Chemistry of Natural Compounds, Vol. 30, No. 5, 1994

SYNTHETIC AND MODIFIED ISOFLAVONOIDS XV. INTERACTION OF SYNTHETIC ANALOGS OF ISOFLAVONES WITH HYDRAZINE HYDRATE AND ITS DERIVATIVES

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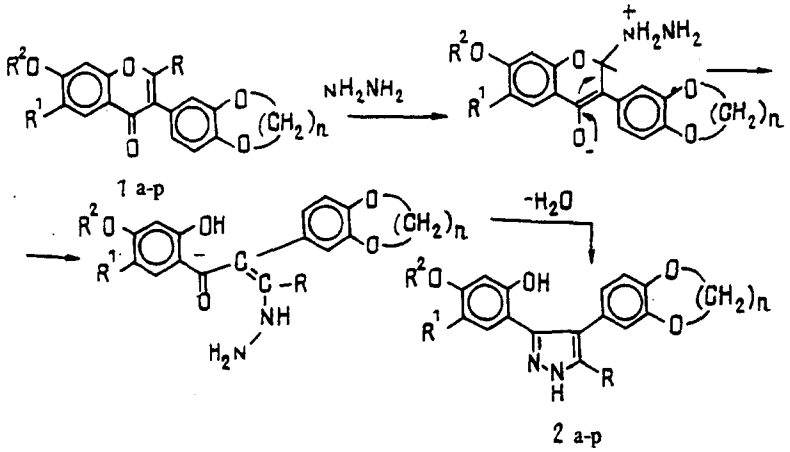
UDC 547.814.5

The reactions of 1,3-benzodioxolane, 1,4-benzodioxane, and 1,5-benzodioxepane analogs of isoflavones with hydrazine derivatives have been studied. It has been found that under the action of hydrazines the new isoflavones recyclize into 3,4-diarylpyrazones. Their structures have been confiremd by their PMR spectra.

It is known [2-5] that under the action of hydrazine hydrate on chromones and thiochromones containing a Me, C_6H_5 or OH group in position 3 the pyrone ring opens and the resulting intermediate compounds rearrange into pyrazole derivatives. We have found that, on being boiled with hydrazine hydrate in alcohol, 7-hydroxy- and 7-methoxyisoflavones with 1,3-benzodioxolane, 1,4-benzodioxane, and 1,5-benzodioxepane nuclei [6-9] recyclize into the 3-(2-hydroxyphenyl)pyrazole derivatives (2a-p*).



1 a-p

2 a-p

a: R=R²=H, R¹=Et, *n*=1; b: R=R²=H, R¹=Pr, *n*=1; c: R=Me, R¹=Et, R²=H, *n*=1; d: R=R¹=R²=H, *n*=2; e: R=R²=H, R¹=Et, *n*=2; g: R=R²=H, R¹=Pr, *n*=1; h: R¹=R²=H, R=Me, *n*=2; i: R=Me, R¹=Et, R²=H, *n*=2; j: R=Me, R¹=Pr, R²=H, *n*=2; k: R=H, R¹=Et, R²=Me, *n*=1; l: R=H, R¹=Pr, R²=Me, *n*=1; m: R=H, R¹=H, R²=Me, *n*=2; n: R=H, R¹=Et, R²=Me, *n*=2; o: R=H, R¹=Pr, R²=Me, *n*=2; p: R=H, R¹=Pr, R²=Me, *n*=3

As a result of the interaction of isoflavone (1p) with methylhydrazine a mixtue of the isomeric pyrazoles (3) and (4) was obtained. We isolated compound (3), formed in larger amount, by fractional crystallization, but the isomeric compound (4) could not be isolated from the reaction mixture in the individual state.

*No compounds (1f) and (2f) are mentioned in this paper — Translator.

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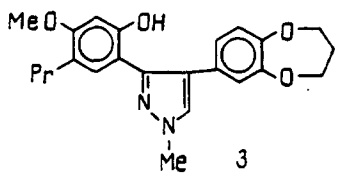
 0009-3130/94/3005-0580$12.50

TABLE 1. Characteristics of Compounds (2) and (3)

Compound	Yield, %	mp. °C	Empirical formula	Reaction time
2 a	90	203	$C_{18}H_{16}N_2O_4$	5.5 h
2b	90	177	$C_{19}H_{18}N_2O_4$	20 min
2c	98	98	$C_{19}H_{18}N_2O_4$	2 h
2d	89	224.5	$C_{17}H_{14}N_2O_4$	20 min
2e	95	189	$C_{19}H_{18}N_2O_4$	20 min
2g	92	177	$C_{20}H_{20}N_2O_4$	10 min
2h	86	217.5	$C_{18}H_{16}N_2O_4$	4 h
2i	97	167	$C_{20}H_{20}N_2O_4$	7 h
2j	94	157	$C_{21}H_{22}N_2O_4$	20 min
2k	98	186	$C_{19}H_{18}N_2O_4$	10 min
2l	96	177	$C_{20}H_{20}N_2O_4$	10 min
2m	96	128	$C_{18}H_{16}N_2O_4$	7 min
2n	85	176	$C_{20}H_{20}N_2O_4$	10 min
2o	96	157	$C_{21}H_{20}N_2O_4$	10 min
2p	74	144	$C_{22}H_{24}N_2O_4$	10 min
3	65.9	93—94	$C_{23}H_{26}N_2O_4$	1 h



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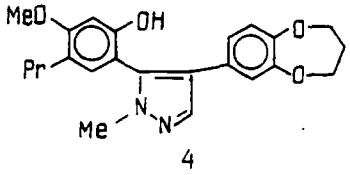

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The amount of compound (4) in the mixture was insignificant. The pyrazoles obtained dissolved readily in 5% caustic soda solution, and with an alcoholic solution of ferric chloride formed blue-green complexes of the chelate type, which showed the presence of a free phenolic hydroxyls in the α-positions to the pyrazole rings of the molecules under investigation. The pyrazole structure of compounds (2) was shown by the separate absorptions of the OH-2 and NH groups [2-5] and aso by the upfield shift of the H-6 proton by an average of 0.90 ppm in comparison with the position of the peak of the H-5 proton in the initial isoflavones (Table 2). The pyrazole stucture of compounds (2a-p) was also shown by the broadened signal of the H-5 proton in the pyrazole ring (spin-spin coupling with the proton on the nitrogen).

