Pakistan J. Sci. Ind. Res., Vol. 29, No. 4, August 1986

SYNTHESIS OF SOME POTENTIALLY ANTICANCER SCHIFF-BASES FROM FURO-COUMARINS AND CHROMONES

O.M. Abdel-Hafez, E.A.M. El-Khrisy and E.A. Abu-Mustafa

Natural Products Laboratory, National Research Centre, Dokki, Cairo, Egypt

(Received November 13, 1985; revised April 3, 1986)

Treatment of 5-amino derivatives of 9-methoxypsoralene, 9-ethoxypsoralene and norvisnagin with aromatic aldehydes, *viz.* benzaldehyde, 2-chlorobenzaldehyde, 4-N, N-dimethylaminobenzaldehyde and 4-nitrobenzaldehyde afforded the corresponding Schiff-bases (Ib-e, IIb-e and IIIb-e), respectively. Treatment of Ib, IIb and IIIb with mercaptoacetic acid, instead of cyclo-addition of thiol group to Schiff-bases to form thiazolidones gave starting amines Ia, IIa and IIIa, respectively.

INTRODUCTION

It has been reported that the biological activity of Schiff bases might be attributed to the azo methine linkage [1]. This observation and the essential role of azo methine linkage in certain biological reactions [2] have prompted these authors to synthesise Some Schiff bases containing the well known biologically active furo-coumarins and chromones [3-5].

RESULTS AND DISCUSSION

5-Amino-9-methoxypsoralene (Ia) selected as a starting material was obtained by the reduction of 5-nitro-9-methoxypsoralene by the method of Brokke and Christensen [6]. The preparation of Schiff bases involved the condensation of 5-amino-9-methoxypsoralene (Ia) with different aromatic aldehydes, viz. benzaldehyde, 2-chlorobenzaldehyde, 4-*N*, *N*-dimethylaminobenzaldehyde and 4-nitrobenzaldehyde. The condensation was accomplished by refluxing the amino derivative with an appropriate aldehyde at definite time. The psoralene Schiff bases, deposited as crystalline solids on cooling, were collected and recrystallised from ethanol. The following compounds were prepared: 5-*N*-benzal-9-methoxypsoralene (Ib), 5-*N*-(2-chlorobenzal)-9-methoxypsoralene (Ic), 5-*N*-(4-N, N-dimethylaminobenzal)-9-methoxypsoralene (Id) and 5-*N*-(4-nitrobenzal)-9-methoxypsoralene (Ie), respectively. The ^{1}H NMR spectrum of Id shows signals at δ 3.09 (6H, s, -N:$(CH_3)_2$); δ 4.23 (3H, s, $-OCH_3$); δ 6.25 and δ 8.85 (2H, d, α-pyrone protons on C_3 and C_4, $J_{3,7}$ = 10 Hz); δ 6.85 and δ 7.63 (2H, d, furan protons, on C_6 and C_7, $J_{6,7}$ = 2.5 Hz); δ 8.45 (1H, s, -N = CH-) and δ 6.74 and δ 7.80 (4H, d, aromatic protons, $J_{o,m}$ = 9 Hz).

5-Amino-9-ethoxypsoralene (IIa) was prepared in a manner similar to a reported method [6]. IIa condensed with appropriate aldehydes in ethanolic solution yielded the following compounds: 5-*N*-benzal-9-ethoxypsoralene (IIb), 5-*N*-(2-chlorobenzal)-9-ethoxypsoralene (IIc), 5-*N*-(4-*N*, *N*-dimethylaminobenzal)-9-ethoxypsoralene (IId) and 5-*N*-(4-nitrobenzal)-9-ethoxypsoralene (IIe) respectively.

The reaction of benzaldehyde, 2-chlorobenzaldehyde, 4-*N*, *N*-dimethylaminobenzaldehyde and 4-nitrobenzaldehyde with 5-amino-norvisnagin [7] (IIIa) afforded 5-*N*-benzal-norvisnagin (IIIb), 5-N-(2-chlorobenzal)-norvisnagin (IIIc), 5-(4-*N*, *N*-dimethylaminobenzal)-norvisnagin (IIId) and 5-*N*-(4-niorobenzal)-norvisnagin (IIIe) respectively. The ^{1}H NMR of compound IIIb shows signals at δ 2.43 (3H, s, $-CH_3$); δ 6.09 (1H, s, vinylic porton on C_3); δ 6.99 and δ 7.60 (2H, d, furan protons on C_6 and C_7, $J_{6,7}$ = 2.2 Hz); δ 9.22 (1H, s, -OH); δ 8.01 (1H, s, -N = CH-) and δ 7.50 – 7.98 (5H, m, aromatic protons).

