A highly regio- and stereoselective synthesis of (*Z*)-3-arylidene-2,3-dihydro-5*H*-1,4-benzodioxepin-5-ones and (*Z*)-3-arylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-5-ones through palladium–copper catalysis

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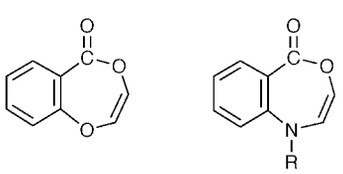
Sodium 2-(prop-2′-ynyloxy)benzoate **1a** reacted with the aryl iodides **2**–**10** in the presence of bis(triphenylphosphine)palladium(II) chloride, cuprous iodide and triethylamine in CH_3CN–DMF to yield the disubstituted alkynes **11**–**19** in good yields (48–58%). Similarly, sodium 2-[*N*-benzyl-*N*-(prop-2′-ynyl)]aminobenzoate **1b** on reaction with aryl iodides under palladium–copper catalysis afforded the disubstituted alkynes **20**–**22**. Compounds **11**–**19** on cyclisation with cuprous iodide in the presence of triethylamine in acetonitrile yielded the 3-arylidene-2,3-dihydro-5*H*-1,4-benzodioxepin-5-ones **23**–**31** in 61–83% yields. Similarly, compounds **20**–**22** on cyclisation gave 3-arylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-5-ones **32**–**34**.

Over the last few decades, palladium-catalysed reactions[1] have been of immense significance because of their role in carboannulation[2] and heteroannulation processes.[3] In our laboratory, we have developed methods based on palladium–copper catalysed heteroannulation of terminal alkynes which have led to various benzofused heterocycles, *e.g.*, benzofurans,[4] phthalides,[5] quinolines and quinolones,[6] benzodioxans,[7] isoindolinones,[8] benzoxazines[9] and isobenzofurans.[10] In continuation of those studies, we became interested in the development of benzofused heterocycles containing seven-membered rings with two heteroatoms, *e.g.* benzodioxepinone I and benzoxazepinone II structures.



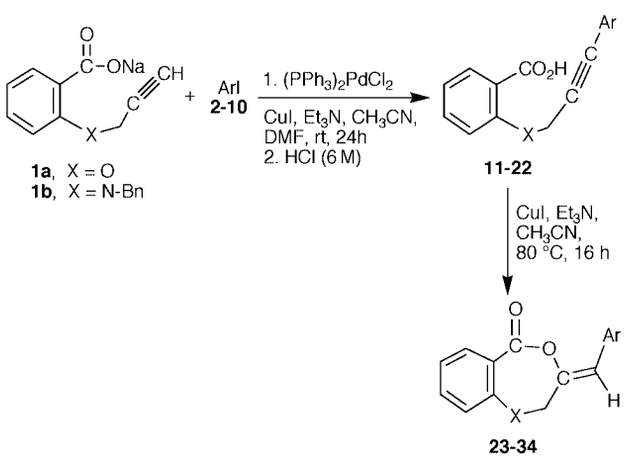
I II

There have been many reports of compounds containing these structures which occur naturally and are also of biological importance.[11] However, a search of the literature revealed only a limited number of methods available for the synthesis of these heterocyclic structures.[12]

In view of this, we wish to report in this paper our results on the synthesis of benzodioxepinone and benzoxazepinone structures.

Results and discussion

When sodium 2-(prop-2′-ynyloxy)benzoate **1a** was treated with aryl iodides **2**–**10** in the presence of bis(triphenylphosphine)-palladium(II) chloride, cuprous iodide and triethylamine in CH_3CN–DMF, the disubstituted alkynes **11**–**19** were obtained in good yields (48–58%). The cyclisation of **11**–**19** with cuprous iodide in the presence of triethylamine in acetonitrile yielded the 3-arylidene-2,3-dihydro-5*H*-1,4-benzodioxepin-5-ones **23**–**31** in 61–83% yields (Scheme 1 and Table 1). Similarly, sodium 2-[*N*-benzyl-*N*-(prop-2′-ynyl)]aminobenzoate **1b** on treatment with aryl iodides **2**, **8** or **9** in the presence of palladium catalyst, cuprous iodide and triethylamine in CH_3CN–DMF led to the disubstituted alkynes **20**–**22** which on cyclisation with cuprous iodide in triethylamine led to the 3-arylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-5-ones **32**–**34** (Scheme 1 and Table 1).



Scheme 1

The starting materials (**1a** and **1b**) were synthesised by propargylation of methyl salicylate or methyl anthranilate with propargyl bromide in the presence of potassium carbonate in acetone and subsequent hydrolysis of the products with potassium hydroxide.† The *N*-benzylation was carried out with benzyl bromide in DMF in the presence of potassium carbonate.

The palladium-catalysed reactions of **1a** or **1b** with aryl iodides were carried out with bis(triphenylphosphine)-palladium(II) chloride in the presence of cuprous iodide as a co-catalyst. The reactions were usually carried out at room temperature when only the disubstituted alkynes were obtained. If the reactions were carried out at a higher temperature (80 °C), the yields of the disubstituted alkynes (**11**–**22**) were much lower, although formation of some cyclic products (8–10%) could also be seen. Usually the sodium salts **1a** or **1b** were used for the palladium catalysed reactions. The corresponding free acids led

† The IUPAC name for propargyl is prop-2-ynyl.

