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BAZI YENİ AZOPİRAZOL SÜBSTİTÜE 1,2,4-TRİAZOL-5-TİONLARIN SENTEZLERİ VE SPEKTROMETRİK ANALİZLERİ

SYNTHESIS AND SPECTROMETRIC ANALYSIS OF SOME NEW AZOPYRAZOLE SUBSTITUTED 1,2,4-TRIAZOLE-5-THIONES

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SUMMARY

In this work, 1,3-dimethyl-2-arylhydrazono-1,2,3-propanetriones were condensed with purpald (4-amino-3-hydrazino-1,4-dihydro-5H-1,2,4-triazole-5-thione) to obtain new azopyrazole derivatives in the acidic medium.

The stuructures of these new azopyrazole derivatives were established utilizing chemical, analytical and spectroscopic methods.

ÖZET

Bu çalışmada, 1,3-dimetil-2-arilhidrazono-1,2,3-propantrionların purpald (4-amino-3-hidrazino-1,4-dihidro-5H-1,2,4-triazol-5-tion) ile asidik ortamda kondensasyonu sonucunda yeni azopirazol türevi bileşikleri kazanılmıştır.

Oluşan azopirazol türevlerinin yapıları kimyasal, analitik ve spektroskopik yöntemler yardımı ile kanıtlanmıştır.

INTRODUCTION

Triazole and pyrazole derivatives have been reported to posses potent hypoglycemic activity (1-3). This paper describes the synthesis and spectroscopic analysis of triazole derivatives having on azopyrazole moiety 3 position.

EXPERIMENTAL PART

All m.p.'s were taken on a Büchi 510 melting point apparatus and

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uncorrected. IR spectra were run on a Perkin Elmer 240 spectrophotometer. ^{1}H-NMR spectra were taken on a Perkin Elmer R32 90 MHz spectrometer. Mass spectra were taken on a VG12F mass spectrometer.

General method for the preparation of 2-arylhydrazono-1,3-dimethyl-1,2,3-propanetriones (1a-h).

The diazonium salts of arylamines (0.01 mol) was added to the mixture of acethylacetone (1 g), water (25 ml), ethanol (25 ml) and sodiumacetate (50 g). The precipitated coloured product was filtred, washed with water and recrystallized from ethanol (4-7). Melting points of compounds 1a-h were given table 1.

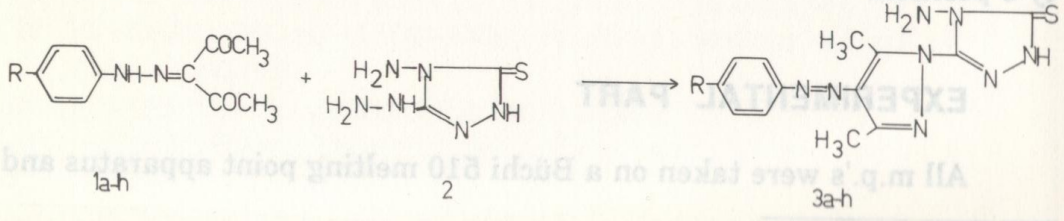
Table-1: Melting points of compounds la-h.

Compound	1a	1b	1c	1d	1e	1f	1g	1h
m.p. (°C) (EtOH)	78	223	250-3	130-2	205-7	220-4	217	187

General method for the preparation of 4-amino-3-[3,5-dimethyl-4-(p-substituedphenylazo)-1H-pyrazole-1-yl]-1,4-dihydro-5H-1,2,4-triazole-5-thiones.

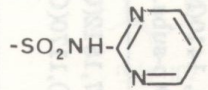
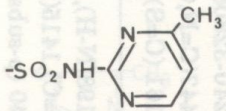
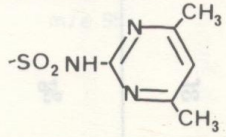
To 2-arylhydrazono-1,3-dimethyl-1,2,3-propanetriones (0.005 mol) in glacial acetic acid (30-50 ml) was added purpald (0.731 g, 0.005 mol) containing concentrated sulfuric acid (1 ml). The mixture was refluxed for 4 hours. After pouring to crash-ice was set aside overnight in the refregerator. The precipitate was filtered and the crude product was recrystallized from ethanol (8) (Table II).

