portions. After cooling, filtering, and washing under carbon dioxide with water, ethanol and ether, 2.69 g. of clustered needles was obtained. The product was recrystallized by the addition of 2 ml. of concentrated hydrochloric acid to its solution in a hot mixture of 115 ml. of methanol and 10 ml. of water. It was found to be a hydrochloride with a melting point at about 270°. It is soluble in *N* sodium hydroxide.

Anal. Calcd. for $C_{11}H_{12}ON_4S \cdot HCl$: C, 46.39; H, 4.60; N, 19.68. Found: C, 46.46; H, 4.71; N, 19.51.

1-(4-Acetamidobenzyl)-3-thiosemicarbazide (VI).—To a suspension of 23.6 g. (0.1 mole) of I in 400 ml. of liquid ammonia was added in small pieces 7.3 g. of sodium. A clear solution resulted, after the addition of the first few pieces. By adding 0.6 g. of ammonium chloride, the persistent blue color was discharged. The residue obtained after evaporation was taken up with 200 g. of ice-water and the insoluble material was filtered and washed with water, ethanol and ether; yield 11.18 g. (47%), m.p. 209° (dec.). After recrystallization from 800 ml. of 50% methanol, the product melted at 217–218°. It is insoluble in *N* hydrochloric acid and alkali.

Anal. Calcd. for $C_{10}H_{14}ON_4S$: C, 50.40; H, 5.92; N, 23.51. Found: C, 50.68; H, 5.92; N, 23.24.

RESEARCH LABORATORIES
HOFFMANN-LA ROCHE INC.
NUTLEY 10, N. J.

RECEIVED APRIL 23, 1951

Condensation of Nitroparaffins with α,β-Unsaturated Ketones Using Calcium Hydride[1]

BY NORTON FISHMAN[2] AND SAVERIO ZUFFANTI

Introduction.—Kloetzel,[3] in 1947, used diethylamine as a condensing agent for the reaction between nitroparaffins and α,β-unsaturated ketones. At room temperature he obtained yields of 58–97.5% in 6–35 days.

The basic character of calcium hydride[4] led us to investigate its efficacy as a condensing agent in this reaction. 2-Nitropropane, benzalacetophenone and calcium hydride produced no reaction even on prolonged standing over a period of several weeks.

In the presence of methanol, however, an immediate reaction results and within 15 hours a 92% yield of 4-methyl-4-nitro-1,3-diphenyl-1-pentanone is obtained. Nitromethane, 1-nitropropane and 2-nitropropane were condensed with benzalacetone and benzalacetophenone using calcium hydride and methanol. At room temperature the reactions were complete in from 1–21 days and the yields ranged from 65–92%.

Experimental

Purification of Materials.—The methanol and nitroparaffins were purified by allowing them to stand over calcium hydride for several weeks and then filtering and fractionating.

It was noted that although the hydride will not react with the pure alcohol or nitroparaffins individually, an instantaneous evolution of hydrogen is observed if the hydride is added to a mixture of the alcohol and the nitroparaffin. From the reaction mixture can be recovered the entire quantity of alcohol and the calcium salt of the nitroparaffin. The benzalacetone and benzalacetophenone were purified by repeated recrystallizations.

(1) Presented before the Chicago Meeting of the American Chemical Society, September 8, 1950. This note is part of the thesis presented by Norton Fishman to Northeastern University, in partial fulfillment of the requirements of the A.M. degree.

(2) Harvard University, Cambridge, Mass.

(3) M. C. Kloetzel, THIS JOURNAL, **69**, 2271 (1947).

(4) S. Zuffanti and J. Sardella, *ibid.*, **72**, 4322 (1950).