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Table 1 Synthesis of 1,4-benzodioxepinones (**23**–**31**) and 4,1-benzoxazepinones (**32**–**34**)

Entry	Monosubstituted alkynes, **1** X	Aryl iodides, ArI Ar	Disubstituted alkynes **11**–**22** (Yield %)[a]	Dioxepinones or oxazepinones (Yield %)[b]
1	O, **1a**	Ph, **2**	**11** (56)	**23** (83)
2	O, **1a**	*o*-$MeOC_6H_4$, **3**	**12** (57)	**24** (80)
3	O, **1a**	*m*-ClC_6H_4, **4**	**13** (55)	**25** (80)
4	O, **1a**	*o*-$MeO_2CC_6H_4$, **5**	**14** (54)	**26** (75)
5	O, **1a**	2-Thienyl, **6**	**15** (58)	**27** (76)
6	O, **1a**	*o*-CH_3CO-OC_6H_4, **7**	**16** (48)	**28** (83)
7	O, **1a**	*p*-$MeOC_6H_4$, **8**	**17** (58)	**29** (79)
8	O, **1a**	2,4-Dimethoxypyrimidin-5-yl, **9**	**18** (58)	**30** (75)
9	O, **1a**	*o*-IC_6H_4, **10**	**19** (50)	**31** (61)
10	N-Bn, **1b**	Ph, **2**	**20** (68)	**32** (84)
11	N-Bn, **1b**	*p*-$MeOC_6H_4$, **8**	**21** (65)	**33** (81)
12	N-Bn, **1b**	2,4-Dimethoxypyrimidin-5-yl, **9**	**22** (64)	**34** (73)

[a] Yields are based on **1** and refer to chromatographically pure isolated materials. [b] Based on the disubstituted alkynes **11**–**22** and refer to the chromatographically pure isolated materials.

to lower yields. The reactions were carried out in a mixture of acetonitrile and dimethyl formamide. Use of DMF alone led to lower yields due to the formation of strongly coloured materials. The use of other catalysts like tetrakis(triphenylphosphine)palladium(0) in the presence of potassium carbonate in dimethyl formamide at 60 °C or palladium(II) acetate in the presence of potassium *tert*-butoxide, tetrabutylammonium chloride, triphenylphosphine in acetonitrile at room temperature for 8 h did not yield the disubstituted alkynes. Various substituted aryl iodides could be used in the palladium-catalysed reactions leading to the disubstituted alkynes. However, when 1,2-diiodobenzene was used, only one of the iodo-groups participated in the palladium-catalysed reactions, the other iodo-group remained unaffected.

The cyclisation of the disubstituted alkynes was carried out by heating with cuprous iodide (5 mol%) in the presence of triethylamine in acetonitrile. The cyclised products were obtained in 61–83% yields. The cyclisation of the disubstituted alkynes could also be carried out by refluxing them in acetonitrile in the presence of $PdCl_2$ (5 mol%) as catalyst. However, the yields were much lower (40%). For the formation of the 4,1-benzoxazepinones, the presence of a benzyl (Bn) or an alkyl group on the nitrogen atom was found to be essential for cyclisation. The cyclisation step leading to the dioxepinone or the oxazepinone structure was found to be highly regio- and stereoselective. Only seven-membered ring heterocycles were formed. The establishment of the *Z*-configuration of the 3-arylidene group follows from the $^3J_{CH}$ values[13] of the vinylic proton and the methylenic carbon of the heterocyclic rings and from the NOE data.[14] The compounds of *Z*-configuration were found to be quite stable. Attempted isomerisation of compound **23** by (i) stirring in concentrated sulfuric acid at room temperature for 2–5 h or (ii) by heating in nitrobenzene in the presence of iodine at 100–110 °C for 16 h did not afford the corresponding *E*-isomer.

Thus, we have reported a highly efficient regio- and stereoselective method for the synthesis of (*Z*)-3-arylidene-2,3-dihydro-5*H*-1,4-benzodioxepin-5-ones and (*Z*)-3-arylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-5-ones starting from readily available materials under extremely mild conditions. We believe this is the first report of a general procedure for the synthesis of benzodioxepinones and benzoxazepinones using palladium–copper catalysis.

Experimental

Mps were determined in an open sulfuric acid bath or on a Reichert (285980) (Austria) bath and are uncorrected. IR spectra were taken on a Perkin-Elmer 298 instrument for samples as KBr plates or liquid films. ^{1}H NMR spectra were recorded on a Varian EM-360, and a Bruker DPX-300 spectrometer for samples in solvents as indicated with tetramethylsilane as internal reference; *J* values given in Hz. TLC was performed on 60F-254 precoated silica gel sheets (E. Merck) and column chromatography was done on silica gel (60–120 mesh) or neutral alumina. Light petroleum refers to the fraction with distillation range 60–80 °C. Elemental analyses were performed on a Perkin-Elmer 240C analyser.

