providing a proton for initial coordination with the nitrogen of the Schiff base.

The results of this investigation seem to favor the second possible mechanism by analogy to reduction by means of sodium borohydride, since the reducing power of dimethylamine borane in glacial acetic acid is much more like that of sodium borohydride than to that of diborane in diethylene glycol dimethyl ether or tetrahydrofuran.

The stoichiometry study further supports the selectivity of this reduction since in all cases a three- to four-fold excess of the reducing agent was used.

EXPERIMENTAL

Reduction method A. Ten grams of the Schiff base were suspended in 20 ml. of glacial acetic acid in a three-necked flask fitted with a reflux condenser, magnetic stirrer, thermometer, and dropping funnel and placed in a cold water bath. An equimolar amount plus 25% excess of the dimethylamine borane was dissolved in 20 ml. of glacial acetic acid and this solution added slowly through the dropping funnel to the Schiff base suspension keeping the temperature approximately at 20°. After the addition was complete, the reaction mixture was heated under reflux for an additional 15 min. and allowed to cool. If precipitation had not occurred, cold water was added slowly until precipitation was complete. The precipitate was collected by suction filtration, washed with cold water, and dried.

Reduction method B. The reduction was performed as in Method A except that when water was added to the cool reaction mixture an oil resulted. The reaction mixture was then completely neutralized with sodium hydroxide and the oil was extracted with diethyl ether. The ether extracts were dried over anhydrous magnesium sulfate and the ether removed under reduced pressure. The remaining oil was crystallized from petroleum ether or an ethanol-water mixture.

Preparation of acetyl derivatives. The acetyl derivatives were prepared from acetic anhydride and pyridine by the usual method and recrystallized from cyclohexane, cyclohexane-benzene, or ethanol-water mixtures.

Acknowledgment. The authors wish to thank the Callery Chemical Company, Callery, Pa., for samples of dimethylamine borane which were used in this investigation.

BLOOMINGTON, IND.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY]

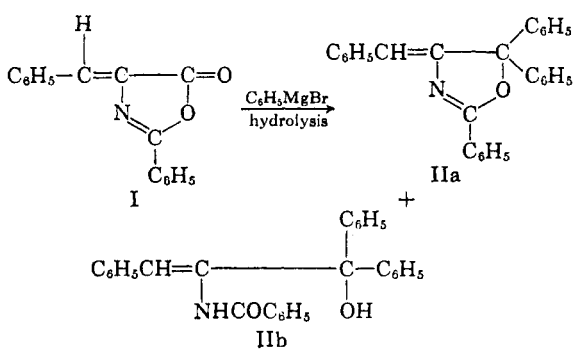
Action of Organomagnesium Compounds, Piperidine, and Aromatic Thiols on 4-Arylazo-2-phenyloxazolin-5-ones

WAFIA ASKER AND ZIEN E. ELAGROUDI

Received June 16, 1960

Treatment of 4-arylazo-2-phenyloxazoline-5-ones (Va-d) with organomagnesium compounds, followed by hydrolysis, effected the opening of the heterocyclic ring and cyclization to the corresponding 1-aryl-5-phenyl-3-diarylmethanol-1*H*-1,2,4-triazoles (VId-h). Similarly, Va-d are rapidly rearranged by the action of piperidine and by the action of aromatic thiols to give 1-aryl-5-phenyl-3-carbpiperide-1*H*-1,2,4-triazoles (VIIa-d) and 1-aryl-5-phenyl-3-arylthiocarboxy-1*H*-1,2,4-triazoles (VIIIa-e).

Although the reaction of 2-phenyl-4-benzylidene-5-(4H)-oxazolone (I) with excess of phenylmagnesium bromide, yielding a mixture of 2,5,5-triphenyl-4-benzylidene-2-oxazoline (IIa) and 1,1-diphenyl-2-benzamidocinnamyl alcohol (IIb), has been widely studied,[1] little attention has been paid to the study of the behavior of the corresponding hydrazone derivatives (V) toward the same reagent.



Recently, it has been shown[2] that 4-phenylazo-2-phenyloxazoline-5-one (Va) is rapidly rearranged by methanolic potassium hydroxide or methanolic ammonia with the formation of 1,5-diphenyl-3-carboxy-1*H*-1,2,4-triazole (VIa) and 1,5-diphenyl-3-carbamido-1*H*-1,2,4-triazole (VIc) respectively.

