Tetrahedron 65 (2009) 8563–8570

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

New efficient synthesis of 4-aminocarbonyl substituted 4*H*-3,1-benzoxazines by a Passerini 3CC/Staudinger/aza-Wittig sequence

Ping He, Jing Wu, Yi-Bo Nie, Ming-Wu Ding *

Key Laboratory of Pesticide & Chemical Biology of Ministry of Education, Central China Normal University, Wuhan, 430079, PR China

ARTICLE INFO

Article history:
Received 1 April 2009
Received in revised form 14 May 2009
Accepted 3 August 2009
Available online 13 August 2009

ABSTRACT

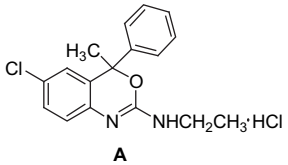
α-Acyloxy-carboxamide azides **1**, obtained from Passerini reaction of easily accessible *o*-azidobenzaldehyde with isocyanides and carboxylic acids, reacted with triphenylphosphine to give various 4-aminocarbonyl substituted 4*H*-1,3-benzoxazines **3** in moderate to high yields via sequential Staudinger and intramolecular aza-Wittig reaction. However, α-hydroxy carboxamide azides **5** were obtained in moderate yields when pyruvic acid was used in the Passerini reaction. Further sequential reaction of azides **5** with triphenylphosphine and isocyanates produced 2-amino-4-aminocarbonyl substituted 4*H*-1,3-benzoxazines **8** via a tandem Staudinger/aza-Wittig/heterocumulene-mediated annulation.

1. Introduction

The isocyanide based multicomponent reactions (I-MCRs) are extremely useful tools for synthesis of combinatorial libraries of compounds and structurally complex molecules.[1] Passerini reaction is one of the main two I-MCRs (Ugi reaction and Passerini reaction) and is a powerful, atom-economical reaction between isonitrile, aldehyde (or ketone), and carboxylic acid components that generates a significantly more complex α-acyloxy-carboxamide adduct. The sequences of classical Passerini isocyanide multicomponent reactions, followed by post-condensation transformations, constitute extremely powerful synthetic tools for the preparation of structurally diverse complex molecules, among them are heterocyclic compounds with elaborate substitution patterns.[2,3]

The aza-Wittig reactions of iminophosphoranes have received increased attention in view of their utility in the synthesis of nitrogen-containing heterocyclic compounds.[4] Thus, it is envisioned that combining the efficiency of the Passerini or Ugi condensation with a post-condensation aza-Wittig reaction would facilitate access to a series of biologically useful heterocycles. The Ugi reaction with a post aza-Wittig cyclization has been utilized in synthesis of some dibenzo[b,f]-1,5-diazocine-6(5*H*)-ones or 1,4-benzodiazepine-5-ones.[5] However, to the best of our knowledge, there is no report about Passerini reaction followed with aza-Wittig reaction to prepare various substituted heterocycles.

The 4*H*-3,1-benzoxazine ring system displays important biological activities and a wide variety of derivatives of this ring system have been used as fungicidal, herbicidal, anti-inflammatory agents, C1r serine protease inhibitors, anticonvulsant, and as DNA-binding antitumor agents.[6] For example, Etifoxine (**A**), a nonbenzodiazepine anticonvulsant drug, has been used for the treatment of psychiatric illnesses with great therapeutic efficacy and less toxicity.[7] There are many known methods for the synthesis of 4*H*-3,1-benzoxazines,[8] however, 4-aminocarbonyl substituted 4*H*-3,1-benzoxazines have not yet been prepared previously probably due to the fact that they are not easily accessible by routine synthetic method. 4-Aminocarbonyl substituted 4*H*-3,1-benzoxazine is a very attractive target for biochemical studies and drug discovery, due to its large number of possible substitution patterns and interesting combination of potential hydrogen bond donors and acceptors on the amide moiety. Recently we have been interested in the synthesis of fused pyrimidinones and imidazolinones via aza-Wittig reaction, with the aim of evaluating their biological activities.[9] Herein we wish to report a fundamentally new approach to the synthesis of 4-aminocarbonyl substituted 4*H*-3,1-benzoxazines by the Passerini reaction between easily accessible 2-azidobenzaldehyde, isocyanides, and various acids, followed by a Staudinger/aza-Wittig cyclization of the Passerini products in the presence of triphenylphosphine (Fig. 1).



A

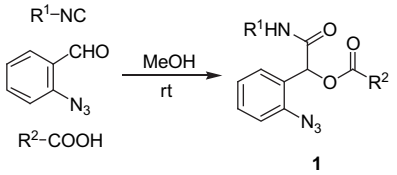
Figure 1. An example of 4*H*-3,1-benzoxazine drug (Etifoxine).

* Corresponding author. Tel.: +86 27 63158845; fax: +86 27 67862041.
E-mail address: ding5229@yahoo.com.cn (M.-W. Ding).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.08.022

2. Results and discussion

A mixture of 2-azidobenzaldehyde[10] (1 equiv), isocyanide (1 equiv), and various acid (1 equiv) was stirred in methanol at room temperature for 5–48 h. The Passerini reaction was carried out smoothly and the products **1** were obtained after recrystallization in moderate to high yields (58–95%) (Scheme 1 and Table 1). As indicated in Table 1, high yields were obtained when aliphatic acids were used (compounds **1a**, **1b**, **1f**, **1k**, and **1q**). Good yields were also reached as most of the aromatic acids were utilized whereas moderate yields were obtained when *o*-substituted aromatic acids were employed (compounds **1d**, **1e**, and **1l**), which is probably due to the steric hindrance of the *o*-substituent.

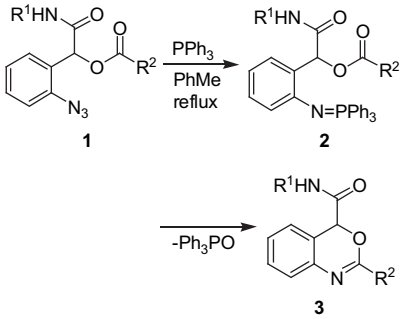


Scheme 1. Preparation of azides **1** via Passerini reaction.

Table 1
Preparation of azides **1** via Passerini reaction

Compound	R^1	R^2	Reaction time (h)	Yield (%)
1a	*t*-Bu	CH_3	5	93
1b	*t*-Bu	CH_2CH_3	10	89
1c	*t*-Bu	3,5-$2CH_3$–C_6H_3	24	79
1d	*t*-Bu	2-CH_3–C_6H_4	48	60
1e	*t*-Bu	2-HO–C_6H_4	48	62
1f	*t*-Bu	CH_2CH_2Ph	12	88
1g	*t*-Bu	4-Cl–C_6H_4	24	81
1h	*t*-Bu	4-NO_2–C_6H_4	24	78
1i	*t*-Bu	4-CH_3O–C_6H_4	24	77
1j	*t*-Bu	Ph	24	73
1k	*t*-Bu	2,4-2Cl–$C_6H_3OCH_2$	10	83
1l	*n*-Bu	2-Cl–C_6H_4	48	58
1m	*n*-Bu	4-Cl–C_6H_4	24	81
1n	*n*-Bu	3-NO_2–C_6H_4	24	80
1o	*n*-Bu	Ph	24	78
1p	*n*-Bu	4-CH_3O–C_6H_4	24	87
1q	*n*-Bu	CH_2CH_3	8	95

The reactions of **1** with triphenylphosphine were examined in toluene at room temperature for 2 h, followed by heating at reflux for 3–36 h. Nitrogen evolution via the Staudinger reaction had ceased during the first 2 h to give iminophosphorane **2**, which could be isolated in good yield, but heating was needed for completion of the intramolecular aza-Wittig reaction of **2** in a reasonable time to afford 4-aminocarbonyl substituted 4*H*-3,1-benzoxazines **3** in 78–92% yields (Scheme 2 and Table 2). The required heating time is



Scheme 2. Preparation of 4*H*-3,1-benzoxazines **3** via intramolecular aza-Wittig reaction.

