Synthesis of Some Triazoles and Thiadiazoles Bearing Phosphorus Substituents

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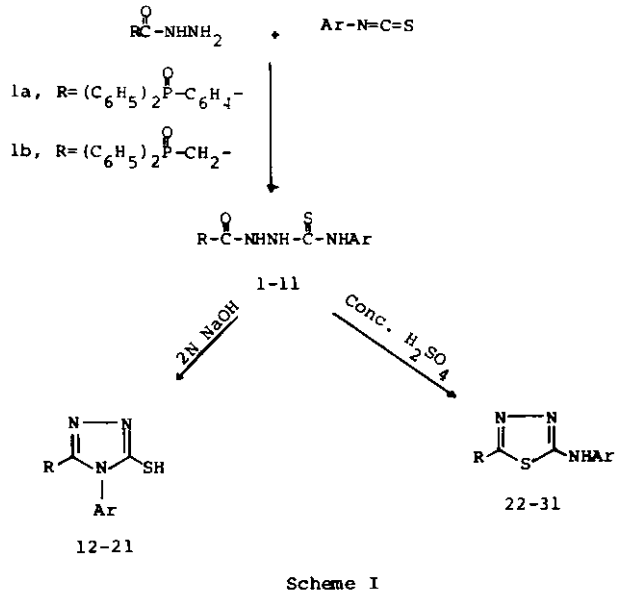
Summary: Several aryl thiosemicarbazides were synthesized by condensing p-(diphenylphosphino)benzoic acid hydrazide and diphenylphosphinoacetic acid hydrazide with suitable aryl isothiocyanates. Cyclisation of these thiosemicarbazides with 2N sodium hydroxide afforded 5-substituted phosphino-4-aryl -3-mercapto-s-triazoles. When cyclisation was affected by concentrated sulphuric acid, 2-arylamino-5-substituted phosphino-1,2,4-thiazoles were obtained.

The chemistry of thiosemicarbazides and their cyclisation products had received great attention in the last years due to their reported [1-5] biological and diverse pharmacological activities. In this investigation, we report the synthesis of some aryl thiosemicarbazides bearing phosphorus substituents, as well as, their conversion into the corresponding triazoles and thiadiazoles.

The various derivatives are synthesized according to the steps outlined in scheme I.



Scheme I

p-(Diphenylphosphino)benzoic acid hydrazide 1_a [6] and diphenylphosphinoacetic acid hydrazide 1_b [7] condense with aryl isothiocyanates with the formation of the corresponding aryl thiosemicarbazides 2-11. The structure of the latter products is based upon the analytical data(Table I), as well as, spectral data(Table II).

On refluxing the thiosemicarbazides 2-11 with 2N sodium hydroxide, ring closure occured with the formation of 5-substituted-phosphino-4-aryl-3-mercapto-s-triazoles 12-21. The IR spectra of these products showed characteristic bands for C=N at 1600 cm^{-1}, as well as, the p=o band at 1180-1190 cm^{-1}. However, when cyclisation of the thiosemicarbazides 2-11 was effected by using concentrated sulphuric acid, 2-arylamino-5-substitutedphosphino-1, 2,4-thiadiazoles 22-31 were obtained. The IR spectra of these thiadiazoles showed characteristic NH absorptions in the region 3250-3350 cm^{-1}, as well as, the characteristic absorption band for C=N at 1600 cm^{-1}.

Experimental

The melting points of these compounds were not corrected. The infrared spect-

Table-1

Physical constans of 1-diphenylphosphinobenzoyl)- and 1-(dipehnylphosphinoacetyl)-4-aryl-3-Thiosemicarbazides

Compound No.	R	Ar	M.P.°C	Yield %	Molecular Formula	Analysis %					
						Calcd.%			Found %		
						C	H	N	C	H	N
2	$(C_6H_5)_2$-P(=O)-C_6H_4	C_6H_5-	194-195	75	$C_{26}H_{22}N_3O_2PS$	66.2	4.7	8.9	65.9	4.3	8.4
3	$(C_6H_5)_2$-P(=O)-C_6H_4-	$C_6H_4Br(p-)$	162-164	75	$C_{26}H_{21}BrN_3O_3PS$	56.7	3.8	7.6	56.8	3.7	7.7
4	$(C_6H_5)_2$-P(=O)-C_6H_4	$C_6H_4Cl(p-)$	161-162	80	$C_{26}H_{21}ClN_3O_2PS$	61.7	4.1	8.3	61.4	3.8	7.9
5	$(C_6H_5)_2$-P(=O)-C_6H_4-	$C_6H_4OCH_3(p-)$	163-164	80	$C_{27}H_{24}N_3O_3PS$	64.7	4.8	8.4	64.2	4.4	8.8
6	$(C_6H_5)_2$-P(=O)-C_6H_4-	$C_6H_4CH_3(p-)$	128-129	75	$C_{27}H_{24}N_3O_2PS$	66.8	4.9	8.7	66.4	4.8	8.4
7.	$(C_6H_5)_2$-P(=O)-CH_2-	C_6H_5	183-184	70	$C_{21}H_{20}N_3O_2PS$	61.6	4.9	10.3	61.7	4.8	10.4
8	$(C_6H_5)_2$-P(=O)-CH_5-	$C_6H_4Br(p-)$	207	75	$C_{21}H_{19}BrN_3O_2PS$	51.6	3.9	8.6	51.6	3.9	8.2
9	$(C_6H_5)_2$-P(=O)-CH_2-	$C_6H_4Cl(p-)$	203	75	$C_{21}H_{19}ClN_3O_2PS$	56.8	4.3	9.5	56.3	3.9	9.1
10	$(C_6H_5)_2$-P(=O)-CH_2-	$C_6H_4OCH_3(p-)$	200-201	70	$C_{22}H_{22}N_3O_3PS$	60.1	5.0	9.6	60.1	5.2	9.4
11	$(C_6H_5)_2$-P(=O)-CH_2-	$C_6H_4CH_3(p-)$	193	70	$C_{22}H_{22}N_3O_2PS$	62.4	5.2	9.9	62.9	5.4	10.0