The aryl iodides **2**–**10** were synthesised according to the known procedures.[7]

Synthesis of the sodium salt of 2-(prop-2′-ynyloxy)benzoic acid 1a

A mixture of methyl salicylate (5 g, 32.89 mmol) and anhydrous potassium carbonate (4.54 g, 32.89 mmol) in dry acetone (20 cm^3) was stirred for 2 h at room temperature. Propargyl bromide (4.69 g, 39.46 mmol) in dry acetone (10 cm^3) was then added very carefully over 30 min. The whole mixture was then heated under reflux for 16 h with constant stirring under a N_2 atmosphere. After removal of acetone, the residue was poured into water (50 cm^3) and extracted with chloroform (3 times 50 cm^3). The combined organic layer was washed with water (3 times 50 cm^3) and dried over anhydrous sodium sulfate. After removal of solvent, the residue was purified by column chromatography over silica gel, using 1 : 1 chloroform–light petroleum as eluting solvent, to yield methyl 2-(prop-2′-ynyloxy)benzoate as a colourless oil, yield 5.80 g (93%) (Found: C, 69.28; H, 5.03. $C_{11}H_{10}O_3$ requires C, 69.46; H, 5.29%); ν_{max} (neat)/cm^{-1} 3280 and 1715; δ_H (60 MHz; CCl_4) 2.43 (1H, t, *J* 2.0, C≡CH), 3.79 (3H, s, -CO_2Me), 4.70 (2H, d, *J* 2.0, -OCH_2), 6.825–7.13 (2H, m, ArH), 7.26–7.82 (2H, m, ArH).

Potassium hydroxide (2.94 g, 52.57 mmol) dissolved in water (10 cm^3) was added dropwise to a methanolic solution (20 cm^3) of methyl 2-(prop-2′-ynyloxy)benzoate (5 g, 26.28 mmol) with constant stirring. This was stirred at room temperature for about 24 h. The residue obtained after the removal of methanol was neutralised with dilute HCl (6 M). It was extracted with chloroform (3 times 50 cm^3). The combined chloroform extract was washed with water (3 times 50 cm^3) and dried over anhydrous sodium sulfate. After removal of solvent, the solid residue was crystallised from ether–light petroleum. 2-(Prop-2′-ynyloxy)benzoic acid was obtained as a white crystalline solid, yield 4.21 g (91%); mp 82–83 °C (Found: C, 68.22; H, 4.64. $C_{10}H_8O_3$ requires C, 68.17; H, 4.57%); ν_{max} (KBr)/cm^{-1} 3280 and 1703; δ_H (60 MHz; CCl_4) 2.50 (1H, t, *J* 2.0, C≡CH), 4.84 (2H, d, *J* 2.0, -OCH_2), 6.89–7.23 (2H, m, ArH), 7.39–7.72 (1H, m, ArH), 8.00–8.16 (1H, m, ArH) and 11.09 (1H, s, -CO_2H).

To a solution of sodium (45 mg, 1.98 mmol) in methanol (10 cm^3), 2-(prop-2′-ynyloxy)benzoic acid (350 mg, 1.98 mmol)

was added and stirred for 5 min and the sodium salt **1a** was obtained after the removal of methanol under reduced pressure in quantitative yield.

Synthesis of the sodium salt of 2-(*N*-benzyl-*N*-prop-2′-ynyl)-aminobenzoic acid 1b

A mixture of methyl anthranilate (5 g, 33.07 mmol) and anhydrous potassium carbonate (4.56 g, 33.07 mmol) in dry DMF (20 cm^3) was stirred for 8 h at room temperature under a N_2 atmosphere. Propargyl bromide (4.72 g, 39.68 mmol) in dry DMF (10 cm^3) was then added slowly over 30 min. The whole mixture was heated at 80 °C for 48 h with constant stirring under a N_2 atmosphere. DMF was removed from the reaction mixture under reduced pressure and the residue was extracted with chloroform (3 times 50 cm^3) and distilled water (50 cm^3). The chloroform extract was washed with water (2 times 50 cm^3) and dried over anhydrous sodium sulfate. After removal of solvent, the residue was purified by column chromatography over silica gel, using 1 : 1 chloroform–light petroleum as eluting solvent to yield methyl 2-(*N*-prop-2′-ynyl)aminobenzoate, yield 4.43 g (71%); mp 63 °C (Found: C, 69.69; H, 5.68; N, 7.29. $C_{11}H_{11}NO_2$ requires C, 69.82; H, 5.86; N, 7.40%); ν_{max} (KBr)/cm^{-1} 3369, 3284 and 1686; δ_H (60 MHz; CCl_4) 2.03 (1H, t, *J* 2.0, C≡CH), 3.66 (3H, s, -CO_2Me), 3.79–3.95 (2H, dd, *J* 4.0), 6.36–6.69 (2H, m, ArH), 7.09–7.42 (1H, m, ArH) and 7.66–7.89 (1H, m, ArH).

A mixture of methyl 2-(*N*-prop-2′-ynyl)aminobenzoate (3 g, 15.85 mmol) and anhydrous potassium carbonate (2.19 g, 15.85 mmol) in dry DMF (15 cm^3) was stirred for 8 h at room temperature under a N_2 atmosphere. Benzyl bromide (4.06 g, 23.77 mmol) in dry DMF (10 cm^3) was then added slowly over 20 min. The whole mixture was heated at 80 °C for 48 h with constant stirring under a N_2 atmosphere. The residue obtained after removal of DMF under reduced pressure was extracted with chloroform (3 times 50 cm^3) and water (50 cm^3). The combined chloroform layer was washed with water (2 times 50 cm^3) and dried over anhydrous sodium sulfate. After removal of solvent, the residue was purified by column chromatography over silica gel using 3 : 1 chloroform–light petroleum as eluent. Methyl 2-(*N*-benzyl-*N*-prop-2′-ynyl)aminobenzoate was obtained as a colourless oil, yield 2.50 g (56.56%) (Found: C, 77.36; H, 6.12; N, 4.92. $C_{18}H_{17}NO_2$ requires C, 77.39; H, 6.13; N, 5.01%); ν_{max} (neat)/cm^{-1} 3285 and 1715; δ_H (60 MHz; CCl_4) 2.03 (1H, t, *J* 2.0, C≡CH), 3.69 (2H, d, *J* 2.0, CH_2C≡C), 3.75 (3H, s, -CO_2Me), 4.33 (2H, s, -NCH_2Ph), 6.79–7.58 (8H, m, ArH) and 7.58–7.75 (1H, m, ArH).

