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Research Paper

Synthesis of Benzodiazepino / Oxazepino / Thiazepino Fused Some Novel Pyrazinocarbazoles and Azacarbazoles

Chemistry

KEYWORDS : Carbazoles, azacarbazoles, quinoxalines, pyrazoles, isoxazoles, pyrimidines, benzodiazepines, benzoxazepines, benzothiazepines.

Neelam K. Yadav — Department of Chemistry, Banasthali Vidyapith, Banasthali (Rajasthan)-304 022, India

D. Kishore — Department of Chemistry, Banasthali Vidyapith, Banasthali (Rajasthan)-304 022, India

Bhawani Singh — Department of Pure & Applied Chemistry, University of Kota, Kota (Rajasthan)-324 005, India

ABSTRACT

Carbazoles, azacarbazoles, quinoxalines, pyrazoles, isoxazoles, pyrimidines, benzodiazepines, benzoxazepines, benzothiazepines possess a wide spectrum of pharmacological profile. Therefore, quinoxalino condensed five-, six- and seven-membered heterocycles have been synthesized with enhanced biological activity. In the present work, benzodiazepino / oxazepino / thiazepino fused pyrazinocarbazoles and azacarbazoles were prepared. The structures of all the compounds have been established on the basis of their elemental analysis and spectral (IR, 1H NMR and MS) data.

Introduction:

Ubiquitous presence of carbazoles and azacarbazoles in a vast array of bio-active molecules (such as ellipticine and olivacine) has stimulated intense research efforts to synthesize their structural analogues where different constitution and chemical reactivity could allow them to be used as novel chemotherapeutic agents. Quinoxaline derivatives exhibit a wide variety of biological activities. It has been reported that some quinoxalines demonstrated various types of biological activities such as antibacterial[1], anti-fungal[2] anti-viral[3-4], anti-depressant[5], anti-inflammatory [6], anti-tubercular, anti-cancer and anti-tumor activities[7-8], *etc.*

The enol ethers, chalcones, oxoketenedithio acetals and dimethyl aminomethylene ketones offer unprecedented opportunities to a chemist for the synthesis of a wide variety of heterocyclic materials. The ubiquitous presence of carbazoles, azacarbazoles, quinoxaline, pyrazoles and isoxazoles in a wide array of molecules exhibiting impressive biological properties has stimulated interest in the reviews, on the synthesis of their structural analogues where different constitution and biological activity could allow them to be used as novel chemotherapeutic agents. This aroused our interest in the synthesis of hetero ring fused pyrazoles and isoxazoles from enol ethers, chalcones, oxoketenedithioacetals and dimethyl aminomethylene ketones derived from the quinoxalino condensed carbazole and azacarbazole derivatives.

Azepines (1,5-Benzodiazepines / oxazepines / thiazepines) are versatile pharmacophoric scaffolds that represent a class of heterocycles which exhibits a wide range of biological applications. Many benzodiazepines, benzoxazepines and benzothiazepines are widely used as anticonvulsant, anti-anxiety, analgesic, sedative, anti-depressive, hypnotic and neuroleptic agents. Some heterocycles containing benzodiazepine moiety have been reported to possess anti-inflammatory, anti-viral, anti-tumour activities[9-11]. The use of 1,5-benzodiazepines have been extended to several diseases such as cancer, viral infection and cardiovascular disorders. Other than their biological importance, benzodiazepines are valuable synthons in the preparation of fused ring compounds, such as triazolo, tetrazolo, quinoxalino and pyrimido-benzodiazepines. As a result of this, research in this area is very active and is directed towards the synthesis of compounds with enhanced pharmacological activity.

Experimental section:

Preparation of 7-Phenyl-6,8,9,16- tetrahydro [1,5] benzodiazepino [7,8-*a*] pyrazino [2,3-h] carbazole-12,13-diol (12a)

A mixture of *o*-phenylenediamine (0.54g, 0.005mole) and **10a** (2.15g, 0.005mole) was refluxed at 150°C in DMF (5ml) for 17 hours. The reaction mixture was cooled to room temperature and solid was collected by filtration and washed thoroughly with water. Recrystallization from aqueous DMF gave **12a** with m.p. 272-274°C and yield of 0.36g (70%). Similarly, the other compounds were prepared with the reactions of *o*-phenylenediamine, *o*-aminophenol and *o*-aminothiophenol from **9a-b** and **10a-b** respectively. Compound **12a:** ^{1}H NMR (DMSO-d_6) δ ppm = 11.87 (1H, s, NH), 11.63 (1H, s, NH), 8.07 (2H, s, CH), 7.40-7.27 (5H, m, ArH), 7.23-6.77 (4H, m, ArH), 4.0 (1H, s, NH), 3.9 (1H, d, CH), 2.68 (2H, t, CH_2), 2.1 (1H, q, CH), 1.5 (2H, q, CH_2); IR (KBr) cm^{-1}= 3280 (NH str.), 2960 (C-H str. ArH), 1590 (C=N str.), 1450, 1540 (C=C str.), 1265(C-H str.).

Results and discussion:

The reaction of **8(a-b)** with ethyl formate in the presence of a base furnished **9(a-b)** and its reaction with aromatic aldehydes generated **10(a-b)**[12]. Corresponding [1,5]-benzodiazepine [1,5]-benzoxazepine and [1,5]-benzothiazepine derivatives **(11a-b)** and **12(a-b)** of carbazoles and azacarbazoles were prepared from enol ethers **(9a-b)** and chalcones **(10a-b)** with reactions of *o*-phenylenediamine, *o*-aminophenol and *o*-aminothiophenol in DMF. ^{1}H NMR spectrum of compound **12a** in DMSO-d_6 displayed signals for the presence protons. A total five singlets, two triplets and one multiplet were found to be present in ^{1}H NMR spectrum of compound **12a**. A singlet for 2H each at δ11.87 was assigned to OH group of quinoxaline ring. Another singlet for 2H at δ8.07 was assigned to protons of benzene nucleus of indole ring. Other singlet at 1H at δ11.34 was assigned to NH group of indole ring. One singlet of 1H at δ9.8 of NH and one singlet of 1H at δ3.1 of CH of azepine ring appeared. Two triplets at δ 2.93 and δ 2.87 were assigned to the CH_2 protons of cyclohexane ring. One multiplet at δ 7.93-8.23 was assigned to the protons of benzene nucleus attached to azepine ring.

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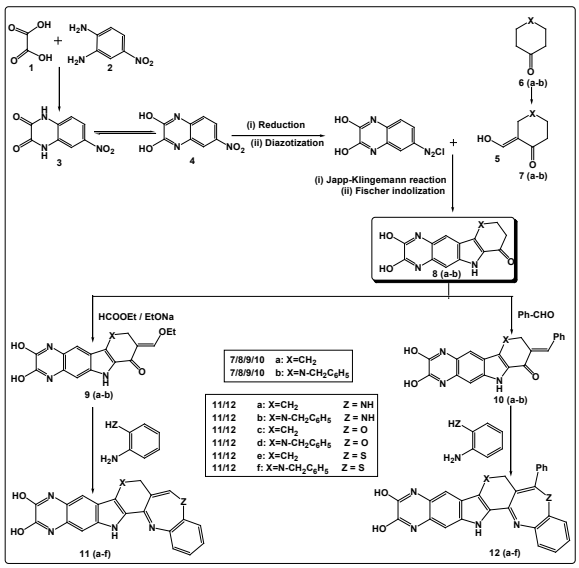

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