

**Figure 1.** Structure of biologically active benzo [1, 4] oxazines **1**-**8.**

 **Figure 2.** Previous and present reports for the synthesis of substituted benzo[1,4]oxazines derivatives.

**Table 1** Optimization studya: Synthesis of 2-oxobenzo[1,4]oxazines **11a** by the reaction of 2,4-dioxo-4-phenylbutanoic acid **9a** and 2-aminophenol **10a**.



|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Entry** | **Solvent** | **Temp (°C)** | | **Method Ab** | | **Method Bc** | |
|  |  | |  | **Time (min)** | **Yieldd (%)** | **Time (min)** | **Yieldd (%)** |
| 1 | Isopropanol | | rt | 180 | 18 | -- | --- |
| 2 | Isopropanol | | 90 | 180 | 45 | 10 | 52 |
| 3 | Isopropanol | | 90 | 300 | 55 | 30 | 58 |
| 4 | DMF | | 90 | 180 | 51 | 30 | 64 |
| 5 | DMF | | 120 | 180 | 58 | 20 | 62 |
| 6 | DMF | | 150 | 120 | 50 | 15 | 69 |
| 7 | DMSO | | 150 | 180 | 59 | 10 | 77 |
| 8 | DMSO | | 150 | 240 | 61 | 5 | 51 |
| 9 | DMSO | | 150 | 300 | 67 | 15 | 72 |
| 10 | DMSO | | 180 | 120 | 65 | 2 | 56 |
| 11 | **Diethylene glycol** | | **150** | 180 | 61 | **5** | **94** |
| 12 | Diethylene glycol | | 150 | 120 | 54 | 3 | 80 |
| 13 | Diethylene glycol | | 150 | 300 | 67 | 7 | 93 |
| 14 | Diethylene glycol | | 170 | 180 | 64 | 2 | 85 |
| 15 | Diethylene glycol | | 160 | 180 | 65 | 2 | 82 |
| 16 | Diethylene glycol | | 170 | 300 | 63 | 5 | 81 |

aReaction conditions: **9a** (0.1 mmol), **10a** (0.1 mmol) in solvent (1.0 mL), 5-300 min, N2 atmosphere. bMethod A: Conventional heating; cMethod B: Microwave Irradiation; dIsolated yield after recrystalization/column chromatography.

**Scheme 1.** Microwave-assisted one-pot green synthesis of 2-oxobenzo[1,4]oxazines analogues (**11a-n**).a & b





aunless otherwise mentioned, all the reactions were carried out with substrates **9a-f** (0.2 mmol), substituted 2-aminophenols **10a-c** (0.2 mmol) in diethylene glycol (2.0 mL) at 150 °C temperature under microwave irradiation. bIsolated yield.

**Scheme 2.** Microwave-assisted one-pot synthesis of functionalized 2-oxoquino[1,4]oxalines **14a**-**h**.a





aunless otherwise mentioned, all the reactions were carried out with substrates **9a-g** or **12** (0.2 mmol) and 1,2-diamino benzene **13** (0.2 mmol) in diethylene glycol (2.0 mL) at 150 °C under microwave irradiation. bIsolated yield.

**Scheme 3.** Gram scale synthesis of **11a, 14c** and **14h.**



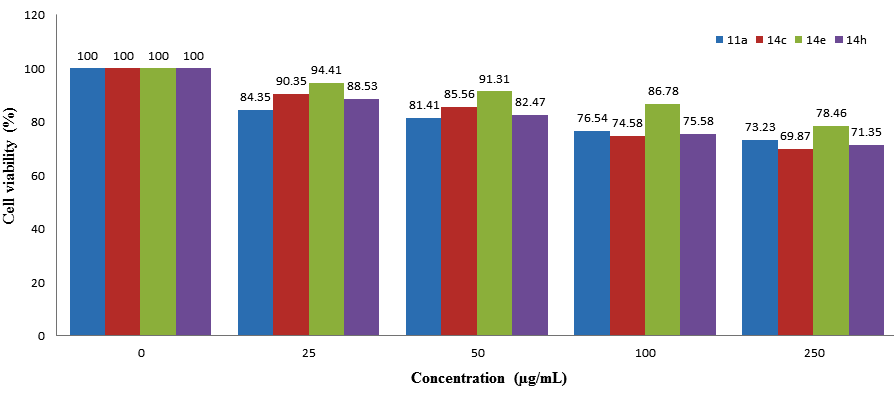
**Scheme 4.** Synthesis of Cephalandole A **16.**



**Table 2.** Antioxidant activity of synthesized compounds **11a-n, 14a-h** and **16** by DPPH radical scavenging and FRAP assay.25

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **S. No.** | **Compound No.** | **Antioxidant activitya** | | |
|  | | **DPPH assay**  **(IC50) (μg/mL)** | **FRAP assay**  **(C0.5FRAP μM)** |
| 1 | **11a** | | 10.20 ± 0.08 | 611.5 ± 23.2 |
| 2 | **11b** | | 19.70 ± 0.31 | 763.2 ± 38.1 |
| 3 | **11c** | | 29.80 ± 0.17 | 306.8 ± 25.8 |
| 4 | **11d** | | 65.32 ± 0.97 | ˃1000 |
| 5 | **11e** | | 25.02 ± 0.21 | 421.7 ± 37.9 |
| 6 | **11f** | | 23.45 ± 0.14 | 845.9 ± 35.1 |
| 7 | **11g** | | 67.40 ± 0.28 | ˃1000 |
| 8 | **11h** | | 78.50 ± 1.41 | 921.6 ± 29.6 |
| 9 | **11i** | | 34.42 ± 0.62 | 291.7 ± 23.1 |
| 10 | **11j** | | 42.98 ± 0.76 | ˃1000 |
| 11 | **11k** | | 21.27 ± 0.11 | 489.2 ± 18.5 |
| 12 | **11l** | | 56.12 ± 1.03 | 348.8 ± 31.4 |
| 13 | **11m** | | 15.70± 0.14 | 598.5 ± 23.4 |
| 14 | **11n** | | 78.76 ± 1.43 | ˃1000 |
| 15 | **14a** | | 27.36 ± 0.44 | 638.4 ± 37.6 |
| 16 | **14b** | | 91.36 ± 2.04 | ˃1000 |
| 17 | **14c** | | 9.89 ± 0.15 | 612.8 ± 17.8 |
| 18 | **14d** | | 28.24 ± 0.46 | 498.4 ± 22.4 |
| 19 | **14e** | | 8.97 ± 0.13 | 689.3 ± 30.0 |
| 20 | **14f** | | 43.54 ± 0.88 | 592.7 ± 41.6 |
| 21 | **14g** | | 38.97 ± 0.97 | ˃1000 |
| 22  23 | **14h** | | 14.27 ± 0.23 | 358.3 ± 17.7 |
| **16** | | 11.87± 0.14 | NDb |
| 24 | **Ascorbic acid** | | 4.57 | --- |
| 25 | **BHT** | | --- | 546.0 ± 13.6 |

aResults are expressed as a mean ± standard deviation (n = 3). DPPH radical scavenging activities are expressed as IC50 concentrations of the compounds (μg/mL) required to inhibit 50 % of the radicals and the maximum inhibition values; bND means not done.



**Figure 3.** Percentage cell viability test.