A similar rearrangement was also reported[3] when 4-benzylidene-2-thio-5-thiazolidone (III) was treated with potassium hydroxide, sodium alkoxides, or primary or secondary amines, giving respectively the 5-substituted 2-thiothiazolidone-4-carboxylic acid (IV), ester and or *N*-substituted amides.

We have now investigated the behavior of 4-arylazo-2-phenyloxazoline-5-ones (Va-d) toward

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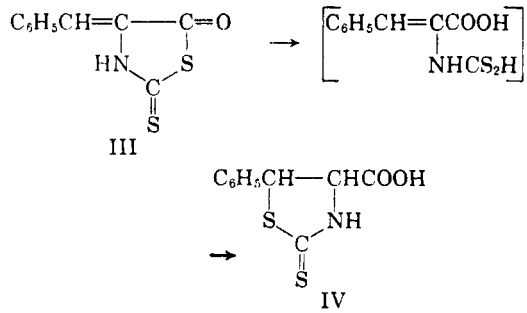
(1) H. Pourrat, *Bull. soc. chim. France*, 828 (1955), A. Mustafa and A. H. E. S. Harhash, *J. Org. Chem.*, 21, 575 (1956), R. Filler and J. D. Wismar, *J. Org. Chem.*, 22, 853 (1957).

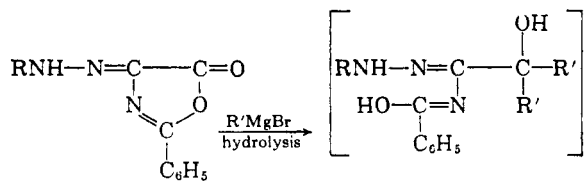
(2) G. W. Sawdey, *J. Am. Chem. Soc.*, 79, 1955 (1957).

(3) I. M. H. Heilbron, *J. Chem. Soc.*, 2102 (1949), J. D. Billmoria and A. H. Cook, *J. Chem. Soc.*, 2323 (1949).



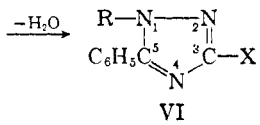
III IV

the action of organomagnesium compounds. Thus, when 4-phenylazo-2-phenyloxazoline-5-one (Va) is treated with excess of phenylmagnesium bromide, opening of the heterocyclic ring is effected, followed by cyclization to give 1,5-diphenyl-3-diphenylmethanol-1*H*-1,2,4-triazole (VId) (*cf.* Scheme A).



(V)

a. R = C_6H_5
b. R = *o*-$CH_3C_6H_4$
c. R = *p*-$CH_3C_6H_4$
d. R = β-$C_{10}H_7$



VI (Scheme A)

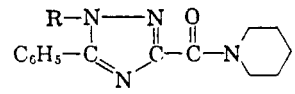
a. R = C_6H_5	X = COOH
b. R = C_6H_5	X = $COOCH_3$
c. R = C_6H_5	X = $CONH_2$
d. R = C_6H_5	X = $C(C_6H_5)_2OH$
e. R = C_6H_5	X = $(p\text{-}CH_3C_6H_4)_2OH$
f. R = *o*-$CH_3C_6H_4$	X = $C(C_6H_5)_2OH$
g. R = *p*-$CH_3C_6H_4$	X = $C(C_6H_5)_2OH$
h. R = β-$C_{10}H_7$	X = $C(C_6H_5)_2OH$

Similar treatment of Vb-d with the same reagent results in the formation of the corresponding substituted I*H*-1,2,4-triazole derivatives (VIf-h) respectively. Treatment of Va with excess of *p*-tolylmagnesium iodide leads to the formation of 1,5-diphenyl-3-di(*p*-tolyl)methanol-I*H*-1,2,4-triazole, VIe.

The reaction appears to be a general and convenient route to I*H*-1,2,4-triazoles of the general type VId-h. No compounds represented by VId-h appear to have been described previously. The properties of the examples prepared in this work are recorded in Table II.

The structures of the I*H*-1,2,4-triazoles (VId-h) were established by elemental analysis and the fact that they are colorless. Further confirmation was obtained by the synthesis of 1,5-diphenyl-3-diphenylcarbinol-I*H*-1,2,4-triazole (VId) *via* the action of phenylmagnesium bromide on 1,5-diphenyl-3-carbomethoxy-I*H*-1,2,4-triazole (VIb). This product proved to be identical with that obtained from the reaction of the same reagent with Va (see above).

4-Arylazo-2-phenyloxazoline-5-ones (Va-d) rearranges readily with piperidine to give the corresponding 1-aryl-5-phenyl-3-carbpiperide-I*H*-1,2,-4-triazole (VIIa-d). The reactions appears to proceed by opening of the heterocyclic ring, followed by cyclization[4] to VII.