Table 2
Preparation of 4-aminocarbonyl substituted 4*H*-3,1-benzoxazines **3** via intramolecular aza-Wittig Reaction

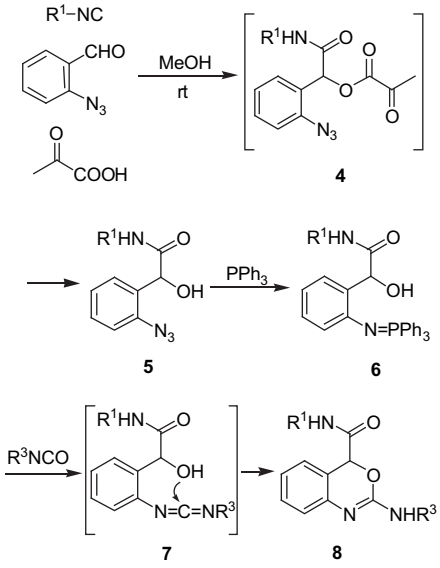
Compound	R^1	R^2	Reaction time (h)	Yield (%)
3a	*t*-Bu	CH_3	3	80
3b	*t*-Bu	CH_2CH_3	4	83
3c	*t*-Bu	3,5-$2CH_3$–C_6H_3	24	78
3d	*t*-Bu	2-CH_3–C_6H_4	36	69
3e	*t*-Bu	2-HO–C_6H_4	24	89
3f	*t*-Bu	CH_2CH_2Ph	8	90
3g	*t*-Bu	4-Cl–C_6H_4	24	88
3h	*t*-Bu	4-NO_2–C_6H_4	24	79
3i	*t*-Bu	4-CH_3O–C_6H_4	24	90
3j	*t*-Bu	Ph	24	87
3k	*t*-Bu	2,4-2Cl–$C_6H_3OCH_2$	8	86
3l	*n*-Bu	2-Cl–C_6H_4	24	70
3m	*n*-Bu	4-Cl–C_6H_4	24	86
3n	*n*-Bu	3-NO_2–C_6H_4	24	80
3o	*n*-Bu	Ph	24	89
3p	*n*-Bu	4-CH_3O–C_6H_4	24	84
3q	*n*-Bu	CH_2CH_3	3	92

related to R^2 substituent: shorter time (3–8 h) is needed as R^2 is alkyl group (compounds **3a**, **3b**, **3f**, **3k**, and **3q**) whereas longer time (24–36 h) is required when R^2 is aromatic group.

When pyruvic acid was used in the Passerini reaction as one of the three reactants, α-hydroxy carboxamide adduct **5** was isolated as the sole product in moderate yield. The formation of product **5** can be viewed as an initial Passerini reaction to afford α-acyloxy-carboxamide adduct **4**, which undergoes further hydrolysis during work-up to give **5**. The similar hydrolysis reaction was also encountered as trifluoroacetic acid was utilized in

Table 3
Preparation of compounds **5**, **6**, **8**

Compound	R^1	R^3	Reaction time (h)	Yield (%)
5a	*t*-Bu		12	68
5b	*n*-Bu		12	65
6a	*t*-Bu		4	87
6b	*n*-Bu		4	90
8a	*t*-Bu	*i*-Pr	12	65
8b	*t*-Bu	4-Cl–C_6H_4	6	60
8c	*t*-Bu	4-F–C_6H_4	6	73
8d	*t*-Bu	3-CH_3–C_6H_4	10	67
8e	*n*-Bu	4-Cl–C_6H_4	6	71



Scheme 3. Preparation of 2-amino-4*H*-3,1-benzoxazines **8**.

Passerini reaction.[11] The obtained azide **5** was further reacted with triphenyl phosphine and the iminophosphorane **6** was obtained in high yield via Staudinger reaction. When solutions of iminophosphoranes **6** in dry toluene were treated with isocyanate at reflux temperature, 2-amino-4-aminocarbonyl substituted 4*H*-3,1-benzoxazines **8** were isolated as crystalline solids in moderate yields (Table 3, Scheme 3). Presumably, the conversion of **6** into **8** involves initial aza-Wittig reaction between the iminophosphorane **6** and the isocyanate to give a carbodiimide **7**, which easily undergoes ring closure to give **8**.

The structure of **3** and **8** was confirmed by their spectrum data. Furthermore a single crystal of **3e** was obtained from a CH_2Cl_2 solution of **3e**. X-ray structure analysis verified again the proposed structure (Fig. 2), and showed that the oxazine ring atoms are not on one plane, but have a torsion angle by 18.91°, while the dihedral angle of the two phenyl rings is 19.88°.

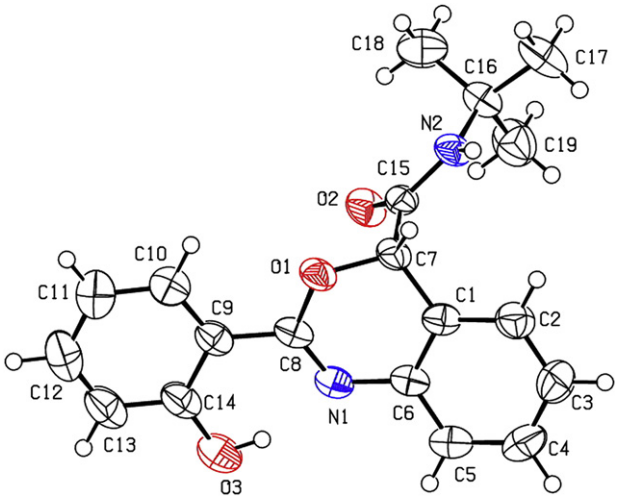


Figure 2. ORTEP diagram of the crystal structure of **3e** (Drawn at the 50% thermal ellipsoids. There are two crystallographic independent molecules in one unit cell. Only one is shown for clarity).

3. Conclusion

In conclusion, we are reporting a new MCR, yielding 4-aminocarbonyl substituted 4*H*-3,1-benzoxazines, by a sequence of a Passerini reaction, Staudinger reaction, and an intramolecular or tandem aza-Wittig ring closure. Due to the easy availability of the synthetic approach and the neutral ring closure condition, this new synthetic approach discussed here has the potential in synthesis of various 4-aminocarbonyl substituted 4*H*-3,1-benzoxazines, which are of considerable interest as potential biological active compounds or pharmaceuticals.

4. Experimental

4.1. General

Melting points were uncorrected. MS were measured on a Finnigan Trace MS spectrometer. IR were recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. NMR were recorded in $CDCl_3$ or DMSO-d_6 on a Varian Mercury 400 or 600 spectrometer and resonances relative to TMS. Elementary analyses were taken on a Vario EL III elementary analysis instrument. The X-ray diffraction data were collected on a *Bruker SMART AXS CCD* diffractometer, Mo Kα, 2θ=1.86–27.50°. 2-Azidobenzaldehyde was easily prepared from the reaction of sodium azide with 2-nitrobenzaldehyde according to the literature reports.[10]

4.2. Synthesis of azides 1 via Passerini reaction

*4.2.1. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl acetate (**1a**).* To a solution of 2-azidobenzaldehyde (0.44 g, 3 mmol) in methanol (15 mL) was added sequentially acetic acid (0.18 g, 3 mmol) and *tert*-butyl isocyanide (0.25 g, 3 mmol) at room temperature. After the reaction mixture was stirred for 5 h at ambient temperature, the solvent was removed off under reduced pressure and the residue was recrystallized from ether/petroleum ether to give 0.81 g (93%) of azide **1a** as white solid. Mp: 82–83 °C, IR (KBr): 3279, 2127, 2095, 1739, 1663, 1557, 1239 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.49–7.16 (m, 4H, Ar-H), 6.14 (s, 1H, OCH), 5.96 (s, 1H, NH), 2.18 (s, 3H, CH_3), 1.35 (s, 9H, $3CH_3$). MS *m*/*z*: 248 (M^+-N_3, 21), 131 (100), 93 (47). Anal. Calcd for $C_{14}H_{18}N_4O_3$: C, 57.92; H, 6.25; N, 19.30. Found: C, 57.71; H, 6.31; N, 19.42.

*4.2.2. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl propionate (**1b**).* Operation as above with propionic acid (0.22 g, 3 mmol) for 10 h, compound **1b** (0.81 g, 89%) was also isolated as white solid. Mp: 96–97 °C, IR (KBr): 3291, 2125, 2098, 1735, 1665, 1558, 1242 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.47–7.15 (m, 4H, Ar-H), 6.16(s, 1H, OCH), 6.00 (s, 1H, NH), 2.51–2.41 (m, 2H, CH_2), 1.35 (s, 9H, $3CH_3$), 1.18 (t, J=7.2 Hz, 3H, CH_3). MS *m*/*z*: 262 (M^+-N_3, 12), 150 (73), 134 (100), 92 (36). Anal. Calcd for $C_{15}H_{20}N_4O_3$: C, 59.20; H, 6.62; N, 18.41. Found: C, 59.47; H, 6.74; N, 18.35.

*4.2.3. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 3,5-dimethylbenzoate (**1c**).* Operation as above with 3,5-dimethylbenzoic acid (0.45 g, 3 mmol) for 24 h, compound **1c** (0.90 g, 79%) was also isolated as white solid. Mp: 161–162 °C, IR (KBr): 3384, 2133, 1698, 1676, 1536, 1254 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.70–7.17 (m, 7H, Ar-H), 6.41 (s, 1H, OCH), 6.13 (s, 1H, NH), 2.36 (s, 6H, CH_3), 1.35 (s, 9H, $3CH_3$). Anal. Calcd for $C_{21}H_{24}N_4O_3$: C, 66.30; H, 6.36; N, 14.73. Found: C, 66.24; H, 6.13; N, 14.96.