The reactions of Ib, IIb and IIIb with mercaptoacetic acid afforded the starting materials Ia, IIa and IIIa. The

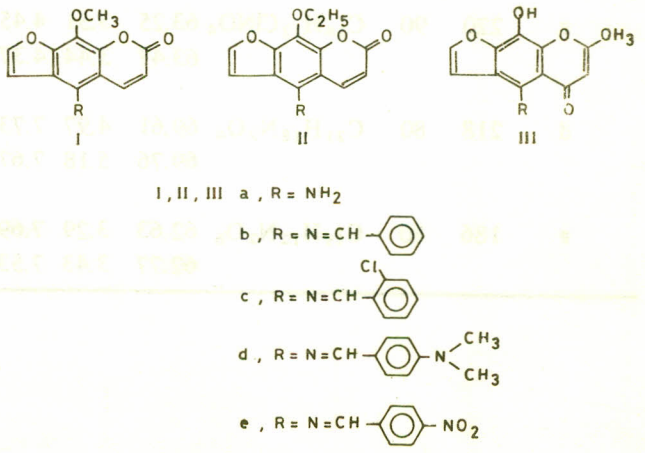

Table 1. Physical data for prepared compounds.

Compound	M.P.	Yield (%)		Analysis Calc./Found C	H	N
Ib	210	80	$C_{19}H_{13}NO_4$	71.47	4.08	4.39
				70.99	4.28	5.01
c	206	85	$C_{19}H_{12}ClNO_4$	64.45	3.39	3.96
				64.75	3.09	4.33
d	189	75	$C_{21}H_{18}N_2O_4$	69.61	5.52	8.58
				69.74	5.22	8.89
e	200	65	$C_{19}H_{12}N_2O_6$	62.64	3.30	7.69
				62.02	3.63	7.35
IIa	182	70	$C_{13}H_{11}NO_4$	63.63	4.51	5.70
				63.85	4.63	5.83
b	162	80	$C_{20}H_{15}NO_4$	72.07	4.50	4.20
				71.98	4.87	4.14
c	196	95	$C_{19}H_{15}ClNO_4$	63.96	4.21	3.93
				64.31	4.17	4.01
d	182	85	$C_{22}H_{20}N_2O_4$	70.21	5.31	7.46
				70.30	5.33	7.62
e	308	95	$C_{20}H_{14}N_2O_6$	63.49	3.70	7.41
				63.23	4.02	7.24
IIIb	170	70	$C_{19}H_{13}NO_4$	71.47	4.07	4.39
				71.03	4.28	4.48
c	220	90	$C_{18}H_{12}ClNO_4$	63.25	3.51	4.45
				63.47	3.44	4.37
d	218	80	$C_{21}H_{18}N_2O_4$	69.61	4.97	7.73
				69.76	5.18	7.67
e	186	80	$C_{19}H_{12}N_2O_6$	62.63	3.29	7.69
				62.77	3.43	7.53

Schiff bases were hydrolysed in the presence of mercaptoacetic acid instead of cycloaddition of the thiol group to the Schiff bases to give some thiazolidones [8].

The ir spectra of the prepared compounds agreed with the assigned structures. For psoralenes it showed a band for C = O at 1720 cm^{-1}. Chromones showed a bands at 1655 cm^{-1} (C = O) and a broad band at 3400 cm^{-1} (OH groups). Some of the physical data for the prepared compounds are given in Table 1.

EXPERIMENTAL

M.p.s are uncorrected. The ^1H NMR spectra were run in DMSO and TMS as reference at the Ilinois University, Chicago, Program for Collaborative Research in the Pharmaceutical Sciences, USA. The prepared compounds were analysed for C, H and N, and the microanalytical data are in full agreement with the suggested structures. 4-Amino-9-methoxypsoralene (Ia) and 5-amino-norvisnagin (IIIa) were prepared according to a reported method.

General procedure for the preparation of Schiff bases (Ib-e, IIb-e and IIIb-e: A mixture of equimolecular quantities of amino derivatives and the aldehyde in 50 ml methanol was refluxed for 10 hr. The reaction mixture was concentrated after cooling, the deposited product was filtered off and recrystallised from ethanol. In the case of reaction of benzaldehyde and the amino derivative, piperidine (1 ml) was added.

REFERENCES

1. S.K. Chakraborti and B. Kumar De, J. Indian Chem. Soc., **50**, 137 (1973).
2. E. Metzler, M. Ikawa and E.E. Snell, J. Am. Chem. Soc., **76**, 648 (1954).
3. T.O. Soine, J. Pharm. Sci., **53**, 231 (1964).
4. M. Hesse and H. Schimd, Moderne Methoden der Pflanzenanalyse, **6**, 109 (1963).
5. L. Musafo and J. Rodighiero, Experientia, **18**, 153 (1962).
6. M.E. Brokke and B.E. Christensen, J. Org. Chem., **23**, 589 (1958).
7. A Schonberg and N. Badran, J. Am. Chem. Soc., **73**, 2960 (1951).
8. A.K. El-Shafei, Kh. M. Hassan and H.S. Kashef, J. Indian Chem. Soc., **54**, 743 (1977).