4-Methyl-4-nitro-1,3-diphenyl-1-pentanone.—Into a 250 ml. flask are placed 10 g. (0.048 mole) of benzalacetophenone, 44 g. (0.49 mole) of 2-nitropropane and 40 ml. of dry methanol. These are mixed thoroughly till the ketone is dissolved and 2 g. (0.048 mole) of calcium hydride is added. Thereafter continuous evolution of hydrogen is observed while the reaction progresses.[5] The mixture is allowed to stand stoppered with a calcium chloride tube for 24 hours, and then the solidified contents are extracted with anhydrous chloroform. The extract is concentrated and the crystals are filtered off, washed with alcohol, and dried. The product, 4-methyl-4-nitro-1,3-diphenyl-1-pentanone, melts at 133–135°. Yields of 85–92% are obtained. The purified crystals melt at 146°.

(5) Note the order of addition, for when calcium hydride is added before the ketone, little or no reaction product is obtained.

DEPARTMENT OF CHEMISTRY
NORTHEASTERN UNIVERSITY
BOSTON, MASS.

RECEIVED MAY 2, 1951

5-Methyl-2-nitraminopyridine

BY LUTHER A. R. HALL AND CALVIN A. VANDERWERF

In the course of work aimed toward the synthesis of certain pyridotriazoles, it was of interest to prepare a number of new compounds derived from 2-aminopyridine. All of these except 5-methyl-2-nitraminopyridine have since been reported by Lappin and Slezak.[1]

5-Methyl-2-nitraminopyridine.—The nitration of 5 methyl-2-aminopyridine was carried out by a modification of the general method of Seide.[2] To a cold (0–5°) solution of 15.0 g. (0.139 mole)[3] of 5-methyl-2-aminopyridine[4] in 33 ml. of concentrated sulfuric acid, 9 g. of fuming nitric acid (sp. gr. 1.50) was added carefully with efficient stirring. The nitration mixture was allowed to stand for 2 hours in an ice-bath during which time its color changed from light yellow to dark orange-brown. It was then poured onto about 75 g. of ice. The product, which came down as a yellow precipitate, weighed 14.9 g. (70.0%). After three recrystallizations from water, the pure product melted at 183.0–183.5° (dec.).

Anal. Calcd. for $C_6H_7N_3O_2$: C, 47.1; H, 4.6. Found: C, 47.1; H, 4.6.

(1) G. R. Lappin and F. B. Slezak, THIS JOURNAL, **72**, 2806 (1950).

(2) O. Seide, *Ber.*, **57**, 791 (1924); *ibid.*, **57**, 1802 (1924).

(3) Small scale runs were preferred in order that adequate cooling might be maintained. The reaction is extremely exothermic, with the product decomposing at temperatures above 50°.

(4) Obtained from the Reilly Tar and Chemical Corp.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF KANSAS
LAWRENCE, KANSAS

RECEIVED APRIL 9, 1951

The Preparation of Some Substituted 2-Thiouracils and 2,4-Dimercaptopyrimidines

BY ELVIRA A. FALCO, PETER B. RUSSELL AND GEORGE H. HITCHINGS

The discovery of the chemotherapeutic activity of certain 5-phenoxy-2-thiouracils (I)[1] against vaccinia virus prompted the preparation of a series of 5-phenoxy, and other 2-thiouracils carrying weighty substituents at the 5- or 6-position.

The preparations of these compounds were carried out by conventional methods.[2,3] The compounds are listed in Table I.

(1) R. L. Thompson, S. A. Minton, Jr., E. A. Falco and G. H. Hitchings, *Federation Proc.*, **10**, 421 (1951); *J. Immunol.*, in press (1951).

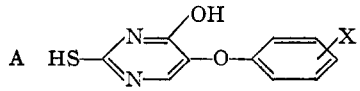
(2) T. B. Johnson and H. H. Guest, *Am. Chem. J.*, **42**, 271 (1909).

(3) T. B. Johnson and J. C. Ambelang, THIS JOURNAL, **60**, 2941 (1938).