*4.2.4. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 2-methylbenzoate (**1d**).* Operation as above with 2-methylbenzoic acid (0.41 g, 3 mmol) for 48 h, compound **1d** (0.66 g, 60%) was also isolated as white solid. Mp: 91–93 °C, IR (KBr): 3391, 2131, 1708, 1687, 1535, 1309, 1217 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.02–7.16 (m, 8H, Ar-H), 6.39 (s, 1H, OCH), 6.15 (s, 1H, NH), 2.62 (s, 3H, CH_3), 1.37 (s, 9H, $3CH_3$). MS *m*/*z*: 267 ($M^+-N_2-C_4H_9$, 4), 177 (6), 118 (100), 91 (17), 57 (10). Anal. Calcd for $C_{20}H_{22}N_4O_3$: C, 65.56; H, 6.05; N, 15.29. Found: C, 65.30; H, 6.11; N, 15.14.

*4.2.5. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 2-hydroxybenzoate (**1e**).* Operation as above with 2-hydroxybenzoic acid (0.41 g, 3 mmol) for 48 h, compound **1e** (0.68 g, 62%) was also isolated as white solid. Mp: 151–153 °C, IR (KBr): 3313, 2132, 1708, 1646, 1461, 1292, 1122 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 10.44 (s, 1H, OH), 7.94–6.91 (m, 8H, Ar-H), 6.40 (s, 1H, OCH), 6.00 (s, 1H, NH), 1.36 (s, 9H, $3CH_3$). MS *m*/*z*: 327 (M^+-N_2, 100), 298 (11), 259 (26), 139 (9). Anal. Calcd for $C_{19}H_{20}N_4O_4$: C, 61.95; H, 5.47; N, 15.21. Found: C, 61.81; H, 5.49; N, 15.29.

*4.2.6. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 3-phenylpropanoate (**1f**).* Operation as above with 3-phenylpropionic acid (0.45 g, 3 mmol) for 12 h, compound **1f** (1.00 g, 88%) was also isolated as white solid. Mp: 103–104 °C, IR (KBr): 3280, 2129, 2095, 1733, 1662, 1557, 1294, 1177 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.43–7.14 (m, 9H, Ar-H), 6.16 (s, 1H, OCH), 5.93 (s, 1H, NH), 3.01–2.97 (m, 2H, CH_2), 2.81–2.75 (m, 2H, CH_2), 1.33 (s, 9H, $3CH_3$). MS *m*/*z*: 281 ($M^+-N_2-C_4H_9$, 6), 253 (13), 193 (7), 133 (86), 121 (91), 105

(100). Anal. Calcd for $C_{21}H_{24}N_4O_3$: C, 66.30; H, 6.36; N, 14.73. Found: C, 66.48; H, 6.21; N, 14.94.

*4.2.7. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 4-chlorobenzoate (**1g**).* Operation as above with 4-chlorobenzoic acid (0.47 g, 3 mmol) for 24 h, compound **1g** (0.94 g, 81%) was also isolated as white solid. Mp: 140–141 °C, IR (KBr): 3288, 2131, 1730, 1655, 1563, 1273, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.04–7.20 (m, 8H, Ar-H), 6.37 (s, 1H, OCH), 6.00 (s, 1H, NH), 1.36 (s, 9H, $3CH_3$). Anal. Calcd for $C_{19}H_{19}ClN_4O_3$: C, 58.99; H, 4.95; N, 14.48. Found: C, 58.93; H, 4.71; N, 14.62.

*4.2.8. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 4-nitrobenzoate (**1h**).* Operation as above with 4-nitrobenzoic acid (0.50 g, 3 mmol) for 24 h, compound **1h** (0.93 g, 78%) was also isolated as white solid. Mp: 125–126 °C, IR (KBr): 3284, 2133, 1733, 1664, 1531, 1275, 1119 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.32–7.24 (m, 8H, Ar-H), 6.38 (s, 1H, OCH), 5.90 (s, 1H, NH), 1.36 (s, 9H, $3CH_3$). Anal. Calcd for $C_{19}H_{19}N_5O_5$: C, 57.43; H, 4.82; N, 17.62. Found: C, 57.57; H, 4.98; N, 17.38.

*4.2.9. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 4-methoxybenzoate (**1i**).* Operation as above with 4-methoxybenzoic acid (0.46 g, 3 mmol) for 24 h, compound **1i** (0.88 g, 77%) was also isolated as white solid. Mp: 130–32 °C, IR (KBr): 3283, 2132, 1724, 1662, 1606, 1259, 1169 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.05–6.94 (m, 8H, Ar-H), 6.39 (s, 1H, OCH), 6.12 (s, 1H, NH), 3.87 (s, 3H, OCH_3), 1.37 (s, 9H, $3CH_3$). Anal. Calcd for $C_{20}H_{22}N_4O_4$: C, 62.82; H, 5.80; N, 14.65. Found: C, 62.64; H, 5.94; N, 14.85.

*4.2.10. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl benzoate (**1j**).* Operation as above with benzoic acid (0.37 g, 3 mmol) for 24 h, compound **1j** (0.77 g, 73%) was also isolated as white solid. Mp: 136–137 °C, IR (KBr): 3303, 2125, 1722, 1670, 1560, 1255, 1113 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.11–7.18 (m, 9H, Ar-H), 6.41 (s, 1H, OCH), 6.13 (s, 1H, NH), 1.38 (s, 9H, $3CH_3$). Anal. Calcd for $C_{19}H_{20}N_4O_3$: C, 64.76; H, 5.72; N, 15.90. Found: C, 64.81; H, 5.63; N, 15.63.

*4.2.11. 1-(2-Azidophenyl)-2-(tert-butylamino)-2-oxoethyl 2-(2,4-dichlorophenoxy) acetate (**1k**).* Operation as above with 2-(2,4-dichlorophenyloxy)acetic acid (0.66 g, 3 mmol) for 10 h, compound **1k** (1.12 g, 83%) was also isolated as white solid. Mp: 95–96 °C, IR (KBr): 3380, 2136, 1753, 1681, 1482, 1196, 1091 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.40–6.79 (m, 7H, Ar-H), 6.21 (s, 1H, OCH), 5.97 (s, 1H, NH), 4.81 (s, 2H, CH_2O), 1.32 (s, 9H, $3CH_3$). MS *m*/*z*: 450 (M^+, 14), 350 (10), 288 (50), 260 (52), 220 (74), 175 (81), 134 (100). Anal. Calcd for $C_{20}H_{20}Cl_2N_4O_4$: C, 53.23; H, 4.47; N, 12.41. Found: C, 53.37; H, 4.59; N, 12.34.

*4.2.12. 1-(2-Azidophenyl)-2-(n-butylamino)-2-oxoethyl 2-chlorobenzoate (**1l**).* Operation as above with 2-chlorobenzoic acid (0.47 g, 3 mmol) for 48 h, compound **1l** (0.67 g, 58%) was also isolated as white solid. Mp: 68–69 °C, IR (KBr): 3289, 2124, 1730, 1656, 1252, 1104 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.96–7.18 (m, 8H, Ar-H), 6.54 (s, 1H, NH), 6.52 (s, 1H, CHO), 3.40–3.28 (m, 2H, NCH_2), 1.57–1.49 (m, 2H, CH_2), 1.40–1.33 (m, 2H, CH_2), 0.92 (t, *J*=7.2 Hz, 3H, CH_3). Anal. Calcd for $C_{19}H_{19}ClN_4O_3$: C, 58.99; H, 4.95; N, 14.48. Found: C, 58.77; H, 4.88; N, 14.71.

*4.2.13. 1-(2-Azidophenyl)-2-(n-butylamino)-2-oxoethyl 4-chlorobenzoate (**1m**).* Operation as above with 4-chlorobenzoic acid (0.47 g, 3 mmol) for 24 h, compound **1m** (0.94 g, 81%) was also isolated as white solid. Mp: 122–124 °C, IR (KBr): 3299, 2131, 1725, 1665, 1258, 1096 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.05–7.19 (m, 8H, Ar-H), 6.46 (s, 1H, OCH), 6.20 (br, 1H, NH), 3.44–3.25 (m, 2H, NCH_2), 1.52–1.46 (m, 2H, CH_2), 1.34–1.28 (m, 2H, CH_2), 0.90 (t, *J*=7.2 Hz, 3H, CH_3). Anal. Calcd for $C_{19}H_{19}ClN_4O_3$: C, 58.99; H, 4.95; N, 14.48. Found: C, 59.14; H, 4.75; N, 14.27.