Potassium hydroxide (1.0 g, 17.82 mmol) dissolved in water (10 cm^3) was added dropwise to a methanolic solution (20 cm^3) of methyl 2-(*N*-benzyl-*N*-prop-2′-ynyl)aminobenzoate (2.5 g, 8.94 mmol) with constant stirring. This was stirred at room temperature for 24 h. The residue obtained after the removal of methanol was neutralised with dilute HCl (6 M) and worked up with chloroform (3 times 50 cm^3) and water (50 cm^3). The solid residue obtained after the removal of chloroform was crystallised from ether–light petroleum. 2-(*N*-Benzyl-*N*-prop-2′-ynyl)-aminobenzoic acid was obtained as a white crystalline solid, yield 1.97 g (83.12%); mp 117–118 °C (Found: C, 76.95; H, 5.69; N, 5.28. $C_{17}H_{15}NO_2$ requires C, 76.93; H, 5.58; N, 5.21%); ν_{max} (KBr)/cm^{-1} 3293 and 1691; δ_H (60 MHz; CCl_4) 2.36 (1H, t, *J* 2.0), 3.66 (2H, d, *J* 2.0), 4.23 (2H, s, -NCH_2Ph), 7.09–7.75 (8H, m, ArH) and 8.06–8.29 (1H, m, ArH).

To a solution of sodium (30 mg, 1.3 mmol) in methanol (10 cm^3), 2-(*N*-benzyl-*N*-prop-2′-ynyl)aminobenzoic acid (350 mg, 1.3 mmol) was added and stirred for 5 min and the sodium salt **1b** was obtained after the removal of methanol under reduced pressure in quantitative yield.

General procedure for the synthesis of 11–22

A mixture of iodoarene **2**–**10** (1 mmol), bis(triphenylphosphine)palladium(II) chloride (2.5 mol%), cuprous iodide (5 mol%) and triethylamine (2.5 equiv.) was stirred in dry acetonitrile (9 cm^3) for about 25 min under an argon atmosphere. The sodium salt of the acetylenic compound **1a** or **1b** (1 mmol) in dry DMF (7 cm^3) was added very slowly and the reaction mixture was stirred at room temperature for 24 h. After removal of solvent, the residue was neutralised with dilute HCl (6 M) and this was extracted with chloroform (3 times 25 cm^3) and water (50 cm^3). The combined chloroform layer was washed with water (3 times 25 cm^3) and dried over anhydrous sodium sulfate. The material obtained after the removal of solvent was purified by chromatography on silica gel (60–120 mesh) using chloroform as eluent, the disubstituted alkynes (**11**–**22**) were obtained as gum.

2-[(3′-Phenyl)prop-2′-ynyloxy]benzoic acid 11. Gum (Found: C, 75.78; H, 5.15. $C_{16}H_{12}O_3$ requires C, 76.17; H, 4.79%); ν_{max} (neat)/cm^{-1} 1702; δ_H (60 MHz; CCl_4) 5.13 (2H, s, -CH_2), 7.0–7.72 (6H, m, ArH) and 8.0–8.33 (3H, m, ArH).

2-[3′-(*o*-Methoxyphenyl)prop-2′-ynyloxy]benzoic acid 12. Gum (Found: C, 72.21; H, 5.13. $C_{17}H_{14}O_4$ requires C, 72.32; H, 4.99%); ν_{max} (neat)/cm^{-1} 1701; δ_H (60 MHz; CCl_4) 3.76 (3H, s, -OCH_3), 5.09 (2H, s, -CH_2), 6.72–7.52 (7H, m, ArH), 8.0–8.2 (1H, m, ArH) and 10.4 (1H, s, -CO_2H, broad).

2-[3′-(*m*-Chlorophenyl)prop-2′-ynyloxy]benzoic acid 13. Gum (Found: C, 67.01; H, 4.15. $C_{16}H_{11}O_3Cl$ requires C, 67.02; H, 3.86%); ν_{max} (neat)/cm^{-1} 1702; δ_H (60 MHz; CCl_4) 5.03 (2H, s, -CH_2), 6.82–7.66 (7H, m, ArH), 7.8–8.13 (1H, m, ArH) and 10.5 (1H, s, -CO_2H, broad).

2-[3′-(*o*-Methoxycarbonylphenyl)prop-2′-ynyloxy]benzoic acid 14. Gum (Found: C, 69.41; H, 4.72. $C_{18}H_{14}O_5$ requires C, 69.67; H, 4.54%); ν_{max} (neat)/cm^{-1} 1715 and 1702; δ_H (60 MHz; CCl_4) 3.89 (3H, s, -CO_2Me), 5.10 (2H, s, -CH_2), 6.81–7.72 (7H, m, ArH) and 8.01–8.26 (1H, m, ArH).