TABLE I

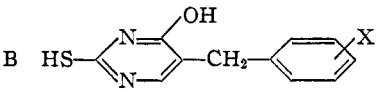
2-THIOURACILS

A



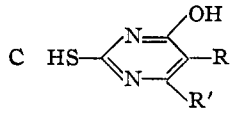
X	Formula	M.p.,[b] °C.	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N	Solvent
2-Cl	$C_{10}H_7ClN_2O_2S$	268–270			11.0			10.7	80% EtOH
4-Cl	$C_{10}H_7ClN_2O_2S$	267–268	47.2	2.8		47.3	2.9		95% EtOH
4-Br	$C_{10}H_7BrN_2O_2S$	284–285	40.1	2.3		40.5	2.4		50% EtOH
4-I	$C_{10}H_7IN_2O_2S$	274–275			8.1			8.5	95% EtOH
2,4-diCl	$C_{10}H_6Cl_2N_2O_2S$	266–267	41.5	2.1	9.7	42.0	2.3	9.7	80% EtOH
2,4-diBr	$C_{10}H_6Br_2N_2O_2S$	270–271	31.7	1.6		32.1	1.9		95% EtOH
2,4,5-triCl	$C_{10}H_5Cl_3N_2O_2S.H_2O$[a]	310			8.2			8.1	EtOH
3-CH_3,4-Cl	$C_{11}H_9ClN_2O_2S$	250–252	49.2	3.4	10.4	48.9	3.8	10.2	Pptd. from dil. NaOH with AcOH
3-CH_3	$C_{11}H_{10}N_2O_2S$	252–253	56.4	4.3	12.0	56.8	4.2	12.2	Pptd. from dil. NaOH with AcOH
3,4-diCH_3	$C_{12}H_{12}N_2O_2S$	250–255			11.3			11.3	Pptd. from dil. NaOH with AcOH
2-Cl,4-C$(CH_3)_3$	$C_{14}H_{15}ClN_2O_2S$	206–208	54.1	4.8	9.0	53.8	4.7	9.1	EtOH
4-C$(CH_3)_3$	$C_{14}H_{16}N_2O_2S$	266–267			10.1			10.3	50% EtOH
4-OCH_3	$C_{11}H_{10}N_2O_3S$	174–178	52.8	4.0	11.2	53.3	4.3	11.2	MeOH
4-COOEt	$C_{13}H_{12}N_2O_4S$	242–246	53.4	4.1	9.6	54.0	3.9	9.8	50% EtOH
2-$CH(CH_3)_2$, 4-Cl,5-CH_3	$C_{14}H_{15}ClN_2O_2S$	244–251	54.1	4.8	9.0	54.4	5.0	9.2	AcOH
4-C_6H_5	$C_{16}H_{12}N_2O_2S$	298–301			9.5			9.3	AcOH
3,4-CH=CH—CH=CH—	$C_{14}H_{10}N_2O_2S$	250–270	62.2	3.7	10.4	62.1	3.8	9.8	MeOH
4-$OCH_2C_6H_5$	$C_{17}H_{14}N_2O_3S$	245–255	62.6	4.3	8.6	63.0	4.2	8.6	EtOH

B



4-Cl	$C_{11}H_9ClN_2OS$	266–271			11.1			10.8	95% EtOH
4-$N(CH_3)_2$	$C_{13}H_{15}N_3OS$	209–210	59.8	5.7		59.6	5.7		95% EtOH
4-OCH_3	$C_{12}H_{12}N_2O_2S$	222–223	58.1	4.8		57.8	4.7		95% EtOH
4-CH_3	$C_{12}H_{12}N_2OS$	240–243	62.1	5.2		62.0	5.0		95% EtOH
3-OCH_3,4-$OCH_2C_6H_5$	$C_{19}H_{18}N_2O_3S$	210–211	64.4	5.1		64.6	5.8		95% EtOH

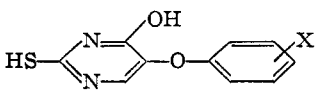
C



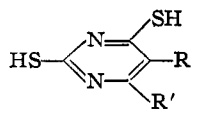
R	R′								
H	-$C_6H_4Cl(4)$	$C_{10}H_7ClN_2OS$	281–282	50.3	2.9	11.7	50.8	2.8	11.6	EtOH–Me_2CO–H_2O (1:1:2)
CH_3[c]	-$C_6H_4Cl(4)$	$C_{11}H_9ClN_2OS$	290–291	52.3	3.6	11.1	52.2	3.6	11.4	EtOH–H_2O (1:1)