*4.2.14. 1-(2-Azidophenyl)-2-(n-butylamino)-2-oxoethyl 3-nitrobenzoate (**1n**).* Operation as above with 3-nitrobenzoic acid (0.50 g, 3 mmol) for 24 h, compound **1n** (0.95 g, 80%) was also isolated as white solid. Mp: 132–133 °C, IR (KBr): 3286, 2130, 1725, 1661, 1534, 1350, 1253 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.92–7.24 (m, 8H, Ar-H), 6.49 (s, 1H, OCH), 6.15 (s, 1H, NH), 3.35–3.27 (m, 2H, NCH_2), 1.53–1.49 (m, 2H, CH_2), 1.34–1.29 (m, 2H, CH_2), 0.90 (t, *J*=7.2 Hz, 3H, CH_3). MS *m*/*z*: 396 (M^+-1, 4), 369 (4), 242 (25), 150 (100), 104 (34). Anal. Calcd for $C_{19}H_{19}N_5O_5$: C, 57.43; H, 4.82; N, 17.62. Found: C, 57.26; H, 4.95; N, 17.68.

*4.2.15. 1-(2-Azidophenyl)-2-(n-butylamino)-2-oxoethyl benzoate (**1o**).* Operation as above with benzoic acid (0.37 g, 3 mmol) for 24 h, compound **1o** (0.82 g, 78%) was also isolated as white solid. Mp: 113–115 °C, IR (KBr): 3274, 2132, 1716, 1654, 1354, 1248 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.11 (d, *J*=7.2 Hz, 2H, Ar-H), 7.62–7.19 (m, 6H, Ar-H), 6.50 (s, 1H, OCH), 6.26 (s, 1H, NH), 3.38–3.25 (m, 2H, NCH_2), 1.53–1.49 (m, 2H, CH_2), 1.36–1.30 (m, 2H, CH_2), 0.91 (t, *J*=7.2 Hz, 3H, CH_3). Anal. Calcd for $C_{19}H_{20}N_4O_3$: C, 64.76; H, 5.72; N, 15.90. Found: C, 64.58; H, 5.96; N, 15.84.

*4.2.16. 1-(2-Azidophenyl)-2-(n-butylamino)-2-oxoethyl 4-methoxybenzoate (**1p**).* Operation as above with 4-methoxybenzoic acid (0.46 g, 3 mmol) for 24 h, compound **1p** (1.00 g, 87%) was also isolated as white solid. Mp: 110–111 °C, IR (KBr): 3277, 2134, 1711, 1671, 1258, 1165 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.05 (d, *J*=8.4 Hz, 2H, Ar-H), 7.60–7.19 (m, 4H, Ar-H), 6.94 (d, *J*=8.4 Hz, 2H, Ar-H), 6.47 (s, 1H, OCH), 6.28 (s, 1H, NH), 3.86 (s, 3H, OCH_3), 3.36–3.25 (m, 2H, NCH_2), 1.52–1.50 (m, 2H, CH_2), 1.35–1.31 (m, 2H, CH_2), 0.91 (t, *J*=7.2 Hz, 3H, CH_3). Anal. Calcd for $C_{20}H_{22}N_4O_4$: C, 62.82; H, 5.80; N, 14.65. Found: C, 62.95; H, 5.63; N, 14.68.

*4.2.17. 1-(2-Azidophenyl)-2-(n-butylamino)-2-oxoethyl propionate (**1q**).* Operation as above with propionic acid (0.22 g, 3 mmol) for 8 h, compound **1q** (0.87 g, 95%) was also isolated as white solid. Mp: 85–86 °C, IR (KBr): 3312, 2107, 1739, 1660, 1543, 1179 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.50–7.15 (m, 4H, Ar-H), 6.25 (s, 1H, OCH), 6.19 (s, 1H, NH), 3.32–3.22 (m, 2H, NCH_2), 2.52–2.43 (m, 2H, CH_2), 1.52–1.46 (m, 2H, CH_2), 1.34–1.27 (m, 2H, CH_2), 1.18 (t, *J*=7.6 Hz, 3H, CH_3), 0.91 (t, *J*=7.2 Hz, 3H, CH_3). Anal. Calcd for $C_{15}H_{20}N_4O_3$: C, 59.20; H, 6.62; N, 18.41. Found: C, 59.36; H, 6.43; N, 18.67.

4.3. Synthesis of some iminophosphoranes 2 via Staudinger reaction

*4.3.1. 2-(tert-Butylamino)-1-(2-(triphenylphosphoranylidene) aminophenyl)-2-oxoethyl 4-nitrobenzoate (**2h**).* To a stirred solution of azide **1h** (0.40 g, 1 mmol) in toluene (10 mL) was added dropwise triphenylphosphine (0.26 g, 1 mmol) in toluene (5 mL) at room temperature. After the reaction mixture was stirred for 2 h at ambient temperature, the solvent was removed off under reduced pressure and the residual was recrystallized from methylene dichloride/petroleum ether to give 0.58 g (92%) of iminophosphorane **2h** as white solid. Mp: 210–213 °C, IR (KBr): 3210, 1725, 1687, 1526, 1319, 1261, 1114 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.56 (s, 1H, CONH), 8.42–6.54 (m, 24H, Ar-H and OCH), 1.07 (s, 9H, $3CH_3$). MS *m*/*z*: 631 (M^+, 26), 482 (100), 382 (46), 261 (57), 253 (59), 183 (50). Anal. Calcd for $C_{37}H_{34}N_3O_5P$: C, 70.35; H, 5.43; N, 6.65. Found: C, 70.51; H, 5.67; N, 6.38.

*4.3.2. 2-(tert-Butylamino)-1-(2-(triphenylphosphoranylidene) aminophenyl)-2-oxoethyl benzoate (**2j**).* Operation as above with azide

1j (0.35 g, 1 mmol), compound **2j** (0.52 g, 88%) was also isolated as white solid. Mp: 212–213 °C, IR (KBr): 3203, 1724, 1684, 1591, 1480, 1261, 1112 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.51 (s, 1H, CONH), 8.25–6.51 (m, 25H, Ar-H and OCH), 1.06 (s, 9H, $3CH_3$). MS *m*/*z*: 586 (M^+, 19), 481 (100), 380 (63), 353 (31), 277 (46), 209 (81), 183 (94), 105 (99). Anal. Calcd for $C_{37}H_{35}N_2O_3P$: C, 75.75; H, 6.01; N, 4.78. Found: C, 75.54; H, 6.12; N, 4.61.

*4.3.3. 2-(tert-Butylamino)-1-(2-(triphenylphosphoranylidene) aminophenyl)-2-oxoethyl 2-(2,4-dichlorophenoxy) acetate (**2k**).* Operation as above with azide **1k** (0.45 g, 1 mmol), compound **2k** (0.62 g, 90%) was also isolated as white solid. Mp: 159–161 °C, IR (KBr): 3189, 1764, 1678, 1592, 1480, 1325, 1196 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.46 (s, 1H, CONH), 7.72–6.50 (m, 23H, Ar-H and OCH), 5.01, 4.91 (dd, *J*=16.2 Hz, 2H, CH_2O), 1.03 (s, 9H, $3CH_3$). MS *m*/*z*: 684 (M^+, 11), 598 (16), 576 (18), 433 (12), 307 (100), 289 (16), 263 (12), 149 (13). Anal. Calcd for $C_{38}H_{35}Cl_2N_2O_4P$: C, 66.57; H, 5.15; N, 4.09. Found: C, 66.63; H, 5.29; N, 4.21.

4.4. Synthesis of 4*H*-3,1-benzoxazines 3 via intramolecular aza-Wittig reaction

*4.4.1. N-(tert-Butyl)-2-methyl-4H-3,1-benzoxazine-4-carboxamide (**3a**).* To a stirred solution of azide **1a** (0.29 g, 1 mmol) in toluene (10 mL) was added dropwise triphenylphosphine (0.26 g, 1 mmol) in toluene (5 mL) at room temperature. After the reaction mixture was stirred for 2 h at room temperature and then for 3 h at reflux temperature, the solvent was removed off under reduced pressure and the residual was recrystallized from methanol to give 0.20 g (80%) of compound **3a** as white solid. Mp: 157–158 °C, IR (KBr): 3290, 1676, 1642, 1541, 1218 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.42–7.13 (m, 4H, Ar-H), 6.07 (s, 1H, CONH), 5.50 (s, 1H, OCH), 2.21 (s, 3H, CH_3), 1.38 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.9, 157.8, 137.4, 129.5, 127.0, 124.8, 124.2, 120.1, 75.2, 51.5, 28.6, 21.5. MS *m*/*z*: 146 (M^+−CONHBu, 100), 104 (11), 77 (23), 57 (34). Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.34; H, 7.56; N, 11.32.