2-[3′-(2-Thienyl)prop-2′-ynyloxy]benzoic acid 15. Gum (Found: C, 64.79; H, 4.04. $C_{14}H_{10}O_3S$ requires C, 65.09; H, 3.90%); ν_{max} (neat)/cm^{-1} 1703; δ_H (60 MHz; CCl_4) 5.06 (2H, s, -CH_2), 6.76–7.69 (5H, m, ArH), 7.90–8.16 (2H, m, ArH) and 10.92 (1H, s, -CO_2H, broad).

2-[3′-(*o*-Acetoxyphenyl)prop-2′-ynyloxy]benzoic acid 16. Gum (Found: C, 69.40; H, 4.79. $C_{18}H_{14}O_5$ requires C, 69.60; H, 4.54%); ν_{max} (neat)/cm^{-1} 1715 and 1701; δ_H (60 MHz; CCl_4), 2.03 (3H, s, -$OCOCH_3$), 5.0 (2H, s, -CH_2), 6.79–7.62 (6H, m, ArH), 7.76–8.06 (2H, m, ArH) and 10.03 (1H, s, -CO_2H, broad).

2-[3′-(*p*-Methoxyphenyl)prop-2′-ynyloxy]benzoic acid 17. Gum (Found: C, 72.09; H, 5.18. $C_{17}H_{14}O_4$ requires C, 72.32; H, 4.99%); ν_{max} (neat)/cm^{-1} 1702; δ_H (60 MHz; CCl_4) 3.79 (3H, s, -OCH_3), 5.09 (2H, s, -CH_2), 6.72–7.56 (6H, m, ArH), 8.03–8.40 (2H, m, ArH) and 10.13 (1H, s, -CO_2H, broad).

2-[3′-(2,4-Dimethoxypyrimidin-5-yl)prop-2′-ynyloxy]benzoic acid 18. Gum (Found: C, 60.94; H, 4.74; N, 8.78. $C_{16}H_{14}N_2O_5$ requires C, 61.14; H, 4.48; N, 8.91%); ν_{max} (neat)/cm^{-1} 1702; δ_H (300 MHz; $CDCl_3$) 4.00 (3H, s, -OCH_3), 4.03 (3H, s, -OCH_3), 5.18 (2H, s, -CH_2), 7.15–7.27 (2H, m, ArH), 7.55–7.61 (1H, m, ArH), 8.16–8.19 (1H, q, ArH) and 8.31 (1H, s, ArH).

2-[3′-(*o*-Iodophenyl)prop-2′-ynyloxy]benzoic acid 19. Gum (Found: C, 50.56; H, 3.25. $C_{16}H_{11}IO_3$ requires C, 50.81; H, 2.93%); ν_{max} (neat)/cm^{-1} 1701; δ_H (60 MHz; CCl_4) 5.05 (2H, s, -CH_2), 6.74–7.68 (7H, m, ArH) and 7.91–8.15 (1H, m, ArH).

2-[*N*-Benzyl-*N*-(3′-phenylprop-2′-ynyl)amino]benzoic acid 20. Gum (Found: C, 80.59; H, 5.79; N, 3.83. $C_{23}H_{19}NO_2$ requires C,

80.91; H, 5.60; N, 4.10%); ν_{max} (neat)/cm^{-1} 1702; δ_H (60 MHz; CCl_4) 3.86 (2H, s, -CH_2-C≡), 4.33 (2H, s, -NCH_2Ph), 7.16–7.8 (13H, m, ArH) and 8.16–8.42 (1H, m, ArH).

2-{*N*-Benzyl-*N*-[3′-(*p*-methoxyphenyl)prop-2′-ynyl]amino}-benzoic acid 21. Gum (Found: C, 77.32; H, 5.95; N, 3.46. $C_{24}H_{21}NO_3$ requires C, 77.60; H, 5.69; N, 3.77%); ν_{max} (neat)/cm^{-1} 1701; δ_H (60 MHz; CCl_4) 3.75 (3H, s, -OCH_3), 3.82 (2H, s, -CH_2C≡), 4.30 (2H, s, -NCH_2Ph), 6.70–6.82 (2H, m, ArH), 7.13–7.92 (10H, m, ArH) and 8.13–8.33 (1H, m, ArH).

2-{*N*-Benzyl-*N*-[3′-(2,4-dimethoxypyrimidin-5-yl)prop-2′-ynyl]amino}benzoic acid 22. Gum (Found: C, 68.21; H, 5.49; N, 10.65. $C_{23}H_{21}N_3O_4$ requires C, 68.47; H, 5.24; N, 10.41%); ν_{max} (neat)/cm^{-1} 1702; δ_H (60 MHz; CCl_4) 4.03 (3H, s, -OCH_3), 4.06 (3H, s, -OCH_3), 3.83 (2H, s, -CH_2C≡), 4.31 (2H, s, -NCH_2Ph), 7.13–7.71 (8H, m, ArH) and 8.17–8.32 (2H, m, ArH).

