[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

RHODANINE DERIVATIVES OF KETONES[1]

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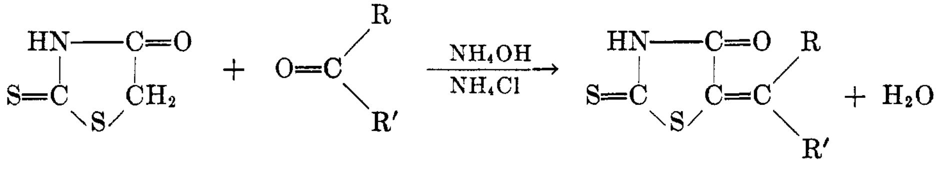
In a study of the fungicidal properties of rhodanine derivatives, an effort has been made to extend the scope of the reaction of rhodanine with carbonyl compounds. Rhodanine condenses readily with aldehydes (1) but its reaction with ketones has received little attention. Feigl (2) and Schwarz (3) state that condensations between rhodanine and ketones are possible, but neither reference contains descriptions of physical properties or analyses.[2] Certain derivatives of rhodanine with diketones have been reported (4–7) but no description of the properties of the rhodanine derivative of a simple ketone has been found in the literature.

Thirty-three representatives of various types of ketone have been condensed with rhodanine. With few exceptions, the reacting carbonyl compounds were methyl or alicyclic ketones. The second group of the methyl ketone was aliphatic, aromatic or heterocyclic.

The method of Girard (8) was used, in which the condensation takes place in an ammonium hydroxide-ethyl alcohol medium containing ammonium chloride.



EXPERIMENTAL

The condensation product was obtained by dissolving 0.15 mole each of the ketone and of rhodanine in 10 ml. of concentrated ammonium hydroxide and sufficient ethyl alcohol for a clear solution. Ten grams of ammonium chloride dissolved in 20 ml. of hot water was added and the resulting solution refluxed on a hot water- or steam-bath until evidence of reaction, usually the formation of a precipitate, was observed. The product either crystallized from solution or was precipitated by dilution with water. After filtration, it was recrystallized from ethyl alcohol, dioxane, acetone, benzene or a suitable mixture of solvents. No effort was made to find optimum conditions for the preparation of individual compounds. The yields varied with the nature of the ketone, being higher with the aliphatic ketones, but averaged about 30%. The melting points and analyses of the individual condensation products are recorded in Table I.

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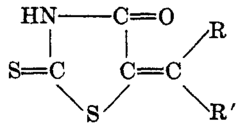
[1] The work described in this paper was done under contract with the Medical Division, Chemical Corps, U. S. Army.

[2] A condensation product between acetone and rhodanine has been mentioned in connection with an unsuccessful attempt to synthesize penicillamine, but no description of the compound is included (9).

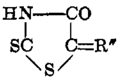
TABLE I

PROPERTIES OF RHODANINE DERIVATIVES



R	R′	M.P., °C. uncor.	ANALYSES			
			Calc'd		Found[a]	
			C	H	C	H
Methyl	Methyl	196–197	41.59	4.07	41.68	3.78[b]
Methyl	Ethyl	119–120	44.89	4.84	45.09	4.72[b]
Methyl	Propyl	120–121	47.73	5.51	47.84	5.63
Methyl	Isopropyl	192–192.5	47.73	5.51	47.79	5.48
Methyl	Butyl[c]	118–119	50.20	6.08	50.44	6.08
Methyl	Isobutyl	97–99	50.20	6.08	50.12	6.41[b]
Methyl	Amyl	120.5–122.0	52.38	6.59	52.52	6.51[b]
Methyl	Hexyl	107–108	54.28	7.04	54.47	7.00
Methyl	Nonyl	106–107	58.90	8.12	58.58	7.90
Ethyl	Ethyl	123	47.73	5.51	48.16	5.30[d]
Methyl	Benzyl	155[e]	57.83	4.45	57.86	4.53
Methyl	Styryl	192–194	59.74	4.24	59.66	4.15
Methyl	β-Naphthoxymethyl	188–190	60.93	4.15	60.84	4.15
Methyl	Phenyl	165–166	56.14	3.86	55.85	3.92[b]
Methyl	*p*-Tolyl	175–176	57.83	4.45	58.16	4.50[b]
Methyl	*p*-Chlorophenyl	204	48.97	2.99	49.36	3.30[b]
Methyl	*p*-Bromophenyl	215–216 d.	42.04	2.57	42.14	2.71
Ethyl	Phenyl	146–147	57.83	4.45	58.06	4.64[b]
Methyl	2-Thienyl	218–221.5 d.	44.79	2.92	45.32	2.70[b,f]
Methyl	2-(5-Chlorothienyl)	205	39.19	2.19	39.32	2.19[g]
Methyl	2-(5-Bromothienyl)	214–215 d.	33.75	1.89	33.97	2.05[g]
Methyl	2-(5-*tert*-Butylthienyl)	192–193	52.49	5.08	52.50	4.91[g]
Methyl	2-Furyl	243.5–244.5	47.98	3.13	47.60	2.63[h]
Methyl	2-(5-Methylfuryl)	248 d.	50.19	3.79	50.30	3.64[g]
Methyl	β-Furylvinyl	210–214 d.	52.57	3.61	52.69	3.73
Ethyl	Furyl	180.5–181.0	50.19	3.79	50.21	3.73[h,b]
Propyl	Furyl	159.5–160.5	52.15	4.38	52.13	4.60[h]

R″ in



Cyclohexylidene	172–173	50.67	5.20	50.95	5.08
2-Methylcyclohexylidene	141–143	52.83	5.76	52.76	5.99
3-Methylcyclohexylidene	146–148	52.83	5.76	52.94	5.60
4-Methylcyclohexylidene	149–150	52.83	5.76	53.17	5.72
4-*tert*-Amylcyclohexylidene	182–183	59.32	7.47	59.45	7.37[i]
Cyclopentylidene	195–196	48.21	4.55	48.44	4.55

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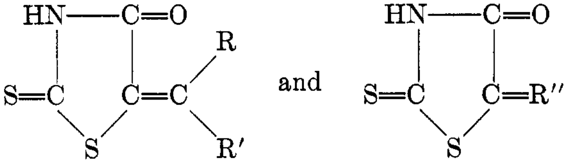
[a] All analyses by Clark Microchemical Laboratory unless otherwise noted. [b] Analyses by University of Pittsburgh Microchemical Laboratory. [c] Ketone prepared by R. J. Grantham. [d] S: Calc'd, 31.85; found, 31.85. [e] Some crystals, m.p. 130–134°, were also obtained. [f] S: Calc'd, 39.85; found, 39.83. [g] Ketone prepared by method of Hartough and Kosak, *J. Am. Chem. Soc.*, **69**, 3093 (1947). We are indebted to the Socony-Vacuum Co. for some of the thiophene compounds used in this work. [h] Ketone supplied by Dr. Robert Levine. [i] Ketone obtained by $K_2Cr_2O_7$-H_2SO_4 oxidation of 4-*tert*-amylcyclohexanol, following the general procedure of Grove and Bovington, *Ann. Applied Biol.*, **34**, 115 (1947) for the preparation of 4-*tert*-butylcyclohexanone; b.p., 75°/27.

SUMMARY

The condensation of rhodanine with carbonyl compounds has been extended to include derivatives of simple ketones. Products of the general formula



have been obtained.

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