*4.4.2. N-(tert-Butyl)-2-ethyl-4H-3,1-benzoxazine-4-carboxamide (**3b**).* Operation as above with azide **1b** (0.30 g, 1 mmol) refluxed for 4 h, compound **3b** (0.22 g, 83%) was also isolated as white solid. Mp: 109–110 °C, IR (KBr): 3353, 1676, 1635, 1532, 1363, 1169 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.41–7.14 (m, 4H, Ar-H), 6.14 (s, 1H, CONH), 5.50 (s, 1H, OCH), 2.46 (q, *J*=7.2 Hz, 2H, CH_2). 1.37 (s, 9H, $3CH_3$), 1.28 (t, *J*=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 167.0, 161.1, 137.3, 129.2, 126.7, 124.8, 124.3, 120.1, 75.0, 51.3, 28.4, 28.1, 10.3. MS *m*/*z*: 260 (M^+, 5), 160 (100), 131 (50), 104 (20), 76 (27). Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.33; H, 7.51; N, 10.74.

*4.4.3. N-(tert-Butyl)-2-(3,5-dimethylphenyl)-4H-3,1-benzoxazine-4-carboxamide (**3c**).* Operation as above with azide **1c** (0.38 g, 1 mmol) refluxed for 24 h, compound **3c** (0.26 g, 78%) was also isolated as white solid. Mp: 144–146 °C, IR (KBr): 3277, 1650, 1557, 1248, 1083 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.70–7.17 (m, 7H, Ar-H), 6.23 (s, 1H, CONH), 5.65 (s, 1H, OCH), 2.39 (s, 6H, $2CH_3$), 1.33 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.1, 155.0, 138.1, 138.0, 133.6, 131.5, 129.5, 127.0, 125.4, 125.1, 124.9, 120.9, 75.5, 51.5, 28.1, 21.2. MS *m*/*z*: 336 (M^+, 57), 231 (99), 206 (65), 192 (100), 165 (64), 105 (51). Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.92; H, 7.04; N, 8.56.

*4.4.4. N-(tert-Butyl)-2-(2-methylphenyl)-4H-3,1-benzoxazine-4-carboxamide (**3d**).* Operation as above with azide **1d** (0.37 g, 1 mmol) refluxed for 36 h, compound **3d** (0.22 g, 69%) was also isolated as white solid. Mp: 140–142 °C, IR (KBr): 3336, 1664, 1593, 1535, 1210, 1103 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84–7.24 (m, 8H, Ar-H), 6.18 (s, 1H, CONH), 5.67 (s, 1H, OCH), 2.63 (s, 3H, CH_3), 1.35 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 156.7, 138.3, 131.7, 131.5, 130.8, 129.6, 129.5, 127.4, 125.9, 125.0, 124.5, 120.6, 75.4, 51.5, 28.5, 21.7. MS *m*/*z*: 322 (M^+, 27), 222 (100), 195 (31), 165 (19), 130 (15), 116 (13). Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.78; H, 6.74; N, 8.75.

*4.4.5. N-(tert-Butyl)-2-(2-methylphenyl)-4H-3,1-benzoxazine-4-carboxamide (**3e**).* Operation as above with azide **1e** (0.37 g, 1 mmol) refluxed for 24 h, compound **3e** (0.29 g, 89%) was also isolated as white solid. Mp: 151–152 °C, IR (KBr): 3303, 1658, 1601, 1571, 1246, 1091 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 13.25 (s, 1H, OH), 7.82 (d, *J*=7.2 Hz, 1H, Ar-H), 7.47–6.91 (m, 7H, Ar-H), 6.18 (s, 1H, CONH), 5.69 (s, 1H, OCH), 1.35 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.3, 161.2, 157.0, 135.6, 134.1, 129.7, 127.5, 127.0, 125.4, 123.9, 120.3, 118.8, 117.7, 113.0, 75.5, 51.7, 28.5. MS *m*/*z*: 324 (M^+, 96), 224 (100), 196 (99), 180 (88), 166 (31), 105 (9). Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.08; H, 6.15; N, 8.78.

*4.4.6. N-(tert-Butyl)-2-phenylethyl-4H-3,1-benzoxazine-4-carboxamide (**3f**).* Operation as above with azide **1f** (0.38 g, 1 mmol) refluxed for 8 h, compound **3f** (0.30 g, 90%) was also isolated as white solid. Mp: 99–100 °C, IR (KBr): 3290, 1657, 1602, 1552, 1363, 1163 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.41–7.16 (m, 9H, Ar-H), 6.03 (s, 1H, CONH), 5.46 (s, 1H, OCH), 3.08–3.04 (m, 2H, CH_2), 2.75 (t, *J*=7.2 Hz, 2H, CH_2), 1.35 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.8, 159.6, 140.3, 137.4, 129.4, 128.4, 128.2, 126.9, 126.2, 124.6, 124.4, 120.2, 75.1, 51.4, 36.4, 32.0, 28.4. MS *m*/*z*: 337 (M^++1, 62), 236 (100), 218 (44), 145 (43), 116 (38), 91 (97). Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.89; H, 7.11; N, 8.52.

*4.4.7. N-(tert-Butyl)-2-(4-chlorophenyl)-4H-3,1-benzoxazine-4-carboxamide (**3g**).* Operation as above with azide **1g** (0.39 g, 1 mmol) refluxed for 24 h, compound **3g** (0.30 g, 88%) was also isolated as white solid. Mp: 144–146 °C, IR (KBr): 3299, 1660, 1629, 1551, 1248, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.09 (d, *J*=7.8 Hz, 2H, Ar-H), 7.45–7.24 (m, 6H, Ar-H), 6.12 (s, 1H, CONH), 5.66 (s, 1H, OCH), 1.34 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.8, 153.8, 138.0, 137.8, 130.1, 129.6, 129.0, 128.7, 127.4, 125.1, 124.9, 120.7, 75.6, 51.5, 28.5. MS *m*/*z*: 341 (M^+-1, 37), 238 (98), 213 (100), 177 (58), 138 (82), 111 (50). Anal. Calcd for $C_{19}H_{19}ClN_2O_2$: C, 66.57; H, 5.59; N, 8.17. Found: C, 66.73; H, 5.38; N, 8.34.

*4.4.8. N-(tert-Butyl)-2-(4-nitrophenyl)-4H-3,1-benzoxazine-4-carboxamide (**3h**).* Operation as above with azide **1h** (0.40 g, 1 mmol) refluxed for 24 h, compound **3h** (0.30 g, 79%) was also isolated as white solid. Mp: 180–181 °C, IR (KBr): 3307, 1660, 1631, 1597, 1522, 1346, 1091 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.32–7.29 (m, 8H, Ar-H), 6.01 (s, 1H, CONH), 6.00 (s, 1H, OCH), 1.36 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.5, 152.8, 149.5, 137.5, 129.8, 128.6, 128.1, 125.6, 124.8, 123.5, 120.7, 75.9, 51.7, 28.5. MS *m*/*z*: 253 (M^+−BuNHCO, 22), 207 (14), 105 (28), 91 (24), 77 (56), 57 (100). Anal. Calcd for $C_{19}H_{19}N_3O_4$: C, 64.58; H, 5.42; N, 11.89. Found: C, 64.65; H, 5.31; N, 11.97.

*4.4.9. N-(tert-Butyl)-2-(4-methoxyphenyl)-4H-3,1-benzoxazine-4-carboxamide (**3i**).* Operation as above with azide **1i** (0.38 g, 1 mmol) refluxed for 24 h, compound **3i** (0.31 g, 90%) was also isolated as white solid. Mp: 121–122 °C, IR (KBr): 3322, 3060, 1663, 1623, 1572, 1254, 1098 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.10 (d, *J*=8.4 Hz, 2H, Ar-H), 7.45–7.20 (m, 4H, Ar-H), 6.97 (d, *J*=9.0 Hz, 2H, Ar-H), 6.19 (s, 1H, CONH), 5.63 (s, 1H, OCH), 3.86 (s, 3H, OCH_3), 1.33 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 167.1, 162.6, 154.6, 138.3, 129.5, 129.4, 126.7, 124.9, 124.7, 123.9, 120.8, 113.8, 75.5, 55.3, 51.4,

28.5. MS *m*/*z*: 338 (M^+, 59), 253 (10), 237 (100), 210 (36), 195 (29), 133 (32). Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28. Found: C, 70.74; H, 6.38; N, 8.46.