General procedure for the synthesis of 23–34

To a solution of the disubstituted alkynes **11**–**22** (1 mmol) in dry acetonitrile, cuprous iodide (5 mol%) and triethylamine (4 equiv.) was added and the whole mixture was refluxed at 80 °C for 16 h under an argon atmosphere. After the removal of solvent under reduced pressure, the residue was purified by column chromatography on silica gel (60–120 mesh) using 1 : 1 chloroform–light petroleum (60–80 °C) as eluent to yield the cyclic products **23**–**34** in good yields (61–83%). The products were finally crystallised from ether–light petroleum.

(*Z*)-2,3-Dihydro-3-(phenylmethylidene)-5*H*-1,4-benzodioxepin-5-one 23. This was synthesised according to the general procedure; crude product was crystallised from diethyl ether–light petroleum, mp 89–91 °C (Found: C, 76.32; H, 5.04. $C_{16}H_{12}O_3$ requires C, 76.17; H, 4.79%); ν_{max} (KBr)/cm^{-1} 1725 and 1660; δ_H (300 MHz; $CDCl_3$) 4.86 (2H, s, -CH_2), 6.03 (1H, s, =CH), 7.03–7.11 (2H, m, ArH), 7.25–7.37 (3H, m, ArH), 7.45–7.51 (1H, m, ArH), 7.59–7.63 (2H, m, ArH) and 7.95 (1H, dd, *J* 7.8 and 1.8, ArH); δ_C (75 MHz; $CDCl_3$) 73.01, 118.30, 119.30, 120.57, 122.57, 128.57, 128.61, 129.54, 132.50, 134.12, 135.06, 143.20, 156.84 and 165.32; δ_C (75 MHz; $CDCl_3$; DEPT 135) 73.09 (inverted), 119.38, 120.65, 122.65, 128.66, 128.76, 129.63, 134.21 and 135.15.

(*Z*)-2,3-Dihydro-3-[(*o*-methoxyphenyl)methylidene]-5*H*-1,4-benzodioxepin-5-one 24. Mp 116–117 °C (Found: C, 71.99; H, 4.94. $C_{17}H_{14}O_4$ requires C, 72.32; H, 4.99%); ν_{max} (KBr)/cm^{-1} 1720 and 1660; δ_H (300 MHz; $CDCl_3$) 3.81 (3H, s, -OCH_3), 4.89 (2H, s, -CH_2), 6.53 (1H, s, =CH), 6.84–6.87 (1H, d, *J* 8.3, ArH), 6.96–7.12 (3H, m, ArH), 7.24–7.30 (1H, m, ArH), 7.46–7.52 (1H, m, ArH) and 7.94–7.98 (2H, m, ArH); δ_C (75 MHz; $CDCl_3$) 55.53, 73.20 ($^3J_{CH}$ = 4.2 Hz), 110.51, 112.97, 118.36, 120.59, 120.86, 121.29, 122.39, 129.78, 130.22, 134.08, 134.93, 143.00, 156.78, 156.87 and 165.64; δ_C (75 MHz; $CDCl_3$; DEPT 135) 55.61, 73.20 (inverted), 110.59, 113.05, 120.66, 120.93, 122.47, 129.86, 130.30, 134.16 and 135.00.

(*Z*)-2,3-Dihydro-3-[(*m*-chlorophenyl)methylidene]-5*H*-1,4-benzodioxepin-5-one 25. Mp 101–102 °C (Found: C, 67.07; H, 4.04. $C_{16}H_{11}O_3Cl$ requires C, 67.02; H, 3.86%); ν_{max} (KBr)/cm^{-1} 1700 and 1660; δ_H (300 MHz; $CDCl_3$) 4.86 (2H, s, -CH_2), 5.96 (1H, s, =CH), 7.05–7.14 (2H, m, ArH), 7.24–7.32 (2H, m, ArH), 7.48–7.57 (3H, m, ArH) and 7.98 (1H, dd, *J* 8.1 and 1.8, ArH); δ_C (75 MHz; $CDCl_3$) 72.61, 117.31, 117.80, 120.46, 122.61, 127.51, 128.49, 129.35, 129.89, 134.27, 134.31, 134.47, 135.22, 144.43, 156.98 and 164.72; δ_C (75 MHz; $CDCl_3$; DEPT 135) 72.60 (inverted), 117.39, 120.54, 122.69, 127.59, 128.57, 129.44, 129.97, 134.39 and 135.30.

(*Z*)-2,3-Dihydro-3-[(*o*-methoxycarbonylphenyl)methylidene]-5*H*-1,4-benzodioxepin-5-one 26. Liquid (Found: C, 69.30; H, 4.73. $C_{18}H_{14}O_5$ requires C, 69.67; H, 4.54%); ν_{max} (neat)/cm^{-1} 1720, 1710 and 1660; δ_H (300 MHz; $CDCl_3$) 3.74 (3H, s, -CO_2Me), 4.81 (2H, s, -CH_2), 6.82 (1H, s, =CH), 6.97–7.04 (2H, m, ArH), 7.22–7.28 (1H, m, ArH), 7.39–7.45 (2H, m, ArH), 7.65–7.68 (1H, m, ArH) and 7.83–7.87 (2H, m, ArH); δ_C (75 MHz; $CDCl_3$) 52.49, 73.09, 117.89, 118.54, 120.97, 122.88, 128.36, 129.31, 130.99, 131.26, 132.59, 133.77, 134.44, 135.42, 144.07, 157.38, 165.64 and 167.70; δ_C (75 MHz; $CDCl_3$; DEPT 135) 52.21, 72.80 (inverted), 117.61, 120.68, 122.59, 128.08, 130.70, 130.98, 132.30, 134.15 and 135.13.

