Proc. Indian Acad. Sci. (Chem. Sci.), Vol. 94, No. 3, June 1985, pp. 487–493.

Synthesis and characterization of α-oximino-β-thiosemicarbazino-acetoacetarylamides and their cyclized product vicinal triazoles

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MS received 5 October 1984; revised 21 January 1985

Abstract. Several α-oximino-β-thiosemicarbazones of acetoacetarylamides have been synthesized by condensing thiosemicarbazide and α-oximinoacetoacetarylamides. α-Oximino-β-thiosemicarbazinoacetoacetarylamides are cyclized employing thionyl chloride or acetic anhydride/sodium acetate to give N-aryl 4-methyl-2-thiocarbamido-1,2,3,triazole-5 carboxylic acid amide. The compounds reported herein are characterized by UV, IR and microanalytical data.

Keywords. α-Oximino-β-thiosemicarbazones of acetoacetarylamides; vicinal triazoles; UV and IR studies.

1. Introduction

α-Oximinohydrazones have been shown to possess biological activity by several investigators (Giammanco 1961; Misra and Verma 1962) by virtue of the presence of the –CONH–N=C– group and the =NOH group, which impart antiparasitic, fungicidal and bactericidal properties to such compounds. α-Oximino-β-hydrazones of acetoacetarylamides have been shown (Patel and Mankad 1968; Patel *et al* 1975) to be utilized quantitatively for the estimation of transition metal ions such as Ni and Pd, either alone or in the presence of other metals. Cyclization of oximinohydrazones affords vicinal triazoles (Rupport and Nilsson 1961). Several investigators (Gugliemo *et al* 1973; Geigy 1972; Fritz *et al* 1973; David *et al* 1972; Osamu *et al* 1972) have reported the synthesis of *vis*-triazoles from oxime hydrazones and shown to possess whitening property and also pharmacological activity.

In view of the above survey, it was considered worthwhile to undertake a systematic study of the preparation and characterization of α-oximino-β-thiosemicarbazones of acetoacetarylamides and their cyclized products vicinal triazoles.

2. Experimental

All the chemicals used are of analytical grade. α-Oximinoacetoacetarylamides have been prepared (Knorr 1887) and crystallized from aqueous ethanol.

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2.1 *General method for the preparation of α-oximino-β-thio-semicarbazones of acetoacetarylamides*

Condensation of the α-oximinoacetoacetarylamides with thiosemicarbazide was carried out by treating *o*-oximinoacetoacetarylamides in ethanol with semicarbazide in equimolar proportions and adding a few drops of concentrated HCl. On keeping for 1–3 hrs., the product separating was filtered and crystallized from aqueous ethanol. In all the cases the yield obtained was in the range of 75 to 80%. The analytical results are recorded in table 1.

2.2 *Preparation of vicinal triazoles*

α-Oximino-β-thiosemicarbazones of acetoacetarylamides (0·5 gm) were mixed with excess of freshly distilled thionyl chloride (about 20 ml). The contents were refluxed at 80–90°C for 3 hrs. Excess thionyl chloride was distilled off at atmospheric pressure while traces were removed by distillation *in vacuo* after adding benzene and petroleum ether successively. The semisolid mass solidified on trituration with dry ether. Ether was allowed to evaporate and the fine solid powder obtained was dried at 50–60°C and then kept in a vacuum desiccator till the odour of thionyl chloride disappeared. The compounds thus obtained were recrystallized from ethanol and are listed in table 2.

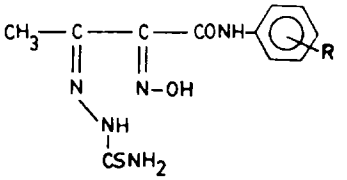
The 2,4,5-trisubstituted 1,2,3-triazoles reported here and prepared by the above method were also synthesized by the action of acetic anhydride (about 20 ml)/sodium acetate (about 0·2 gm) on the corresponding α-oximinothiosemicarbazones (about 0·1 to 0·2 gm) at the reflux temperature of acetic anhydride for 3 hrs, followed by the distillation of excess acetic anhydride and pouring of the residual reaction mass onto ice. The solid products separated in each case were crystallized from ethanol. The melting points of the products were found to be the same as those prepared by the above method.

2.3 *Physical measurements*

Nitrogen content were estimated by micro Duma's method. UV measurements were carried out using ethanol as a solvent. IR spectra in the form of their KBr pellets were recorded (400 cm^{-1} to 4000 cm^{-1}).

3. Results and discussion

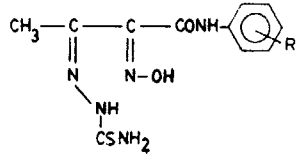
α-Oximino-β-thiosemicarbazinoacetoacetarylamides have been assigned anti-configuration (Patel and Mankad 1964) as



where R = H, *o*-CH_3, *p*-CH_3, *o*-Cl, *m*-Cl, *p*-Cl, *o*-OCH_3, *p*-OCH_3, 2:4 $(CH_3)_2$.

Table 1 shows the UV data for oximino thiosemicarbazones. The absorption pattern was characterized by the presence of two bands around 235–255 nm and 304–305 nm.