*4.4.10. N-(tert-Butyl)-2-phenyl-4H-3,1-benzoxazine-4-carboxamide (**3j**).* Operation as above with azide **1j** (0.35 g, 1 mmol) refluxed for 24 h, compound **3j** (0.27 g, 87%) was also isolated as white solid. Mp: 155–156 °C, IR (KBr): 3305, 1658, 1627, 1549, 1249, 1099 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.16 (d, 2H, Ar-H), 7.55–7.25 (m, 6H, Ar-H), 6.19 (s, 1H, CONH), 5.68 (s, 1H, OCH), 1.34 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 167.0, 154.7, 138.0, 131.9, 131.7, 129.6, 128.5, 127.7, 127.2, 125.1, 125.0, 120.9, 75.6, 51.5, 28.6. MS *m*/*z*: 308 (M^+, 3), 208 (98), 180 (39), 152 (46), 105 (24), 77 (100). Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.16; H, 6.41; N, 9.29.

*4.4.11. N-(tert-Butyl)-2-((2,4-dichlorophenoxy)methyl)-4H-3,1-benzoxazine-4-carboxamide (**3k**).* Operation as above with azide **1k** (0.45 g, 1 mmol) refluxed for 8 h, compound **3k** (0.35 g, 86%) was also isolated as white solid. Mp: 123–124 °C, IR (KBr): 3285, 1653, 1484, 1296, 1068 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.46–7.11 (m, 7H, Ar-H), 6.45 (s, 1H, CONH), 5.60 (s, 1H, OCH), 4.81 (dd, J_1=13.2 Hz, J_2=10.8 Hz, 2H, CH_2), 1.25 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.8, 154.4, 152.7, 136.1, 130.3, 129.6, 128.0, 127.9, 126.2, 124.9, 124.7, 120.7, 116.8, 75.2, 70.2, 51.7, 28.4. MS *m*/*z*: 406 (M^+, 16), 371 (6), 307 (76), 288 (14), 146 (100), 117 (25). Anal. Calcd for $C_{20}H_{20}Cl_2N_2O_3$: C, 58.98; H, 4.95; N, 6.88. Found: C, 58.87; H, 4.84; N, 6.96.

*4.4.12. N-(n-Butyl)-2-(2-chlorophenyl)-4H-3,1-benzoxazine-4-carboxamide (**3l**).* Operation as above with azide **1l** (0.39 g, 1 mmol) refluxed for 24 h, compound **3l** (0.24 g, 70%) was also isolated as white solid. Mp: 91–92 °C, IR (KBr): 3254, 1652, 1579, 1436, 1236, 1102 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84–7.26 (m, 8H, Ar-H), 6.70 (s, 1H, CONH), 5.88 (s, 1H, OCH), 3.37–3.31 (m, 2H, NCH_2), 1.54–1.47 (m, 2H, CH_2), 1.37–1.28 (m, 2H, CH_2), 0.85 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.3, 155.2, 137.6, 132.6, 131.8, 131.4, 130.5, 129.6, 127.9, 127.0, 125.3, 124.6, 120.1, 75.3, 39.1, 31.3, 19.9, 13.6. MS *m*/*z*: 342 (M^+, 22), 239 (100), 215 (27), 177 (43), 150 (44), 76 (91). Anal. Calcd for $C_{19}H_{19}ClN_2O_2$: C, 66.57; H, 5.59; N, 8.17. Found: C, 66.42; H, 5.48; N, 8.27.

*4.4.13. N-(n-Butyl)-2-(4-chlorophenyl)-4H-3,1-benzoxazine-4-carboxamide (**3m**).* Operation as above with azide **1m** (0.39 g, 1 mmol) refluxed for 24 h, compound **3m** (0.24 g, 70%) was also isolated as white solid. Mp: 166–167 °C, IR (KBr): 3299, 1660, 1632, 1489, 1235, 1100 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, J=8.8 Hz, 2H, Ar-H), 7.44–7.20 (m, 6H, Ar-H), 6.42 (s, 1H, CONH), 5.77 (s, 1H, OCH), 3.29 (q, J=6.8 Hz, 2H, NCH_2), 1.48–1.41 (m, 2H, CH_2), 1.31–1.23 (m, 2H, CH_2), 0.86 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.7, 153.8, 138.0, 137.7, 131.9, 130.0, 129.6, 129.1, 128.7, 128.5, 127.3, 125.1, 124.8, 120.4, 75.5, 39.1, 31.3, 19.8, 13.6. MS *m*/*z*: 342 (M^+, 7), 244 (100), 179 (10), 139 (24), 77 (10). Anal. Calcd for $C_{19}H_{19}ClN_2O_2$: C, 66.57; H, 5.59; N, 8.17. Found: C, 66.48; H, 5.74; N, 8.09.

*4.4.14. N-(n-Butyl)-2-(3-nitrophenyl)-4H-3,1-benzoxazine-4-carboxamide (**3n**).* Operation as above with azide **1n** (0.40 g, 1 mmol) refluxed for 24 h, compound **3n** (0.28 g, 80%) was also isolated as white solid. Mp: 163–164 °C, IR (KBr): 3278, 1657, 1633, 1530, 1350, 1242 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.96–7.27 (m, 8H, Ar-H), 6.33 (s, 1H, CONH), 5.86 (s, 1H, OCH), 3.33 (q, J=6.8 Hz, 2H, NCH_2), 1.51–1.45 (m, 2H, CH_2), 1.32–1.27 (m, 2H, CH_2), 0.88 (q, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.4, 152.6, 148.3, 137.3, 133.5, 133.4, 129.9, 129.6, 128.0, 126.1, 125.6, 124.8, 122.7, 120.4, 75.8, 39.2, 31.3, 19.9, 13.6. MS *m*/*z*: 353 (M^+, 3), 253 (100), 207 (33), 178 (11). Anal. Calcd for $C_{19}H_{19}N_3O_4$: C, 64.58; H, 5.42; N, 11.89. Found: C, 64.31; H, 5.57; N, 11.82.

*4.4.15. N-(n-Butyl)-2-phenyl-4H-3,1-benzoxazine-4-carboxamide (**3o**).* Operation as above with azide **1o** (0.35 g, 1 mmol) refluxed for 24 h, compound **3o** (0.27 g, 89%) was also isolated as white solid. Mp: 131–133 °C, IR (KBr): 3262, 1649, 1574, 1239, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, J=8.0 Hz, 2H, Ar-H), 7.55–7.23 (m, 7H, Ar-H), 6.35 (s, 1H, CONH), 5.82 (s, 1H, OCH), 3.34–3.28 (m, 2H, NCH_2), 1.48–1.42 (m, 2H, CH_2), 1.30–1.24 (m, 2H, CH_2), 0.85 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.9, 154.6, 137.9, 131.9, 131.5, 129.6, 128.6, 127.8, 127.3, 125.2, 125.0, 120.5, 75.5, 39.1, 31.3, 19.9, 13.6. MS *m*/*z*: 208 (M^+−BuNHCO, 73), 179 (15), 152 (24), 104 (27), 77 (100). Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.28; H, 6.41; N, 9.15.

*4.4.16. N-(n-Butyl)-2-(4-methoxyphenyl)-4H-3,1-benzoxazine-4-carboxamide (**3p**).* Operation as above with azide **1p** (0.38 g, 1 mmol) refluxed for 24 h, compound **3p** (0.28 g, 84%) was also isolated as white solid. Mp: 128–130 °C, IR (KBr): 3272, 1654, 1626, 1574, 1253, 1097 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.10 (d, J=8.8 Hz, 2H, Ar-H), 7.46–7.19 (m, 4H, Ar-H), 6.97 (d, J=8.8 Hz, 2H, Ar-H), 6.38 (s, 1H, CONH), 5.75 (s, 1H, OCH), 3.86 (s, 3H, OCH_3), 3.32–3.27 (m, 2H, NCH_2), 1.47–1.41 (m, 2H, CH_2), 1.29–1.24 (m, 2H, CH_2), 0.86 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.0, 162.6, 154.6, 138.2, 129.6, 129.5, 126.7, 124.9, 124.8, 123.9, 120.4, 113.8, 75.4, 55.4, 39.1, 31.3, 19.8, 13.6. MS *m*/*z*: 338 (M^+, 12), 238 (100). Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28. Found: C, 70.91; H, 6.68; N, 8.07.

*4.4.17. N-(n-Butyl)-2-ethyl-4H-3,1-benzoxazine-4-carboxamide (**3q**).* Operation as above with azide **1q** (0.30 g, 1 mmol) refluxed for 3 h, compound **3q** (0.24 g, 92%) was also isolated as white solid. Mp: 79–80 °C, IR (KBr): 3347, 1672, 1633, 1530, 1368, 1174 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.44–7.15 (m, 4H, Ar-H), 6.27 (s, 1H, CONH), 5.64 (s, 1H, OCH), 3.35–3.29 (m, 2H, NCH_2), 2.48 (q, J=7.6 Hz, 2H, CH_2), 1.54–1.47 (m, 2H, CH_2), 1.38–1.27 (m, 5H, CH_2 and CH_3), 0.92 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.9, 161.4, 137.3, 129.5, 126.8, 124.8, 124.4, 119.9, 74.9, 39.0, 31.3, 28.2, 19.9, 13.6, 10.4. MS *m*/*z*: 261 (M^++1, 31), 160 (93), 131 (34), 91 (100), 77 (38). Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.14; H, 7.87; N, 10.98.