Details of the PMR spectra, analyses, yields, and constants for compounds (2a-p) are given in Tables 1 and 2.

Thus, investigations of the interaction of benzodioxolane, benzodioxane, and benzodioxepane analogs of isoflavones with hydrazine derivatives have shown that these compounds are convenient intermediates for the synthesis 3,4-diarylpyrazoles. The formation of the pyrazoles takes place readily and with high yields, which permits this reaction to be used for preparative purposes.

EXPERIMENTAL

The course of the reactions and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 plates. The eluent used was benzene—methanol (9:1). PMR spectra were measured on a Bruker WP-100 SU instrrument in DMSO-d_6 with TMS as internal standard. The elemental analyses of all the compounds corresponded to the calculated figures.

TABLE 2. Chemical Shifts in the PMR Spectra (δ, ppm, J, Hz) of the 3-(2-Hydroxyphenyl)-4-hetarylpyrazoles (in DMSO-d_6)

Compound	Protons of the phenol moiety					Pyrazole protons		Protons of the hetero residue	
	OH-2, s	H-3, s	OH-4 or OMe-4, s	R^1-5	H-6, s	N-H or N-Me, s	H-3 or Me-3, s	H-4 (H-5) or H-6 H-6 (H-7) or H-8 H-7 (H-8) or H-9	$-O(CH_2)_nO$ n=1, 2, 3
2a	9.38	6.49	9.38	2.44 q; 1.03 t	6.80	12.81	7.78	6.80 m	5.95 s
2b	9.35	6.45	9.35	2.43 t; 1.51 m; 0.81 t	6.71	12.77	7.77	6.81 m	5.93 s
2c	9.37	6.43	10.81	2.37 q; 0.91 t	6.81	12.94	2.25	6.81 m	6.05 s
2d	9.54	6.49 d, (2.0)	9.79	6.34 d.d, (8.0; 2.0)	7.01 d, (8.0)	12.86	7.83	6.82 m	4.23 s
2e	9.38	6.48	9.38	2.46 q; 1.04 t	6.79	12.75	7.78	6.79 m	4.21 s
2g	9.38	6.55	9.64	2.44 t; 1.54 m; 0.87 t	6.84	12.84	7.82	6.84 m	4.22 s
2h	9.53	6.38 d, (2.0)	10.98	6.16 d.d, (8.0; 2.0)	6.94 d, (8.0)	12.93	2.19	6.75 m	4.22 s
2i	9.87	6.35	9.87	2.42 q; 0.88 t	6.73	9.87	2.21	6.73 m	4.25 s
2j	9.75	6.43	9.75	2.32 t; 1.35 m; 0.78 t	6.77	9.75	2.20	6.77 m	4.27 s
2k	10.15	6.60	3.79	2.47 q; 1.02 t	6.97	13.06	7.86	6.85 m	6.00 s
2l	9.59	6.53	3.76	2.34 t; 1.40 m; 0.79 t	6.85	12.66	7.81	6.81 m	5.96 s
2m	9.90	6.52 d, (2.0)	3.73	6.40 d.d, (8.0; 2.0)	7.07 d, (8.0)	12.75	7.70	6.78 m	4.19 s
2n	9.58	6.52	3.77	2.39 q; 0.98 t	6.90	12.63	7.79	6.79 m	4.20 s
2o	10.14	6.56	3.78	2.40 t; 1.44 m; 0.81 t	6.90	13.10	7.81	6.79 m	4.22 s
2p	9.60	6.53	3.76	2.34 t; 1.39 m; 0.80 t	6.90	12.66	7.75	6.87 m	4.08 t; 2.07 q
3	9.9	6.5	3.88	2.30 t; 1.30 m; 0.79 t	6.8	3.75	7.87	6.8(H-6), 6.8(H-8), 6.9(H-9)	4.10 t; 2.09 q

3-(2-Hydroxyphenyl-4-hetarylpyrazoles (2a-p). To a solution of 10 mmole of the appropriate isoflavone (1a-p) in the minimum amount of hot alcohol (in some cases it is possible to perform the reaction with a hot suspension of the isoflavone in alcohol) was added 60 ml (120 mmole) of a 2 N alcoholic solution of hydrazine hydrate. The reaction mixture was boiled for from 10 min to 7 h. The end of the reaction was determined with the aid of TLC. The reaction mixture was diluted with water until precipitation was complete, and the precipitate was filtered off from the cold solution. The product was recrystallized from alcohol or aqueous alcohol.

4-(1,5-Benzodioxepan-7-yl)-3-(2-hydroxy-4-methoxy-5-propylphenyl)-1-methylpyrazole (3). To a hot solution of 3.66 g (10 mmole) of the isoflavone (1p) in 70 ml of alcohol was added 2 ml (40 mmole) of methylpyrazine. After an hour's boiling, the reaction mixture was evaporated to a volume of 15-20 ml, and the resulting precipitate was filtered off and washed with alcohol. By crystallization from alcohol, 2.6 g (65.9%) of pyrazole (3) was obtained.

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