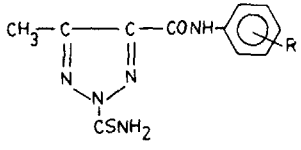
Table 1. Analytical and UV spectral data of α-oximino-β-thiosemicarbazones of acetoacetarylamides.



No.	R	Molecular formula	M.P.°C (D)	Colour	% Nitrogen		λ_{max} (nm)	(log ε_{max})
					Literature	Found		
1	H	$C_{11}H_{13}O_2N_5S$	176–7	White	25·10	23·15	305	(4·4)
							245	(4·2)
2	*o*-CH_3	$C_{12}H_{15}O_2N_5S$	151–2	White	23·88	23·84	304	(4·4)
							235	(4·1)
3	*p*-CH_3	$C_{12}H_{15}O_2N_5S$	175	White	23·88	23·95	305	(4·4)
							245	(4.3)
4	*o*-Cl	$C_{11}H_{12}O_2N_5SCl$	160–2	Light yellow	22·33	22·10	305	(4.4)
							235	(4.2)
5	*m*-Cl	$C_{11}H_{12}O_2N_5SCl$	180	White	22·33	22·20	305	(4·4)
							245	(4.3)
6	*p*-Cl	$C_{11}H_{12}O_2N_5SCl$	170	White	22.33	22.46	305	(4.5)
							250	(4.4)
7	*o*-OCH_3	$C_{12}H_{15}O_3N_5S$	158–9	White	22·65	22·60	305	(4.4)
							245	(4·2)
8	*p*-OCH_3	$C_{12}H_{15}O_3N_5S$	171	Yellow	22·65	22·70	305	(4.4)
							255	(4.3)
9	2:4 $(CH_3)_2$	$C_{13}H_{17}O_2N_5S$	187–9	White	22·81	22·90	305	(4.4)
							238	(4.1)

D—decomposed.

Table 2. Analytical and UV spectral data of vicinal triazoles.



No.	R	Molecular formula	M.P.°C (D)	Colour	% Nitrogen		λ_{max} (nm)	($\log \varepsilon_{max}$)
					Literature	Found		
1	H	$C_{11}H_{11}ON_5S$	160	Reddish yellow	26·82	26·46	275	(5·8)
2	*o*-CH_3	$C_{12}H_{13}ON_5S$	80	Buff yellow	25·46	25·51	270	(5·4)
3	*p*-CH_3	$C_{12}H_{13}ON_5S$	154	Yellow	25·46	25·73	265	(5·8)
4	*o*-Cl	$C_{11}H_{10}ON_5SCl$	230	Dark yellow	23·69	23·27	268	(5.6)
5	*m*-Cl	$C_{11}H_{10}ON_5SCl$	155	Yellow	23·69	23·88	268	(5.8)
6	*p*-Cl	$C_{11}H_{10}ON_5SCl$	140	Yellow	23·69	23·99	270	(5·6)
7	*o*-OCH_3	$C_{12}H_{13}O_2N_5S$	170	Lemon yellow	24·05	23·65	260	(5·7)
8	*p*-OCH_3	$C_{12}H_{13}O_2N_5S$	90	Dark yellow	24·05	23·69	275	(5·6)
9	2:4$(CH_3)_2$	$C_{13}H_{15}ON_5S$	225	Light yellow	24·23	24·80	262	(5·4)

D—decomposed.

Table 3. IR spectral data of α-oximino-β-thiosemicarbazones of acetoacetarylamides and their cyclized product vicinal triazoles.