4.5. Synthesis of azides 5 via Passerini reaction

*4.5.1. 2-(2-Azidophenyl)-N-(tert-butyl)-2-hydroxyacetamide (**5a**).* To a solution of 2-azidobenzaldehyde (0.44 g, 3 mmol) in methanol (15 mL) was added sequentially pyruvic acid (0.26 g, 3 mmol) and *tert*-butyl isocyanide (0.25 g, 3 mmol) at room temperature. After the reaction mixture was stirred for 12 h at ambient temperature, the solvent was removed off under reduced pressure and the residue was chromatographed on silicon gel to give 0.51 g (68%) of azide **5a** as white solid. Mp: 129–131 °C, IR (KBr): 3391, 3226, 2135, 2098, 1652, 1526, 1309, 1067 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.44–7.16 (m, 4H, Ar-H), 6.28 (s, 1H, CONH), 5.18 (s, 1H, OCH), 4.15 (s, 1H, OH), 1.32 (s, 9H, $3CH_3$). Anal. Calcd for $C_{12}H_{16}N_4O_2$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.28; H, 6.37; N, 22.71.

*4.5.2. 2-(2-Azidophenyl)-N-(n-butyl)-2-hydroxyacetamide (**5b**).* Operation as above with *n*-butyl isocyanide (0.25 g, 3 mmol), compound **5b** (0.48 g, 65%) was also isolated as white solid. Mp: 48–49 °C, IR (KBr): 3387, 3217, 2138, 2084, 1648, 1528, 1312, 1074 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.46–7.17 (m, 4H, Ar-H), 6.41 (s, 1H, CONH), 5.29 (s, 1H, OCH), 4.17 (s, 1H, OH), 3.33–3.21 (m, 2H, NCH_2), 1.49–1.43 (m, 2H, CH_2), 1.31–1.26 (m, 2H, CH_2), 0.89 (t,

J=7.2 Hz, 3H, CH_3). Anal. Calcd for $C_{12}H_{16}N_4O_2$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.17; H, 6.68; N, 22.51.

4.6. Synthesis of iminophosphoranes 6 via Staudinger reaction

*4.6.1. N-(tert-Butyl)-2-hydroxy-2-(2-(triphenylphosphorany-lidene)aminophenyl)acetamide (**6a**).* To a stirred solution of azide **5a** (0.25 g, 1 mmol) in toluene (10 mL) was added dropwise triphenylphosphine (0.26 g, 1 mmol) in toluene (5 mL) at room temperature. After the reaction mixture was stirred for 4 h at ambient temperature, the solvent was removed off under reduced pressure and the residue was recrystallized from methylene dichloride/petroleum ether to give 0.42 g (87%) of iminophosphorane **6a** as white solid. Mp: 206–208 °C, IR (KBr): 3395, 3203, 1664, 1536, 1302 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.84 (s, 1H, CONH), 7.73–6.44 (m, 19H, Ar-H), 5.76 (s, 1H, OH), 5.70 (d, J=4.0 Hz, 1H, OCH), 1.09 (s, 9H, $3CH_3$). MS m/z: 482 (M^+, 78), 381 (100), 353 (42), 277 (68), 183 (91), 151 (53). Anal. Calcd for $C_{30}H_{31}N_2O_2P$: C, 74.67; H, 6.48; N, 5.81. Found: C, 74.71; H, 6.42; N, 5.68.

*4.6.2. N-(n-Butyl)-2-hydroxy-2-(2-(triphenylphosphorany-lidene)-aminophenyl)acetamide (**6b**).* Operation as above with azide **5b** (0.25 g, 1 mmol), iminophosphorane **6b** (0.43 g, 90%) was also isolated as white solid. Mp: 145–147 °C, IR (KBr): 3389, 3212, 1658, 1545, 1304 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.88 (s, 1H, CONH), 7.72–6.43 (m, 19H, Ar-H), 5.82 (s, 1H, OCH), 5.58 (s, 1H, OH), 3.22–2.96 (m, 2H, NCH_2), 1.13–1.04 (m, 4H, $2CH_2$), 0.65 (t, J=7.2 Hz, 3H, CH_3). MS m/z: 482 (M^+, 42), 381 (78), 353 (37), 277 (85), 183 (100), 209 (74), 151 (76). Anal. Calcd for $C_{30}H_{31}N_2O_2P$: C, 74.67; H, 6.48; N, 5.81. Found: C, 74.47; H, 6.34; N, 5.86.

4.7. Synthesis of 2-amino-4*H*-3,1-benzoxazines 8

*4.7.1. N-(tert-Butyl)-2-(isopropylamino)-4H-3,1-benzoxazine 4-carboxamide (**8a**).* To a stirred solution of azide **5a** (0.25 g, 1 mmol) in toluene (10 mL) was added dropwise triphenylphosphine (0.26 g, 1 mmol) in toluene (5 mL) at room temperature. After the reaction mixture was stirred for 4 h at room temperature, *iso*-propyl isocyanate (0.09 g, 1 mmol) was added. The reaction mixture was refluxed for 12 h and the solvent was evaporated under reduced pressure. The residue was recrystallized from methanol to give 0.19 g (65%) of compound **8a** as white solid. Mp: 147–148 °C, IR (KBr): 3409, 3328, 1680, 1630, 1587, 1480, 1242 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.30–6.98 (m, 4H, Ar-H), 5.98 (s, 1H, CONH), 5.40 (s, 1H, OCH), 4.43–4.33 (m, 1H, NCH), 4.07 (br, 1H, NH), 1.37 (s, 9H, $3CH_3$), 1.26–1.24 (m, 6H, $2CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.8, 151.7, 141.6, 129.5, 124.0, 122.8, 122.1, 119.6, 76.6, 51.4, 43.3, 28.5, 23.0. MS m/z: 289 (M^+, 17), 189 (92), 147 (100). Anal. Calcd for $C_{16}H_{23}N_3O_2$: C, 66.41; H, 8.01; N, 14.52. Found: C, 66.25; H, 8.17; N, 14.45.

*4.7.2. N-(tert-Butyl)-2-(4-chlorophenylamino)-4H-3,1-benzoxazine-4-carboxamide (**8b**).* Operation as above with 4-chlorophenyl isocyanate (0.15 g, 1 mmol) refluxed for 6 h, compound **8b** (0.21 g, 60%) was also isolated as white solid. Mp: 231–232 °C, IR (KBr): 3409, 3305, 1682, 1483, 1222 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 9.62 (s, 1H, CONH), 7.92–6.93 (m, 9H, Ar-H and NH), 5.71 (s, 1H, OCH), 1.26 (s, 9H, $3CH_3$). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 167.6, 149.8, 140.4, 138.9, 129.0, 128.4, 125.3, 124.3, 122.9, 120.7, 120.3, 75.7, 50.6, 28.3. MS m/z: 357 (M^+, 4), 257 (93), 147 (29), 120 (100), 104 (24), 92 (36). Anal. Calcd for $C_{19}H_{20}ClN_3O_2$: C, 63.77; H, 5.63; N, 11.74. Found: C, 63.49; H, 5.78; N, 11.56.

*4.7.3. N-(tert-Butyl)-2-(4-fluorophenylamino)-4H-3,1-benzoxazine-4-carboxamide (**8c**).* Operation as above with 4-fluorophenyl isocyanate (0.14 g, 1 mmol) refluxed for 6 h, compound **8c** (0.25 g, 73%) was also isolated as white solid. Mp: 233–234 °C, IR (KBr): 3408, 3377, 1666, 1643, 1509, 1482, 1214 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 9.52 (s, 1H, CONH), 7.90–6.93 (m, 9H, Ar-H and NH), 5.69 (s, 1H, OCH), 1.26 (s, 9H, $3CH_3$).^{13}C NMR (DMSO-d_6, 100 MHz): δ 167.7, 158.5, 156.1, 149.9, 140.6, 136.4, 129.0, 124.3, 122.6, 120.7, 115.2, 114.9, 75.7, 50.6, 28.3. MS m/z: 341 (M^+, 22), 241 (100), 120 (22), 92 (17), 57 (80). Anal. Calcd for $C_{19}H_{20}FN_3O_2$: C, 66.85; H, 5.91; N, 12.31. Found: C, 66.94; H, 5.75; N, 12.53.