Table II

Spectral Data of 1-(diphenylphosphinoacetyl)-4-aryl-3-Thiosemicarbazides.

Compound No.	Characteristic bands in Ir spectra (cm^{-1})			pmr Chemical shifts δ (ppm)		
	C=S	C=O	NH	$-CH_2-$	Aromatic	NH
7	1100	1660	3200-3300	3.6(d)	7.56(m)	10.13(m)
8	1110	1675	3150-3250	3.6(d)	7.4(m)	10.3(m)
9	1100	1680	3200-3300	3.6(d)	7.5(m)	10.16(m)
10	1100	1660	3150-3200	3.6(d)	6.85-7.63(m)	10.1(m)
11	1110	1670	3200-3300	3.6(d)	6.9-7.63(m)	10.27(m)

ra were recorded on a Unicam SP 1200 spectrophotometer using KBr-wafer technique. Proton magnetic resonance spectra were obtained on a Varian A60 instrument using deuterated dimethylsulphoxide as a solvent.

1-(Diphenylphosphinobenzoyl)- and 1-(diphenylphosphinoacetyl)-4-aryl-3-thiosemicarbazides (2-11)

To a solution of 1_a or 1_b (0.01 mole)in 25 ml absolute ethanol, the aryl isothiocyanate (0.011 mole) was added with stirring. The reaction mixture was heated under reflux for 3 hours. Excess ethanol was removed under reduced pressure. The solid obtained was filtered off, washed thoroughly with water -ethanol mixture and finally recrystallized from ethanol. These thiosemicarbazides were characterized by their elemental analyses (Table I), as well as, their spectral data (Table II).

5-Substitutedphosphino-4-aryl-3-mercapto-s-triazoles (12-21).

A mixture oi 0.01 mole of the thiosemicarbazide and 40 ml 2N sodium hydroxide solution was refluxed for 2 hours. The reaction mixture was then cooled, filtered, and the filtrate was acidified with 2N hydrochloric acid. The solid product obtained was filtered off, washed thoroughly with water and recrystallized from ethanol. The physical constants of these triazoles (12-21) are recorded in Table III.

2-Arylamino-5-substitutedphosphino-1, 2,4-thiadiazoles (22-31).

The thiosemicarbazide (0.01 mole) was added portionwise with stirring to 100 ml concentrated sulphuric acid cooled at O°C. After complete addition, the reaction mixture was stirred for additional 3 hours at room temperature and allowed to stand overnight. The solution was then poured or crushed ice, the solid obtained filtered off, washed thoroughly with water, and finally recrystallized from acetic acid. The physical constants of these thiadiazoles (22-31)are recorded in Table IV.

References

1. S.S.Parmar, A.K.Gupta,T.K. Gupta and H.H. Singh, *J.Med.Chem.* **15**, *999 (1972).*
2. S.S.Parmar,V.K.Rastogi,V.K. Agarwal,J.N.Sinah and A.Chandhari, *Can.J.Pharm.Soc.*, **9**, *107(1974)*
3. T.George,D.V.Mehta,R.Tahilramani,J.David and P.K.Talwalker, *J.Med.Chem.* **14**, *335 (1971).*
4. J.S.Kaltenbronn, *Belgian Patent 647,400 (1964); Chem.Abstr.*, **63**, *14787c (1965).*

Table-III

Physical Constants of 5-substituted phosphino-4-aryl-3-mercapto-s-Triazoles.