No.	NH Stretch	OH Stretch	C=N Stretch	N–O Stretch	C=S Stretch	Triazole ring vibration	Ring breathing and C–H in plain vibration	–NH– I	II	III
1	3226 s, 3333 s, 3400 s	2833 s	1610 vs	960 vs	1083 s	—	—	1681 vs, 1612	1555 vs	1325 m
1[c]	3300 s, 3450 s	—	1615 s	—	1330 s	1240 s, 1160 s	1130 s, 1070 m, 905 s, 875 s	1665 s	1540 vs	1300 s
2	3050 s, 3380 s, 3400 s	2857 s	1600 s	962 s	1064 s	—	—	1670 s, 1653 s	1520 s, 1527 s	1315 vs
2[c]	3300 s, 3450 s	—	1600 s	—	1360 s	1250 s, 1170 s	1050 s, 1130 s, 1070 s, 900 s	1675 s	1540 s	1300 s
3	3070 s, 3280 s, 3400 s	2874 s	1600 s	964 vs	1064 s	—	—	1670 vs	1555 s	1300 vs
3[c]	3300 s, 3460 s	—	1605 s	—	1325 s	1255 s, 1245 m	1130 s, 1050 s, 990 s, 900 s	1675 s	1540 s	1300 vs
4	3077 s, 3215 s, 3333 s	2890 w	1603 s	960 vs	1057 s	—	—	1680 s, 1658 m	1546 s, 1520 s	1300 vs
4[c]	3300 s, 3440 s	—	1600 s	—	1330 s	1220 s, 1190 s, 1160 m	1130 s, 1075 s, 1010 m, 920 s	1690 s	1530 s	1300 s
5	3080 s, 3030 s, 3475 s	2885 s	1610 vs	960 vs	1058 s	—	—	1672 vs	1555 s	1300 vs
5[c]	3280 s, 3450 m	—	1605 s	—	1320 s	1245 s, 1180 s, 1160 s	1130 s, 1075 m, 1010 s, 920 s	1675 s	1540 s	1310 s
6	3050 s, 3175 s, 3280 s	2833 s	1605 vs	952 vs	1050 m	—	—	1695 s	1543 s	1300 vs
6[c]	3300 s, 3460 s	—	1610 s	—	1325 s	1260 m, 1225 s, 1180 s	1125 s, 1070 s, 1030 s, 990 m, 900 s	1675 s	1550 s	1300 s
7	3115 s, 3333 s, 3472 s	2874 w	1610 vs	966 vs	1058 s	—	—	1672 vs, 1658 s	1550 s	1300 vs
7[c]	3300 s, 3460 m	—	1605 s	—	1330 m	1250 s, 1220 s, 1180 m	1130 s, 1100 m, 1050 s, 1015 s,	1670 s	1550 s	1300 vs
8	3077 s, 3872 s, 3530 s	2890 s	1610 vs	963 vs	1057 m	—	990 m —	1672 vs	1550 s	1300
8[c]	3300 s, 3450 s	—	1600 s	—	1360 m	1240 s, 1200 m, 1170 s	1090 s, 1015 m, 990 s, 890 s	1680 vs	1535 s	1320 s
9	3050 s, 3300 s, 3475 s	2890 s	1600 s	960 vs	1057 m	—	—	1667 s	1545 m	1290 vs
9[c]	3300 s, 3490 m	—	1600 s	—	1360 m	1260 m, 1220 s, 1160 s	1140 s, 1060 m, 1040 s, 990 s	1680 s	1545 s	1300 vs

Serial numbers represent the α-oximinothiosemicarbazones from table 1, those with superscript c are the corresponding triazoles; s = strong, vs = very strong, m = medium, w = broad.

The UV spectra of acetoacetarylamides and thiosemicarbazide moieties in ethanol show a maxima around 245–252 nm and 230–240 nm respectively. On comparing these data with those given in table 1 it is revealed that the band at 303–305 nm can be assigned to the new chromophoric system [N=C–C(=N)–C=O] and shows a bathochromic displacement to the extent of 53–64 nm (compared to the parent amide λ_{max} 245–252 nm) with increase in absorption intensity. The band observed at 235–255 nm is due to the thiosemicarbazide moiety which shows an increase in intensity compared to acetoacetarylamides (Patel and Mankad 1964).

The IR spectra of α-oximino-β-thiosemicarbazinoacetoacetarylamides have exhibited bands in the region 3100–3400 cm^{-1} which may be attributed to free NH_2 of carbazide moiety, bonded NH of amide and OH of oxime stretchings (Hadzi and Jan 1965). The bands around 1600 cm^{-1} and 940–970 cm^{-1} are assigned to C=N and N–O stretchings respectively (Ungnado *et al* 1963). The secondary amide and C–Cl stretching vibrations are located at their usual positions (Rao 1961).

The 2,4,5-trisubstituted vicinal triazoles prepared here do not show a tendency to form metal complexes with transition metal ions which indicates the absence of free =N–OH and the formation of a triazole ring. It is suggested that under reaction conditions the compounds undergo a steric change from anti-to amphi-configuration (δ) and then follow the cyclodehydrazation.

The UV spectral data of 2,4,5-trisubstituted 1,2,3-triazoles (table 2) show one intense band in the region 260–275 nm ($\log \varepsilon$ = 5·4–5·8) which is attributed to the triazole ring (Rao 1961; Khadem *et al* 1963). Table 3 shows the IR spectral data of vicinal triazoles. The most important feature of these spectra is the presence and location of the vicinal triazole ring vibrations and ring breathing bands. The bands around 1160–1180 cm^{-1}, 1220–1260 cm^{-1} are attributed to vicinal triazole ring vibrations. The peaks around 1130 cm^{-1}, 1050–1100 cm^{-1}, 1000 cm^{-1} and 900 cm^{-1} are assigned to vicinal triazole ring breathing and C–H in-plane deformations. These values are in agreement with the values reported for vicinal triazole ring system (Rao and Venkatraghavan 1964). The absence of a N–O band in triazoles indicates the formation of the triazole ring with the disappearance of the –OH of the oximino group of oximinothiosemicarbazone during the cyclodehydration reaction. The bands around 3450 cm^{-1} and 3300 cm^{-1} are assigned to primary amine N–H and *trans* associated secondary amide N–H stretchings respectively. The band around 1330 cm^{-1} may be assigned to C=S stretching (Wiles *et al* 1967). The bands due to C=N and secondary amide (C=O) stretchings are located at their usual positions (Rao 1961).

Acknowledgement

The authors wish to thank Prof. B N Mankad and Prof. R P Patel, Department of Chemistry, Sardar Patel University for taking keen interest in the work and providing necessary research facilities.

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