HETEROCYCLES 4[1a,b,c]: SYNTHESIS OF 2,2-DIMETHYL-2H-PYRANO[2,3-a]CARBAZOLES

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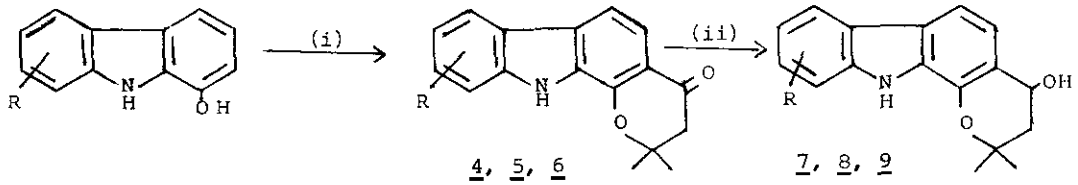
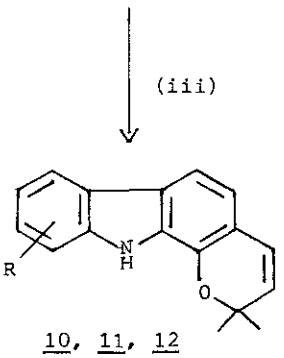
Abstract – Condensation of methyl 1-hydroxy-carbazolecarboxylates 1, 2 and 3 with 3,3-dimethylacrylic acid in presence of zinc chloride-phosphorous oxychloride ($ZnCl_2$-$POCl_3$) afforded corresponding 3,4-dihydro-2,2-dimethyl-4-oxo-2H-pyrans, 4,5 and 6 respectively. These on sodium borohydride ($NaBH_4$) reduction followed by dehydration using p-toluenesulphonyl chloride-pyridine yielded 2,2-dimethyl-2H-pyrano[2,3-a]carbazoles, 10, 11 and 12 respectively.

Pyranocarbazoles with carbomethoxy group are so far not known, eventhough there is a possibility of the formation of these compounds from Mukonine[2] or Koeninbine[3a,b]. Usually all naturally occuring pyranocarbazoles are 2,2-dimethyl-2H-pyrano[3,2-a]carbazoles[2-8]. In literature, Koenimbine was synthesised from 2,6-dihydroxy-3-methylcarbazole and 3-hydroxyisovaleraldehyde dimethyl acetal[9]. A simple pyrano-[3,2-a]carbazole was prepared from Fries rearrangement of 2-(3',3'-dimethylacryl-oyl)oxy-3-methylcarbazole followed by cyclization, reduction and dehydration[10]. Girimbine was synthesised from sodium salt of 1-formyl-2-hydroxy-3-methylcarbazole and allyltriphenyl phosphonium chloride by Narasimhan et al[11]. We report here the synthesis of 2,2-dimethyl-2H-pyrano[2,3-a]carbomethoxycarbazoles 10, 11 and 12. The synthons for these products are methyl 1-hydroxycarbazolecarboxylates, which were prepared recently from various diazotised aminobenzoic acid and 2-hydroxymethylene cyclohexanone followed by cyclization, esterification and aromatisation[1b].

In the present study, methyl 8-hydroxycarbazolecarboxylates, 1, 2 and 3 were condensed with 3,3-dimethylacrylic acid in presence of $ZnCl_2$-$POCl_3$ to give corresponding 3,4-dihydro-2,2-dimethyl-4-oxo-2H-pyrans 4, 5 and 6, respectively. These dihydro-4-oxopyranocarbazoles, 4, 5 and 6 were reduced by using $NaBH_4$ in methanol to corresponding 3,4-dihydro-2,2-dimethyl-4-hydroxy-2H-pyrans, 7, 8 and 9, respectively.

The dehydration of methyl 3,4-dihydro-2,2-dimethyl-4-hydroxy-2H,11H-pyrano[2,3-a] carbazole-10-carboxylate, 7, was attempted by tosylation followed by dehydrotosylation in refluxing pyridine. It was found that tosyl derivatives were very difficult to isolate in pure state and hence, it was decided to carry out the dehydration reaction without isolating the tosyl derivative. Thus, the procedure for tosylation was modified and conditions were optimised, such that, the dehydrated product is obtained in one step. Thus, 7 was dehydrated by using p-tolenesulphonyl chloride-pyridine to dehydro product, 10. Its IR spectrum showed the presence of NH(3360 cm^{-1}), an ester carbonyl (1700 cm^{-1}) and a carbon carbon double bond (1630 cm^{-1}). Its ^{1}H NMR spectrum showed the presence of two olefinic protons, as a clear AB system, each with a coupling constant of 10Hz characteristic of cis protons on olefinic carbon atoms. The olefinic proton nearer to the benzene ring appeared substantially downfield at δ5.53. The other olefinic proton signal appeared at δ5.65. Based on all these details and elemental analysis, the compound was assigned the structure, 10[12].