(*Z*)-2,3-Dihydro-3-[(2-thienyl)methylidene]-5*H*-1,4-benzodioxepin-5-one 27. Mp 95–96 °C (Found: C, 65.38; H, 4.27. $C_{14}H_{10}O_3S$ requires C, 65.09; H, 3.90%); ν_{max} (KBr)/cm^{-1} 1720 and 1660; δ_H (300 MHz; $CDCl_3$) 4.86 (2H, s, -CH_2), 6.34 (1H, s, =CH), 6.98–7.16 (4H, m, ArH), 7.35–7.50 (2H, m, ArH) and 7.92 (1H, dd, *J* 9.0 and 1.8, ArH); δ_C (75 MHz; $CDCl_3$) 72.68, 114.14, 118.94, 121.10, 123.10, 127.28, 128.83, 129.51, 134.36, 135.24, 135.40, 141.23, 157.03 and 165.52; δ_C (75 MHz; $CDCl_3$; DEPT 135) 72.39 (inverted), 113.85, 120.81, 122.83, 127.00, 128.54, 129.22, 134.08 and 135.12.

(*Z*)-2,3-Dihydro-3-[(*o*-acetoxyphenyl)methylidene]-5*H*-1,4-benzodioxepin-5-one 28. Mp 113–114 °C (Found: C, 69.50; H, 4.69. $C_{18}H_{14}O_5$ requires C, 69.60; H, 4.54%); ν_{max} (KBr)/cm^{-1} 1760, 1735 and 1670; δ_H (300 MHz; $CDCl_3$) 2.26 (3H, s, -CH_3), 4.87 (2H, s, -CH_2), 6.10 (1H, s, =CH), 7.05–7.14 (3H, m, ArH), 7.24–7.34 (2H, m, ArH), 7.48–7.54 (1H, m, ArH) and 7.97–8.01 (2H, m, ArH); δ_C (75 MHz; $CDCl_3$) 21.26, 72.98, 118.89, 118.12, 120.77, 122.79, 122.922, 125.44, 126.69, 129.79, 130.69, 134.75, 135.51, 145.08, 148.61, 157.34, 165.19 and 169.42; δ_C (75 MHz; $CDCl_3$; DEPT 135) 20.98, 72.69 (inverted), 111.60, 120.48, 122.50, 122.63, 126.40, 129.50, 130.40, 134.46 and 135.22.

(*Z*)-2,3-Dihydro-3-[(*p*-methoxyphenyl)methylidene]-5*H*-1,4-benzodioxepin-5-one 29. Mp 99–100 °C (Found: C, 72.51; H, 5.12. $C_{17}H_{14}O_4$ requires C, 72.32; H, 4.99%); ν_{max} (KBr)/cm^{-1} 1720 and 1660; δ_H (300 MHz; $CDCl_3$) 3.77 (3H, s, -OCH_3), 4.83 (2H, s, -CH_2), 5.96 (1H, s, =CH), 6.83–6.88 (2H, m, ArH), 7.01–7.09 (2H, m, ArH), 7.43–7.58 (3H, m, ArH) and 7.92 (1H, dd, *J* 8.1 and 1.8, ArH); δ_C (75 MHz; $CDCl_3$) 55.25, 73.14, 114.06, 118.47, 119.18, 120.58, 122.45, 125.14, 130.99, 133.97, 134.92, 141.37, 156.71, 159.71 and 165.68; δ_C (75 MHz; $CDCl_3$; DEPT 135) 55.38, 73.27 (inverted), 114.18, 119.31, 120.70, 122.58, 131.12, 134.10 and 135.04.

(*Z*)-2,3-Dihydro-3-[(2,4-dimethoxypyrimidin-5-yl)methylidene]-5*H*-1,4-benzodioxepin-5-one 30. Mp 146–147 °C (Found: C, 60.90; H, 4.34; N, 8.72. $C_{16}H_{14}N_2O_5$ requires C, 61.14; H, 4.48; N, 8.91%); ν_{max} (KBr)/cm^{-1} 1725 and 1660; δ_H (300 MHz; $CDCl_3$) 3.90 (3H, s, -OCH_3), 3.92 (3H, s, -OCH_3), 4.78 (2H, s, -CH_2), 6.08 (1H, s, =CH), 6.95–7.05 (2H, m, ArH), 7.39–7.45 (1H, m, ArH), 7.87–7.91 (1H, m, ArH) and 8.78 (1H, s, ArH); δ_C (75 MHz; $CDCl_3$) 54.26, 55.01, 72.27, 108.31, 108.38, 117.68, 120.46, 122.49, 134.31, 135.14, 143.88, 156.98, 158.57, 164.36, 164.69 and 167.86; δ_C (75 MHz; $CDCl_3$; DEPT 135) 54.34, 55.09, 72.35 (inverted), 108.46, 120.54, 122.57, 134.39, 135.22 and 158.65.