^{1}H-NMR of compd.3a: DMSOd_6/TMS, δ (ppm), 2.49(s, 3H, C_5-CH_3); 2.58 (s, 3H, C_3-CH_3); 3.29 (s, 1/2 H, -SH); 5.75 (s, 2H,-NH_2); 7.50-7.65 (m, 3H, Ar-H); 7.76-7.90 (m, 2H, Ar-H); 14.28 (s, 1/2 H, -NH).



Scheme - 1

Table-II. Physical Data for Compounds 3a-h.

Compound	R	m.p.(°C)	Yield (%)	Molecular Formula (Mol. Wt.)	Elemental Analysis (Calc./Found) C	H	N
3a	–H	252	77	$C_{13}H_{14}N_8S$ (314.37)	49.67 49.91	4.49 4.75	35.65 36.01
3b	$-NO_2$	277(dec.)	51	$C_{13}H_{13}N_9O_2S$ (359.36)	43.45 43.83	3.65 3.81	35.08 35.78
3c	–COOH	262	71	$C_{14}H_{14}N_8O_2S$ (358.38)	46.92 46.92	3.94 3.90	31.27 31.10
3d	$-COOC_2H_5$	245-48	61	$C_{16}H_{18}N_8O_2S$ (386.40)	49.73 49.73	4.69 4.74	29.00 28.81
3e	$-SO_2NH_2$	236	53	$C_{13}H_{15}N_9O_2S_2$ (393.39)	39.69 40.21	3.84 3.66	32.04 32.71
3f		218	57	$C_{17}H_{17}N_{11}O_2S_2$ (471.53)	43.30 42.42	3.63 3.47	32.68 32.42
3g		257	91	$C_{18}H_{19}N_{11}O_2S_2$ (485.55)	44.53 45.20	3.94 3.90	31.73 31.68
3h		244	58	$C_{19}H_{21}N_{11}O_2S_2.1/2\,H_2O$ (508.59)	45.68 44.87	4.24 4.36	30.84 30.29

RESULT AND DISCUSSION

4-Amino-3-[3,5-dimethyl-4-(p-substituedphenylazo)-1H-pyrazole-1-yl]-1,4-dihydro-5H-1,2,4-triazole-5-thiones (compd. 3a-h) were synthesized from 2-arylhydrazono-1,3-dimethyl-1,2,3-propanetriones (1a-h) and purpald (4-amino-3-hydrazino-1,4-dihydro-5H-1,2,4-triazole-5-thione) (8).

Table-III: IR and Mass Data for Compounds 3a-h.

Compound	IR(KBr) (cm^{-1})	MASS (m/e)
3a	3293-3136(N-H), 1595,1570, 1489,1465 (C=N,C=C), 1412 (N=N), 1154 (C=S), 770,700 (mono subs. benzene)	314(M^+) (base), 299, 237, 222, 209, 123, 122, 115, 108, 107, 101, 95, 77, 68, 65
3b	3300-3136 (N-H), 1592,1561, 1470 (C=N, C=C), 1520,1339 (NO_2),1412(N=N), 1145(C=S), 857 (p-subs.)	359(M^+), 237, 222, 209, 197, 195, 123, 122, 115, 108, 107, 103 (base), 101, 95, 77, 68, 65
3c	3298(N-H), 1678(C=O), 1592, 1500,1478 (C=N, C=C), 1410 (N=N), 1146 (C=S), 865 (p-subs.)	358(M^+) (base), 343, 237, 222, 209, 194, 137, 123, 122, 115, 108, 107, 101, 95, 77, 68, 65
3d	3260-3160(N-H),1715(C=O), 1600,1570,1488(C=N,C=C), 1409(N=N), 1164(C=S), 860 (p-subs.)	386(M^+), 370 (base), 325, 237, 222, 210, 194, 137, 123, 122, 115, 108, 107, 103, 101, 95, 77, 68, 65
3e	3270-3300(N-H),1587,1495 (C=N,C=C),1411(N=N),1162 (C=S), 862 (p-subs.)	279(M^+-114), 223, 199, 178(base), 177, 135, 123, 122, 115, 108, 107, 101, 95, 77, 68, 65
3f	3240-3280(N-H),1587,1479, 1447(C=N,C=C), 1410(N=N), 1161 (C=S), 850(p-subs.)	292 (M^+-179), 186, 185 (base), 123, 108, 107, 95, 77, 68, 65
3g	3198(N-H), 1587,1512(C=N, C=C),1415(N=N),1170(C=S), 840 (p-subs.)	420(M^+-65), 209, 199 (base) 178, 123, 122, 109, 108, 107, 95, 77, 68, 65
3h	3140(N-H), 1600,1480(C=N, C=C),1410(N=N),1140(C=S), 860 (p-subs.)	435(M^+-64), 209, 197, 195, 123, 95 (base), 68, 67

Scheme - 2 : Mass fragmentation of compound 1.