10, 11, 12

1 R = 1-$COOCH_3$

2 R = 2-$COOCH_3$

3 R = 3-$COOCH_3$

4, 7, 10 R = 10-$COOCH_3$ (i) $ZnCl_2$-$POCl_3$

5, 8, 11 R = 9-$COOCH_3$ (ii) $NaBH_4/CH_3OH$

6, 9, 12 R = 8-$COOCH_3$ (iii) TsCl – Pyridine

Similarly 2,2-dimethyl-2H-pyrano[2,3-a]carbazoles, 11 and 12, were prepared and confirmed their structures by spectral data and elemental analysis.

TABLE I

+Compound No	mp °C	Yield %	ν_{max} cm^{-1}	Molecular formula	Analysis Calcd	Found
4	193–195	75	3450	$C_{19}H_{17}NO_4$	C 70.58	70.53
			1600		H 5.30	5.58
			1675		N 4.33	4.38
5	223–225	67	3390	$C_{19}H_{17}NO_4$	C 70.58	70.48
			1690		H 5.30	5.30
			1625		N 4.33	4.20
6	190–191	90	3350	$C_{19}H_{17}NO_4$	C 70.58	70.38
			1700		H 5.30	5.56
			1675		N 4.33	4.37
7	146–147	91	3450	$C_{19}H_{19}NO_4$	C 70.15	70.01
			3200		H 5.84	5.90
			1700		N 4.30	4.33
8	228–229	85	3500	$C_{19}H_{19}NO_4$	C 70.15	70.30
			3360		H 5.84	5.70
			1690		N 4.30	4.20
9	135–136	88	3500	$C_{19}H_{19}NO_4$	C 70.15	70.25
			3200		H 5.84	5.60
			1690		N 4.30	4.20
10	193–194	55	3360	$C_{19}H_{17}NO_3$	C 74.25	74.40
			1700		H 5.58	5.40
			1630		N 4.56	4.30
11	191–192	64	3380	$C_{19}H_{17}NO_3$	C 74.25	74.10
			1700		H 5.58	5.37
			1625		N 4.56	4.29
12	115–116	69	3300	$C_{19}H_{17}NO_3$	C 74.25	74.25
			1690		H 5.58	5.40
			1620		N 4.56	4.30

+ All compounds were crystallised from Petroleum ether–ethyl acetate mixture

TABLE II

Compound No	UV, λ_{max} in nm (log ϵ)
10	198(3.52), 247(3.64) and 317(3.20)
11	196(3.25), 248(3.52) and 326(3.34)
12	195(3.38), 255(3.12) and 310(3.40)

TABLE III

Compound No	^{1}H-NMR ($CDCl_3$, δ (ppm)), (100 MHz)
4	1.62(s,6H,$(CH_3)_2C_2<$), 2.88(s,2H,C_3-methylene), 4.1(s,3H,C_{10}-$COOCH_3$), 7.3(m,1H,C_8-H), 7.65(d,1H,C_5-H,J=6Hz), 7.82(d,1H,C_6-H, J=6Hz), 8.14(d,1H,C_7-H,J=8Hz), 8.30(d,1H,C_9-H,J=8Hz), 10.16 (broad s,1H,D_2O exchangeable).
5	1.60(s,6H,$(CH_3)_2C_2<$), 2.95(s,2H,C_3-methylene), 3.95(s,3H,C_9-$COOCH_3$), 7.2(s,1H,C_{10}-H), 7.56(d,1H,C_6-H,J=8Hz), 7.86(d,1H,C_5-H, J=8Hz),8.3(m,2H,C_7-H and C_8-H), 12.2(s,1H,-NH, D_2O exchangeable)
6	1.60(s,6H,$(CH_3)_2C_2<$), 2.90(s,2H,C_3-methylene), 4.0(s,3H,C_8-$COOCH_3$), 7.52(d,1H,C_{10}-H,J=8Hz), 7.7(d,1H,C_5-H,J=6Hz), 7.82(d, 1H,C_6-H,J=6Hz), 8.2(d,1H,C_9-H,J=8Hz), 8.64(broad s,1H,-NH,D_2O exchangeable), 8.83(s,1H,C_7-H).
10	1.57(s,6H,$(CH_3)_2C_2<$), 4.09(s,3H,C_{10}-$COOCH_3$),5.65(d,1H,C_3-H, J=10Hz), 6.53(d,1H,C_4-H,J=10Hz), 6.95(d,1H,C_5-H,J=6Hz), 7.26(m, 1H,C_8-H), 7.59(d,1H,C_6-H,J=6Hz),8.11(d,1H,C_7-H,J=8Hz), 8.24(d, 1H,C_9-H,J=8Hz), 9.45(broad s,1H,-NH,D_2O exchangeable).
11	1.57(s,6H,$(CH_3)_2C_2<$), 4.00(s,3H,C_9-$COOCH_3$), 5.67(d,1H,C_3-H, J=10Hz), 6.53(d,1H,C_4-H,J=10Hz), 6.95(d,1H,C_5-H,J=6Hz), 7.61(d, 1H,C_6-H,J=6Hz), 8.00(m,2H,C_7-H and C_8-H), 8.18(s,1H,C_{10}-H),8.35 (broad s,1H,-NH,D_2O exchangeable).
12	1.58(s,6H,$(CH_3)_2C_2<$), 4.1(s,3H,C_8-$COOCH_3$), 5.65(d,1H,C_3-H, J=10Hz), 6.53(d,1H,C_4-H,J=10Hz), 6.95(d,1H,J=6Hz), 7.4(d,1H,C_5-H,J=6Hz), 7.6(d,1H,C_6-H,J=6Hz), 8.14(d,1H,C_9-H,J=8Hz),8.4(s,1H, NH,D_2O exchangeable), 8.76(s,1H,C_7-H).