(*Z*)-2,3-Dihydro-3-[(*o*-iodophenyl)methylidene]-5*H*-1,4-benzodioxepin-5-one 31. Liquid (Found: C, 50.87; H, 3.10. $C_{16}H_{11}IO_3$ requires C, 50.81; H, 2.93%); ν_{max} (neat)/cm^{-1} 1720 and 1660; δ_H (300 MHz; $CDCl_3$) 4.88 (2H, s, -CH_2), 6.24 (1H, s, =CH), 6.94–7.13 (3H, m, ArH), 7.34–7.36 (1H, m, ArH), 7.47–7.50 (1H, m, ArH), 7.78–7.84 (2H, m, ArH) and 7.95 (1H, dd, *J* 7.8 and 1.6, ArH); δ_C (75 MHz; $CDCl_3$) 72.87, 100.71, 118.24, 120.89, 122.44, 122.99, 128.80, 130.15, 130.81, 134.61, 135.56, 135.84, 139.79, 144.86, 157.43 and 165.24; δ_C (75 MHz; $CDCl_3$;

DEPT 135) 72.58 (inverted), 120.60, 122.15, 122.770, 128.51, 129.86, 130.52, 134.32, 135.27 and 139.50.

(*Z*)-1,2,3,5-Tetrahydro-1-benzyl-3-(phenylmethylidene)-4,1-benzoxazepin-5-one 32. Mp 159–161 °C (Found: C, 80.80; H, 5.82; N, 3.88. $C_{23}H_{19}NO_2$ requires C, 80.91; H, 5.60; N, 4.10%); ν_{max} (KBr)/cm^{-1} 1720 and 1670; δ_H (300 MHz; $CDCl_3$) 3.97 (2H, s, -CH_2-C=C), 4.55 (2H, s, -NCH_2Ph), 5.68 (1H, s, =CH), 6.90–6.92 (2H, m, ArH), 7.23–7.36 (9H, m, ArH), 7.55–7.58 (2H, m, ArH) and 7.85–7.89 (1H, m, ArH); δ_C (75 MHz; $CDCl_3$) 56.19, 57.96 ($^3J_{CH}$ = 3.2 Hz), 114.57, 117.40, 119.94, 120.24, 127.36, 127.70, 127.73, 128.56, 128.92, 129.06, 133.21, 133.80, 134.02, 136.94, 145.46, 149.15 and 167.45; δ_C (75 MHz; $CDCl_3$; DEPT 135) 56.29 (inverted), 58.06 (inverted), 114.67, 117.50, 120.34, 127.46, 127.83, 129.02, 129.17, 133.90 and 134.12.

(*Z*)-1,2,3,5-Tetrahydro-1-benzyl-3-[(*p*-methoxyphenyl)methylidene]-4,1-benzoxazepin-5-one 33. Mp 113–115 °C (Found: C, 77.49; H, 5.92; N, 3.43. $C_{24}H_{21}NO_3$ requires C, 77.60; H, 5.69; N, 3.77%); ν_{max} (KBr)/cm^{-1} 1720 and 1670; δ_H (300 MHz; $CDCl_3$) 3.80 (3H, s, -OCH_3), 3.96 (2H, s, -CH_2-C=C), 4.54 (2H, s, -NCH_2Ph), 5.67 (1H, s, =CH), 6.85–6.93 (4H, m, ArH), 7.33–7.38 (6H, m, ArH), 7.51–7.54 (2H, m, ArH) and 7.83–7.86 (1H, m, ArH); δ_C (75 MHz; $CDCl_3$) 55.66, 56.54, 58.68, 114.37, 115.36, 117.91, 120.71, 120.97, 126.25, 127.80, 128.03, 129.26, 130.86, 133.92, 134.229, 137.74, 143.98, 139.44, 159.50 and 168.31; δ_C (75 MHz; $CDCl_3$; DEPT 135) 55.37, 56.25 (inverted), 58.39 (inverted), 114.08, 115.07, 117.61, 120.42, 127.51, 127.74, 128.97, 130.57, 133.63 and 134.00.

(*Z*)-1,2,3,5-Tetrahydro-1-benzyl-3-[(2,4-dimethoxypyrimidin-5-yl)methylidene]-4,1-benzoxazepin-5-one 34. Mp 114–115 °C (Found: C, 68.70; H, 5.18; N, 10.80. $C_{23}H_{21}N_3O_4$ requires C, 68.47; H, 5.24; N, 10.41%); ν_{max} (KBr)/cm^{-1} 1720 and 1660; δ_H (300 MHz; $CDCl_3$) 3.95 (2H, s, -CH_2-C=C), 3.98 (3H, s, -OCH_3), 3.99 (3H, s, -OCH_3), 4.58 (2H, s, -NCH_2Ph), 5.77 (1H, s, =CH), 6.88–6.93 (2H, m, ArH), 7.26–7.39 (6H, m, ArH), 7.90–7.93 (1H, m, ArH) and 8.84 (1H, s, ArH); δ_C (75 MHz; $CDCl_3$) 54.53, 55.29, 56.57, 57.63, 103.31, 109.31, 117.63, 119.36, 120.43, 127.60, 128.10, 129.31, 134.49, 134.54, 137.23, 146.81, 149.65, 158.35, 164.24, 167.17 and 167.96; δ_C (75 MHz; $CDCl_3$; DEPT 135) 54.25, 55.01, 56.29 (inverted), 57.34 (inverted), 103.02, 117.34, 120.15, 127.322, 127.81, 129.03, 134.25 and 158.06.

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14 An NOE experiment on **23** showed *ca.* 3.87% enhancement of the intensity of the –CH_2– peak on irradiation of the vinylic proton at δ 6.03.

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