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NOTE

Synthesis and Biological Activity of some New Quinazolines and Quinolines

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In view of the biological activities of quinazolines[1] and in continuation of our work on the synthesis of condensed quinazolines and quinolines, we report here the construction of the pyrimidine ring from 3-ethylamino-5,5-dimethylcyclohexenone (**2**) obtained from the condensation of ethylamine with 5,5-dimethylcyclohexandione (**1**). Treatment of **2** with cinnamoyl isothiocyanate resulted in cyclocondensation affording quinazolines of type **4**. The conversion of compound **2** to the corresponding quina-zoline (**4a**) presumably takes place via the intermediate **3**. Compound **4a** was also obtained from condensation of ethylamine with thioamide **5** that was in turn obtained from the reaction of **1** with cinnamoyl isothiocyanate. Compound **2** on reaction with anisoyl isothiocyanate in refluxing acetone afforded quinazoline **4b**. Addition of malononitrile to quinazoline **4a** afforded pyridoquinazoline **7** via the initial formation of Michael type product **6** which then underwent cycloaddition. Hydrazinolysis is quinazoline **4b** using hydrazine hydrate yielded pyrazoloquinzaolin **8**. Reaction of **2** with benzylidenemalonitrile (**9**) resulted in cycloaddition affording quinoline type **1** via the initial formation of Michael type adduct **10** followed by cyloaddition.

Compounds **2**, **4a,b**, **7**, **8** and **11** were tested *in vitro* for biological activity[2,3] against a variety of bacteria such as *Salmonella* Spp., *Proteus* Spp., *Bacillus subtilis* and *Staphylococcus albus*. The activity was compared with that of penicillin G procaine (reference) at concentration 0.02 g dm^{-3}, which indicated that the compounds have little significant activity.

Experimental

M.ps. are uncorrected. Ir spectra (KBr) were recorded on a Pye-Unicam Sp-1100 spectrophotometer and ^1H nmr spectra on a Varian A 60 (EM 360 L) spectrometer. Microanalyses were carried out at Microanalytical Centre, Cairo University.

Ethylaminocyclohexanone (**2**) : A mixture of **1** (0.01 mol) and $C_2H_5NH_2$ (0.01 mol) in methanol (10 ml) was refluxed for 1 h. The resulting solid obtained upon evaporation and cooling was crystallised from aqueous methanol as colourless crystals (80%), m.p. 50–52°, ν_{max} 3 400–3 200 (NH), 1 645 cm^{-1} (CO).

Thioamide (**5**) : A mixture of cinnamoyl isothiocyanate[3] (0.01 mol) and **1** (0.01 mol) in acetone (15 ml) was refluxed for 0.5 h, then cooled and the resulting yellow solid was crystallised from methanol, (60%), m.p. 128–30°, ν_{max} 3400–3200 (NH), 1660, 1655, 1640 cm^{-1} (CO).

2-Substituted-quinazolinone (**4**) : (a) A mixture of appropriate isothiocyanate (0.01 mol) and enaminone (**2**; 0.01 mol) in acetone (15 ml) was refluxed for 2 h, then cooled and the resulting solid was crystallised from methanol. (b) A mixture of **5** (0.01 mol) and $C_2H_5NH_2$ (0.01 mol) in ethanol (10 ml) was refluxed for 1 h, then cooled and the yellow solid was crystallised from aqueous methanol (yields 70–80%); **4a**, m.p. 218–20°; **4b**, 200–01°, ν_{max} 1 900 (C=S), 1 665 cm^{-1} (CO), δ ($CDCl_3$) 1.3, 1.6, 1.8 (9H, s, 3 × CH_3), 1.9, 2.0, 2.3 (6H, m, 3 × CH_2), 3.9 (3H, s, CH_3), 6.2–7.5 (4H, m, ArH).

Pyridoquinazolinone (**7**) : A mixture of **4a** (0.01 mol), malononitrile (0.01 mol) and TEA (3 drops) in ethanol (10 ml) was refluxed for 0.5 h. The solid obtained upon cooling was crystallised from metharol as colourless crystals, m.p. 222–24°, ν_{max} 3 400–3 100 (NH_2), 2 225(CN), 1 410 (CS), 1 465 cm^{-1} (CO), δ 1.2, 1.4, 1.6 (9H, s, 3 × CH_3), 2.0 2.1, 2.2 (6H, m, 3 × CH_2), 5.6 (1H, s, 4H pyridine).

Pyrazoloquinazolinone (**8**) : A mixture of **4b** (0.01 mol) and $NH_2NH_2.H_2O$ (0.015 mol) in methanol (10 ml) was

refluxed for 1 h. The colourless solid obtained upon cooling was crystallised from methanol as colourless crystals (50%), m.p. 208–10°, ν_{max} 1 590 cm^{-1} (C=N), δ 1.2, 1.3, 1.5 (9H, s, 3 × CH_3), 2.0, 2.2, 2.3 (6H, m, 3 × CH_2), 6.1–7.2 (4H, m, ArH).

2-Amino-3-cyano-1-ethylquinoline (**11**) : A mixture of **2** (0.01 mol), **9** (0.01 mol) and TEA (3 drops) in ethanol (10 ml) was refluxed for 0.5 h. The solid obtained upon cooling was crystallised from methanol as colourless crystals (60%), m.p. 207–09°, ν_{max} 3 400–3 225 (NH_2), 2 225 (CN), 1 655 cm^{-1} (CO), δ 1.1, 1.2, 1.4 (9H, s, 3 × CH_3), 1.9, 2.1, 2.3 (6H, m, 3 × CH_2), 5.0 (2H, s, NH_2), 5.4 (1H, s, 4H pyridine), 6.2–7.0 (5H, m, ArH).

References

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