[a] Calcd. for H_2O; 5.3; found, 4.8. [b] With decomposition. [c] The ethyl α-methyl-p-chlorobenzoylacetate required for the preparation of this compound was prepared by the action of methyl iodide on ethyl p-chlorobenzoylacetate (Thorpe and Brunskill, THIS JOURNAL, **37**, 1261 (1915)). It boiled at 195–204° (20 mm.). *Anal.* Calcd. for $C_{12}H_{13}ClO_3$: C, 59.9; H, 5.4. Found: C, 59.5; H, 5.5.

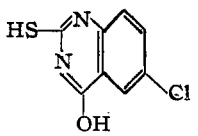
Several of these thiouracils were converted to the corresponding dimercaptopyrimidines (II) by the action of phosphorus pentasulfide.[4,5]



I



II



III

Experimental

2-Thiouracils.—These compounds were prepared by the condensation of thiourea with the sodium salt of the required β-carbonyl ester in ethanol.[2,3] The preparations of the requisite esters have been described.[6,7]

(4) G. B. Elion and G. H. Hitchings, *ibid.*, **69**, 2138 (1947).

(5) P. B. Russell, G. B. Elion, E. A. Falco and G. H. Hitchings, *ibid.*, **71**, 2279 (1949).

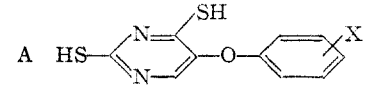
(6) E. A. Falco, P. B. Russell and G. H. Hitchings, *ibid.*, **73**, 3753 (1951).

(7) E. A. Falco, S. DuBreuil and G. H. Hitchings, *ibid.*, **73**, 3758 (1951).

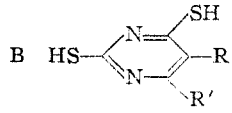
TABLE II

2,4-DIMERCAPTOPYRIMIDINES

A



B



X	R	R	Formula	M.p.,[b] °C.	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N	Solvent
4-Cl			$C_{10}H_7ClN_2OS_2$	292–294	44.4	2.6	10.4	44.3	2.3	10.6	Ppt'd. from dil. NaOH with AcOH
2,4-diCl			$C_{10}H_6N_2Cl_2OS_2$	271–275	39.3	2.0	9.2	39.8	2.4	8.8	EtOH
3-CH_3,4-Cl			$C_{11}H_9ClN_2OS_2$	285–287	46.4	3.2	9.8	46.8	3.2	10.3	EtOH
2-Cl,4-$C(CH_3)_3$			$C_{14}H_{15}ClN_2OS_2$				8.6			8.2	MeOH
	-$CH_2C_6H_4Cl(4)$	H	$C_{11}H_9ClN_2S_2$	255	49.2	3.4	10.4	49.6	3.5	10.8	EtOH
	-$C_6H_3Cl_2(3,4)$[a]	H	$C_{10}H_6Cl_2N_2S_2$	300–303	41.5	2.1	9.7	41.9	2.2	9.7	EtOH
	-H	-$C_6H_4Cl(4)$	$C_{10}H_7ClN_2S_2$	277–278			11.0			11.4	EtOH
	-CH_3	-$C_6H_4Cl(4)$	$C_{11}H_9ClN_2S_2$	265–266	49.2	3.4		49.2	3.4		EtOH

[a] Prepared from 5-(3',4'-dichlorophenyl)-2-thiouracil (P. B. Russell and G. H. Hitchings, THIS JOURNAL, 73, 3763 (1951). [b] With decomposition.

2,4-Dimercaptopyrimidines.—These compounds were prepared by the treatment of the corresponding thiouracil with phosphorus pentasulfide.[4,5]

6-Chloro-4-hydroxy-2-mercaptoquinazoline.—6-Chlorobenzoyleneurea[8,9] was converted to the 4-hydroxy-2-mercaptoquinazoline by the method described earlier.[5] The benzoyleneurea on treatment with phosphorus pentasulfide, gave 6-chloro-2,4-dimercaptoquinazoline which sublimes at 300–350° (not molten below 350°).