EXPERIMENTAL

General Procedures

Condensation of methyl esters of 1-hydroxycarbazoles with 3,3-dimethylacrylic acid

Methyl 8-hydroxycarbazolecarboxylate (1.0 g, 0.004 mole) was condensed with 3,3-dimethylacrylic acid (0.50 g, 0.005 mole) in the presence of freshly fused Zinc chloride (3 g) and phosphorous oxychloride (4 ml). The reaction mixture was kept under calcium chloride guard tube for 24 h. The reaction mixture was then decomposed by pouring it over crushed ice. The solid obtained was adsorbed on silica-gel and chromatographed using petroleum ether-ethyl acetate (4:1). The product obtained by removal of solvent, was crystallised from the suitable solvent mixture.

Reduction of methyl esters of 3,4 dihydro-2,2-dimethyl-4-oxopyranocarbazoles with sodium borohydride

Methyl 3,4-dihydro-2,2-dimethyl-4-oxo-2H,11H-pyrano[2,3-a]carbazolecarboxylate (0.35g, 0.001 mole) was dissolved in methanol (20 ml) and the solution cooled in ice bath to 10°C. Sodium borohydride (0.05 g, 0.002 mole) was added in 2 portions at 0.5 h intervals. The reaction mixture was stirred at room temperature for 3 h. The solution was concentrated and diluted with water. The mixture was extracted with ether. The ether solution was washed with water and dried. The compound obtained was crystallised from petroleum ether-ethyl acetate (1:4).

Dehydration of methyl esters of 3,4-dihydro-2,2-dimethyl-4-hydroxy-2H-pyranocarbazoles with p-toluenesulphonyl chloride and pyridine.

Methyl 3,4-dihydro-2,2-dimethyl-4-hydroxy-2H, 11H-pyrano[2,3-a]carbazole carboxylate (0.1 g, 0.003 mole), p-toluenesulphonyl chloride (0.01 g) and pyridine (10 ml)were refluxed for about 24 h. The reaction mixture was then cooled and poured over crushed ice. The resulting solid was purified by passing through a silica gel column and eluting with petroleum ether ethyl acetate (1:1).

REFERENCES

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1.a) D. Sowmithran and K.J. Rajendra Prasad, Synthesis, 1985, 5, 545.

b) D. Sowmithran and K.J. Rajendra Prasad, Heterocycles, 1986, 24(3), 711.

c) D. Sowmithran and K.J. Rajendra Prasad, Indian J. Chem., (In press)

2. D.P. Chakraborty, K.C. Das, B.P. Das and B.K. Chowdhury, Trans. Bose Res. Inst., 1975, 38, 3; Chem. Abstr., 1977, 86, 510292.

3.a) N.S. Narasimhan, M.V. Paradkar and V.P. Chitguppi, Tet. Lett., 1968, 5502.

b) N.S. Narasimhan, M.V. Paradkar and S.L. Kelkar, Indian J. Chem., 1970, 8(B), 473.

4. D.P. Chakraborty, B.K. Barman and P.K. Bose, Science and Cult.(India), 1964 30, 445.

5. D.P. Chakraborty, P. Bhattacharya, A. Islam and S. Roy, Chem. and Ind.(London), 1974, 303.

6. D.P. Chakraborty and K.C. Das, Chem. Commun., 1968, 967.

7. S.P. Kureel, R.S. Kapil and S.P. Popli, Experientia, 1969, 25, 790.

8. I. Mester and J. Reisch, Ann. Chem., 1977, 1725.

9. S.P. Kureel, R.S. Kapil and S.P. Popli, Chem and Ind.(London), 1970, 1267.

10. D.P. Chakraborty and A. Islam, J. Indian Chem. Soc., 1971, 48, 91.

11. N.S. Narasimhan, M.V. Paradkar and A.M. Gokhale, Tet. Lett., 1970, 1665.

12. D. Sowmithran, Studies in Heterocycles, Ph.D. Thesis, IIT, Bombay (1983).

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