All the synthesized compounds 3a-h were characterized by their elementary analyses, IR, ^{1}H-NMR (for compd. 3a) and mass spectral data. IR spectra in KBr disk of compounds 3a-h showed the characteristic absorption bands of thiolactam NH(3300-3136 cm^{-1}), C=S (1140-1170 cm^{-1}) and N=N (1415-1409 cm^{-1}) (9,10). These IR spectral data indicated that 3a-h exist in the thion form in the solid state. But the NMR spectrum of 3a in DMSO-d_6 exibited both NH (14.28 ppm) and SH (3.29 ppm) signals (9,11). These data showed that compounds 3a exist in the thion-thiol tautomeric equilibria in DMSO-d_6 (Fig. 1).

Mass spectral data of compounds 3a-h were given table III. The fragmentation pattern of compound 3a was shown scheme 2 (12,13).

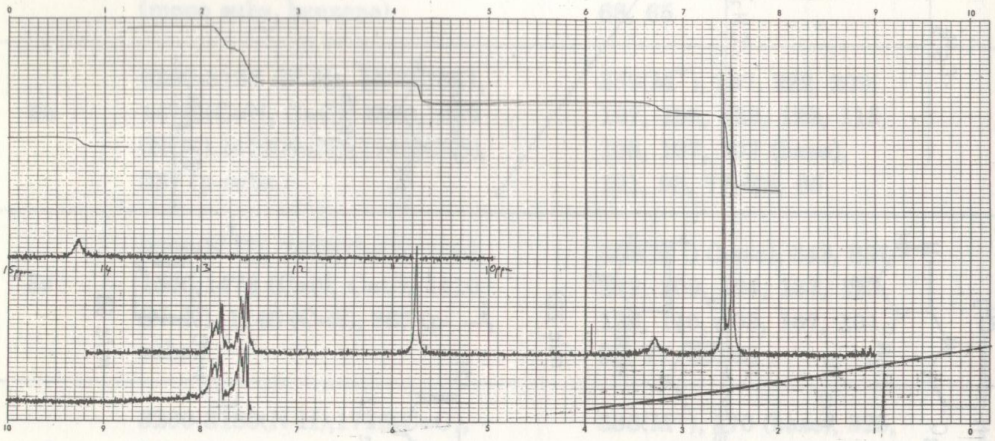


Fig. 1. NMR spectrum of compound 3a.

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REFERENCES

1. Smith, D.L., Forist, A.A., Dulin, W.E.: *J.Med.Chem.*, **8**, 350-3 (1965).
2. Gerritsen, G.C., Dulin, W.E.: *Diabetes*, **14**, 507-15 (1965).
3. Mhasalkar, M.Y., Shah, M.H., Nikam, S.T., Anantanarayanan, K.G., Deliwala, C.V.: *J.Med.Chem.*, **13**, 672-4 (1970).
4. Prakash, A., Gambhir, I.R.: *J.Indian Chem.Soc.*, **41**, (12), 849-54 (1964); *C.A.*, **62**, 11800c (1965).
5. Elquero, J., Jacquier, R., Tarrago, G.: *Bull.Soc.Chim. France*, 2981-9 (1966).
6. Morgan, G.T., Drew, H.D.K.: *J.Chem.Soc.*, **117**, 1456-65 (1920); *C.A.*, **15**, 1493-4 (1921).
7. Ergenç, N., Rollas, S.: *İstanbul Ecz.Fak.Mec.*, **11**, 8-23 (1975).
8. Ergenç, N., Rollas, S.: *İbid*, **11**, 138-57 (1975).
9. Ueno, K.: *J.Am.Chem.Soc.*, **79**, 3205-8 (1957).
10. Rollas, S.: *İstanbul Ecz.Fak.Mec.*, **17**, 155-63 (1981).
11. Ertan, R., Ayhan, G.: *Farmasötik Bilimler Dergisi*, **15**, 1-11 (1990).
12. Bowie, J.H., Lewis, G.E., Cooks, R.G.: *J.Chem.Soc.*, **B**, 621-8 (1967).
13. Zalipsky, J.J., Patel, D.M., Reavey-Catwell, N.H.: *J.Pharm.Sci.*, **67**, 387-91 (1987).

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