Calcd for $C_{22}H_{23}N_5O$: C, 70.76; H, 6.21; N, 18.75. Found: C, 70.84; H, 6.32; N, 18.53.

**(*E*)-4-[1-(*tert*-Butyl)-1*H*-tetrazol-5-yl]-2-styryl-4*H*-1,3-benzoxazine (6s)**

Yield: 0.262 g (73%); white solid; mp 179–180 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.48 (d, *J* = 6.6 Hz, 2 H, Ar-H), 7.41–7.17 (m, 7 H, Ar-H), 7.12 (s, 1 H, CH), 6.70 (d, *J* = 7.8 Hz, 1 H, Ar-H), 6.67 (d, *J* = 16.2 Hz, 1 H, =CH), 1.80 (s, 9 H, $3CH_3$).

$^{13}$C NMR ($CDCl_3$, 100 MHz): δ = 154.3, 151.9, 139.2, 138.5, 134.6, 130.1, 129.6, 128.7, 127.4, 127.1, 125.3, 124.2, 120.6, 68.1, 62.5, 30.1.

MS (EI, 70 eV): *m*/*z* (%) = 359 (18) [M]$^+$, 234 (100), 216 (12), 130 (20), 77 (21).

Anal. Calcd for $C_{21}H_{21}N_5O$: C, 70.17; H, 5.89; N, 19.48. Found: C, 70.39; H, 5.97; N, 19.34.

**2-(4-Chlorophenyl)-4-[1-(4-chlorophenyl)-1*H*-tetrazol-5-yl]-4*H*-1,3-benzoxazine (6t)**

Yield: 0.380 g (90%); white solid; mp 155–156 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.78 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.36–7.17 (m, 8 H, Ar-H and CH), 7.06 (d, *J* = 8.4 Hz, 2 H, Ar-H), 6.88 (d, *J* = 7.2 Hz, 1 H, Ar-H).

$^{13}$C NMR ($CDCl_3$, 150 MHz): δ = 153.8, 152.7, 138.1, 137.3, 137.1, 131.7, 130.6, 129.7, 129.5, 128.9, 128.5, 127.6, 126.8, 126.1, 124.6, 118.6, 68.8.

HRMS: *m*/*z* calcd for [$C_{21}H_{13}Cl_2N_5O$ + Na]$^+$: 444.0389; found: 444.0379.

**4-[1-(4-Chlorophenyl)-1*H*-tetrazol-5-yl]-2-(*p*-tolyl)-4*H*-1,3-benzoxazine (6u)**

Yield: 0.341 g (85%); white solid; mp 153–154 °C.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 7.73 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.34–7.07 (m, 10 H, Ar-H and CH), 6.86 (d, *J* = 7.8 Hz, 1 H, Ar-H), 2.40 (s, 3 H, $CH_3$).

$^{13}$C NMR ($CDCl_3$, 150 MHz): δ = 153.9, 153.8, 142.4, 137.8, 136.9, 131.8, 130.5, 129.6, 129.0, 128.2, 127.6, 127.1, 126.8, 125.9, 124.4, 118.7, 68.6, 21.6.

HRMS: *m*/*z* calcd for $[C_{22}H_{16}ClN_5O + H]^+$: 402.1116; found: 402.1114.

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## Supporting Information

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