Anal. Calcd. for $C_8H_5ClN_2S_2$: C, 42.0; H, 2.2. Found: C, 41.8; H, 2.2.

Treatment of this compound with concentrated ammonium hydroxide solution on the steam-bath gave 4-amino-6-chloro-2-mercaptoquinazoline, which crystallizes from water as needles melting at 300–305° (dec.).

Anal. Calcd. for $C_8H_6ClN_3S$: C, 45.4; H, 2.8. Found: C, 45.1; H, 3.0.

On refluxing this compound with 3 *N* hydrochloric acid, 6-chloro-4-hydroxy-2-mercaptoquinazoline was obtained as colorless needles from water, m.p. 353–354° (dec.).

Anal. Calcd. for $C_8H_5ClN_2OS$: C, 45.2; H, 2.4. Found: C, 45.4; H, 2.3.

Acknowledgment.—We wish to thank S. W. Blackman and N. Martinez, Jr., for the microanalyses reported here.

(8) R. L. McKee, M. K. McKee and R. W. Bost, *ibid.*, **69**, 940 (1947).

(9) F. H. S. Curd, J. K. Landquist and F. L. Rose, *J. Chem. Soc.*, 1759 (1948).

THE WELLCOME RESEARCH LABORATORIES
TUCKAHOE, NEW YORK RECEIVED APRIL 13, 1951

Catalyst Specificity in Friedel–Crafts Copolymerization

BY R. E. FLORIN

It has been established recently that copolymerization of two vinyl monomers can proceed by three different mechanisms—free-radical, carbonium-ion and carbanion—which depend upon the catalyst used and lead to products of different composition.[1] The relative rates at which two monomers M_1 and M_2 enter the polymer are given in all cases by the copolymerization equation

$$\frac{d[M_1]}{d[M_2]} = \frac{[M_1]\,r_1[M_1] + [M_2]}{[M_2]\,r_2[M_2] + [M_1]}$$

where $[M_1]$ and $[M_2]$ are concentrations of monomers and r_1 and r_2 are certain ratios of rate constants, but the numerical values of r_1 and r_2 differ sharply for the three mechanisms.

When a given pair of monomers is copolymerized by any free-radical catalyst, *e.g.*, persulfate ion or any organic peroxide, the reactivity parameters r_1 and r_2 are found to be strictly constant for the monomer pair and temperature, regardless of the solvent or specific catalyst employed. It was desired to test whether a similar constancy would hold for all catalysts of the Friedel–Crafts type, which are thought to effect polymerization by a carbonium-ion mechanism. In the present study, mixtures of styrene (M_1) and 3,4-dichlorostyrene (M_2) were copolymerized at 0° with the catalysts aluminum chloride, aluminum bromide, stannic chloride, titanium tetrachloride, boron fluoride, zinc chloride (at 30°) and sulfuric acid, and the values of r_1 and r_2 were calculated from analytical data by the method of Mayo and Lewis.[2]

Experimental

General methods of polymerization, purification and analysis have been reported in an earlier note.[3] In most experiments of the present series, the solvent was carbon tetrachloride. Monomer mixtures, of composition identified by the numerals and described in Table I, were diluted with an equal volume of carbon tetrachloride (unless otherwise specified) and polymerized by adding small portions of catalyst solutions identified by letter symbols and described below. In the more rapid experiments, temperature control was probably not very satisfactory; during the addition of typical portions of aluminum chloride and bromide solutions to styrene, the temperature rose from 0 to 5°. After sufficient reaction, the whole product was diluted, precipitated with methanol, purified by double reprecipita-

(1) For a comprehensive review, see F. R. Mayo and C. Walling, *Chem. Revs.*, **46**, 191 (1950).

(2) F. R. Mayo and F. M. Lewis, THIS JOURNAL, **66**, 1594 (1944).

(3) R. E. Florin, *ibid.*, **71**, 1867 (1949).