*4.7.4. N-(tert-Butyl)-2-(3-methylphenylamino)-4H-3,1-benzoxazine-4-carboxamide (**8d**).* Operation as above with 3-methylphenyl isocyanate (0.13 g, 1 mmol) refluxed for 10 h, compound **8d** (0.23 g, 67%) was also isolated as white solid. Mp: 188–190 °C, IR (KBr): 3384, 3301, 1666, 1641, 1593, 1483, 1222 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 9.39 (s, 1H, NH), 7.88 (s, 1H, NH), 7.88–6.77 (m, 8H, Ar-H), 5.69 (s, 1H, OCH), 2.28 (s, 3H, CH_3), 1.27 (s, 9H, $3CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6, 149.9, 140.7, 139.6, 137.5, 128.9, 128.6, 128.3, 124.3, 122.5, 120.7, 119.5, 116.2, 115.3, 75.6, 50.5, 28.3, 21.3. MS m/z: 337 (M^+, 28), 237 (100), 91 (17), 57 (34). Anal. Calcd for $C_{20}H_{23}N_3O_2$: C, 71.19; H, 6.87; N, 12.45. Found: C, 71.26; H, 6.73; N, 12.64.

*4.7.5. N-(n-Butyl)-2-(4-chlorophenylamino)-4H-3,1-benzoxazine-4-carboxamide (**8e**).* Operation as above with azide **5b** (0.25 g, 1 mmol) and 4-chlorophenyl isocyanate (0.15 g, 1 mmol) refluxed for 6 h, compound **8e** (0.25 g, 71%) was also isolated as white solid. Mp: 185–186 °C, IR (KBr): 3402, 3308, 1680, 1487, 1220 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 9.63 (s, 1H, NH), 8.28 (s, 1H, NH), 7.75–6.94 (m, 8H, Ar-H), 5.76 (s, 1H, OCH), 3.37–3.03 (m, 2H, NCH_2), 1.40–1.35 (m, 2H, CH_2), 1.27–1.19 (m, 2H, CH_2), 0.83 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.0, 149.6, 140.2, 138.6, 129.1, 128.6, 128.4, 125.4, 124.6, 122.8, 120.5, 119.8, 75.7, 38.2, 31.0, 19.4, 13.6. MS m/z: 357 (M^+, 32), 258 (100), 120 (25), 92 (17). Anal. Calcd for $C_{19}H_{20}ClN_3O_2$: C, 63.77; H, 5.63; N, 11.74. Found: C, 63.95; H, 5.46; N, 11.78.

5. Crystallographic material

Crystallographic data for **3e** have been deposited in the Cambridge Crystallographic Data Center as supplementary publication numbers CCDC 725169. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

We gratefully acknowledge financial support of this work by the National Natural Science Foundation of China (No. 20772041) and the Key Project of Chinese Ministry of Education (No. 107082).

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.08.022.

References and notes

1. (a) Zhu, J.; Bienaymé, H. *Multicomponent Reactions*; Wiley-VCH: New York, NY, 2005; (b) Domling, A. *Chem. Rev.* **2006**, *106*, 17; (c) Banfi, L.; Riva, R. *Org. React.* **2005**, *65*, 1.
2. (a) Fan, L.; Adams, A. M.; Polisar, J. G.; Ganem, B. *J. Org. Chem.* **2008**, *73*, 9720; (b) Owens, T. D.; Semple, J. E. *Org. Lett.* **2001**, *3*, 3301.
3. (a) Beck, B.; Larbig, G.; Mejat, B.; Magnin-Lachaux, M.; Picard, A.; Herdtweck, E.; Domling, A. *Org. Lett.* **2003**, *5*, 1047; (b) Beck, B.; Magnin-Lachaux, M.; Herdtweck, E.; Domling, A. *Org. Lett.* **2001**, *3*, 2875; (c) Wright, D. L.; Robotham, C. V.; Aboud, K. *Tetrahedron Lett.* **2002**, *43*, 943; (d) Bossio, R.; Marcaccini, S.; Pepino, R.; Torroba, T. *Synthesis* **1993**, 783.

4. (a) Chan, J.; Faul, M. *Tetrahedron Lett.* **2006**, *47*, 3361; (b) Palacios, F.; Herran, E.; Alonso, C.; Rubiales, G.; Lecea, B.; Ayerbe, M.; Cossio, F. P. *J. Org. Chem.* **2006**, *71*, 6020; (c) Lertpibulpanya, D.; Marsden, S. P.; Rodriguez-Garcia, I.; Kilner, C. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 5000; (d) Palacios, F.; Alonso, C.; Aparicio, D.; Rubiales, G.; Santos, J. M. *Tetrahedron* **2007**, *63*, 523; (e) Zanatta, N.; Schneider, J. M. F. M.; Schneider, P. H.; Wouters, A. D.; Bonacorso, H. G.; Martins, M. A. P.; Wessjohann, L. A. *J. Org. Chem.* **2006**, *71*, 6996.
5. (a) Corres, N.; Delgado, J. J.; García-Valverde, M.; Marcaccini, S.; Rodríguez, T.; Rojo, J.; Torroba, T. *Tetrahedron* **2008**, *64*, 2225; (b) Sanudo, M.; García-Valverde, M.; Marcaccini, S.; Delgado, J. J.; Rojo, J.; Torroba, T. *J. Org. Chem.* **2009**, *74*, 2189.
6. (a) Dias, N.; Goosens, J. F.; Baldeyrou, B.; Lansiaux, A.; Colson, P.; Di Salvo, A.; Bernal, J.; Turnbull, A.; Mincher, D.; Bailly, C. *Bioconjugate Chem.* **2005**, *16*, 949; (b) Hays, S. J.; Caprathe, B. W.; Gilmore, J. L.; Amin, N.; Emmerling, M. R.; Michael, W.; Nadimpalli, R.; Nath, R.; Raser, K. J.; Stafford, D.; Watson, D.; Wang, K.; Jaen, J. C. *J. Med. Chem.* **1998**, *41*, 1060; (c) Sugiyama, H.; Hosoda, K.; Kumagai, Y.; Takeuchi, M.; Okada, M. U.S. Patent 4.596.801, 1986; (d) Kobzina, J.W. U.S. Patent 4,030,906, 1977.
7. Kuch, H.; Schmitt, K.; Seidl, G.; Hoffmann, I. U.S. Patent 3,725,404, 1973.
8. (a) Costa, M.; Cà, N. D.; Gabriele, B.; Massera, C.; Salerno, G.; Soliani, M. *J. Org. Chem.* **2004**, *69*, 2469; (b) Ma, S.; Li, J.; Sun, Y.; Zhao, J.; Zhao, X.; Yang, X.; Zhang, L.; Wang, L.; Zhou, Z. *Tetrahedron* **2006**, *62*, 7999; (c) Molina, P.; Arques, A.; Molina, A. *Synthesis* **1991**, 21; (d) Garrat, P. J.; Hobbs, C. J.; Wrigglesworth, R. *Tetrahedron* **1989**, *45*, 829; (e) Gauss, W.; Krabbe, H. J. *Synthesis* **1978**, 377.
9. (a) Ding, M. W.; Xu, S. Z.; Zhao, J. F. *J. Org. Chem.* **2004**, *69*, 8366; (b) Zhao, J. F.; Xie, C.; Xu, S. Z.; Ding, M. W.; Xiao, W. J. *Org. Biomol. Chem.* **2006**, *4*, 130; (c) Yuan, J. Z.; Fu, B. Q.; Ding, M. W.; Yang, G. F. *Eur. J. Org. Chem.* **2006**, 4170; (d) Ding, M. W.; Fu, B. Q.; Cheng, L. *Synthesis* **2004**, 1067; (e) Li, H. X.; Xie, C.; Ding, M. W.; Liu, Z. M.; Yang, G. F. *Synlett* **2007**, 2280; (f) Liu, M. G.; Hu, Y. G.; Ding, M. W. *Tetrahedron* **2008**, *64*, 9052; (g) Huang, N. Y.; Liang, Y. J.; Ding, M. W.; Fu, L. W.; He, H. W. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 831.
10. (a) Akritopoulou-Zanze, I.; Gracias, V.; Djuric, S. W. *Tetrahedron Lett.* **2004**, *45*, 8439; (b) Pelkey, E. T.; Gribble, G. W. *Tetrahedron Lett.* **1997**, *38*, 5603; (c) Capperucci, A.; Degl'Innocenti, A.; Funicello, J. M.; Mauriello, G.; Scafato, P.; Spagnolo, P. *J. Org. Chem.* **1995**, *60*, 2254.
11. Semple, J. E.; Owens, T. D.; Nguyen, K.; Levy, O. E. *Org. Lett.* **2000**, *2*, 2769.