Compound No.	R	Ar	M.P.°C	Yield %	Molecular formula	Analysis % Calcd.% C	H	N	Found % C	H	N
12	$(C_6H_5)_2$-P(=O)-C_6H_4-	C_6H_5-	304-305	60	$C_{26}H_{20}N_3OPS$	68.9	4.4	9.3	68.6	4.5	8.9
13	$(C_6H_5)_2$-P(=O)-C_6H_4-	C_6H_4Br(p-)	271-272	60	$C_{26}H_{19}BrN_3OPS$	58.7	3.6	7.2	59.2	3.8	8.1
14	$(C_6H_5)_2$-P(=O)-C_6H_4-	C_6H_4Cl(p-)	283-285	65	$C_{26}H_{19}ClN_3OPS$	64.0	3.9	8.6	63.7	4.1	8.6
15	$(C_6H_5)_2$-P(=O)-C_6H_4-	$C_6H_4OCH_3$(p-)	254-256	70	$C_{27}H_{22}N_3PS$	67.1	4.6	8.7	66.9	5.0	8.3
16	$(C_6H_5)_2$-P(=O)-C_6H_4-	$C_6H_4CH_3$(p-)	266-268	60	$C_{27}H_{22}N_3OPS$	69.9	4.7	9.0	70.1	4.4	8.8
17	$(C_6H_5)_2$-P(=O)-CH_2-	C_6H_5-	295-296	55	$C_{21}H_{17}N_3OPS$	64.6	4.4	10.8	64.9	5.2	10.4
18	$(C_6H_5)_2$-P(=O)-CH_2-	C_6H_4Br(p-)	300-302	60	$C_{21}H_{16}BrN_3OPS$	53.7	3.4	9.0	53.5	3.7	9.2
19	$(C_6H_5)_2$-P(=O)-CH_2-	C_6H_4Cl(p-)	186-188	60	$C_{21}H_{16}ClN_3OPS$	59.4	3.8	-	59.1	3.8	
20	$(C_6H_5)_2$-P(=O)-CH_2	$C_6H_4OCH_3$(p-)	281-282	50	$C_{22}H_{19}N_3O_2PS$	62.9	4.5	10.0	62.6	4.7	9.6
21	$(C_6H_5)_2$-P(=O)-CH_2	$C_6H_4CH_3$(p-)	298-300	60	$C_{22}H_{19}N_3OPS$	65.4	4.7	10.4	65.5	4.7	10.3

Table-IV

Physical Constants of 2-arylamino-5-substitutedphosphino,1,2,4-Thiadiazoles.

Compound No.	R	Ar	M.P.°C	Yield %	Molecular formula	Analysis % Calcd. % C	H	N	Found % C	H	N
22	$(C_6H_5)_2$-P(=O)-C_6H_4-	C_6H_5-	254-255	60	$C_{26}H_{20}N_3OPS$	68.9	4.4	9.3	68.4	4.3	9.0
23	$(C_6H_5)_2$-P(=O)-C_6H_4-	C_6H_4Br(p-)	285-286	70	$C_{26}H_{19}BrN_3OPS$	58.7	3.6	7.9	59.1	3.5	7.7
24	$(C_6H_5)_2$-P(=O)-C_6H_4-	C_6H_4Cl(p-)	280-281	65	$C_{26}H_{19}ClN_3OPS$	64.0	3.9	8.6	64.1	4.0	8.3
25	$(C_6H_5)_2$-P(=O)-C_6H_4-	$C_6H_4OCH_3$(p-)	268-270	55	$C_{27}H_{22}N_3O_2PS$	-	-	8.7	-	-	8.4
26	$(C_6H_5)_2$-P(=O)-C_6H_4-	$C_6H_4CH_3$(p-)	232-233	60	$C_{27}H_{22}N_3OPS$	69.9	4.7	-	69.5	4.4	
27	$(C_6H_5)_2$-P(=O)-CH_2-	C_6H_5-	276-277	65	$C_{21}H_{17}N_3OPS$	64.6	4.4	10.8	64.2	4.2	10.4
28	$(C_6H_5)_2$-P(=O)-CH_2-	C_6H_4Br(p-)	283	60	$C_{21}H_{16}BrN_3OPS$	53.7	3.4	9.0	53.7	3.7	8.5
29	$(C_6H_5)_2$-P(=O)-CH_2-	C_6H_4Cl(p-)	250-252	65	$C_{21}H_{16}ClN_3OPS$	59.4	3.8	9.9	59.3	3.5	9.6
30	$(C_6H_5)_2$-P(=O)-CH_2-	$C_6H_4OCH_3$(p-)	299-300	65	$C_{22}H_{19}N_3O_2PS$	62.9	4.5	10.0	62.6	4.3	9.7
31	$(C_6H_5)_2$-P(=O)-CH_2-	$C_6H_4CH_3$(p-)	247-248	60	$C_{22}H_{19}N_3OPS$	65.4	4.7	10.4	64.9	5.0	10.1

5. M.W.Whitehouse and R.A.Scherrer, *"Anti-inflammatory Agents:Chemistry and Pharmacology" Vol.I, Academic Press,New York,N.Y. 1974,pp.101-104.*

6. M.El-Deek,M.A.Hassan and S. El-Hamshary, *Ain Shams Science Bulletin, 21 (A), 176-184 (1977).*

7. S.M.Kirova, *German Patent DA-18150,24 August (1977).*