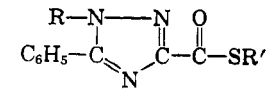
VII

a. R=C_6H_5
b. *o*-$CH_3C_6H_4$
c. *p*-$CH_3C_6H_4$
d. β-$C_{10}H_7$

The assigned structures for the products VIIa-d, were inferred from the facts that they are colorless, insoluble in aqueous sodium hydroxide solution, and gave the correct analytical values. When, VIIa is treated with methanolic potassium hydroxide solution, 1,5-diphenyl-3-carboxy-I*H*-1,-2,4-triazole (VIa) was obtained. The identity of VIa was established by comparison with an authentic sample prepared after Sawdey.[2]

Similar rearrangement has now been observed when Va-d are treated with aromatic thiols, to give the corresponding 1-aryl-5-phenyl-3-arylthiocarboxy-I*H*-1,2,4-triazoles(VIIIa-e). The reaction appears to proceed by opening of the 2-phenyloxazoline-5-one ring[5] and cyclization to VIII.

VIIIa-e are colorless, insoluble in aqueous sodium hydroxide solution and give the correct analytical values. When VIIIb is treated with methanolic potassium hydroxide solution, VIa is obtained together with *p*-thiocresol.



VIII

a. R = R′ = C_6H_5
b. R = C_6H_5, R′ = *p*-$CH_3C_6H_4$
c. R = *o*-$CH_3C_6H_4$, R′ = *p*-$CH_3C_6H_4$
d. R = R′ = *p*-$CH_3C_6H_4$
e. R = β-$C_{10}H_7$, R′ = *p*-$CH_3C_6H_5$

EXPERIMENTAL

Action of Grignard reagents on 4-arylazo-2-phenyloxazoline 5-ones (Va-d). The following exemplifies the procedure. A suspension of 1 g. of Va[2] in dry benzene (50 ml.) was added to a solution of phenylmagnesium bromide (prepared from 0.9 g. of magnesium, 9 g. of bromobenzene and 50 ml. of dry ether). The reaction mixture was heated on a steam bath for 3 hr. After standing overnight at 25°, it was poured slowly into 100 ml. of saturated aqueous ammonium chloride solution, extracted with ether, dried, and evaporated. The oily residue was washed several times with hot petroleum

(4) H. T. Clarke, J. R. Johnson, and R. Robinson, *The Chemistry of Penicillin*, Princeton University Press, Princeton, N. J., 1949, p. 735.

(5) *Cf.* ref. 4, p. 737.

TABLE I

4-ARYLAZO-2-PHENYLOXAZOLIN-5-ONE (V)

4-Arylazo derivative	M.P.[a]	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
Vb[b]	166	65	$C_{16}H_{13}N_3O_2$	68.81	68.87	4.66	4.67	15.05	15.07
Vc[b]	215	60	$C_{16}H_{13}N_3O_2$	68.81	68.51	4.66	4.32	15.05	15.01
Vd[c]	230	60	$C_{19}H_{13}N_3O_2$	72.38	71.84	4.12	4.02	13.33	13.64

TABLE II

1-ARYL-5-PHENYL-3-DIARYLMETHANOL-1*H*-1,2,4-TRIAZOLES (VId-h)

4-Arylazos derivative	Product	M.P.[a]	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
Va	VId	180	60	$C_{27}H_{21}N_3O$	80.39	80.08	5.21	5.09	10.42	10.16
Va	VIe	189	70	$C_{29}H_{25}N_3O$	80.74	80.28	5.80	5.74	9.74	9.85
Vb	VIf	152	60	$C_{28}H_{23}N_3O$	80.57	79.91	5.51	5.42	10.07	10.05
Vc	VIg	145	55	$C_{28}H_{23}N_3O$	80.57	79.83	5.51	5.63	10.07	9.96
Vd	VIh	201	50	$C_{31}H_{23}N_3O$	82.11	81.48	5.29	4.96	9.27	9.46

TABLE III

1-ARYL-5-PHENYL-3-CARBPIPERIDE-1*H*-1,2,4-TRIAZOLES (VII)

4-Arylazos derivative	Product	M.P.[a]	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
Va	VIIa	193	94	$C_{20}H_{20}N_4O$	72.29	72.43	6.02	5.95	16.86	16.59
Vb	VIIb	127	90	$C_{21}H_{22}N_4O$	72.83	72.96	6.36	6.27	16.18	16.05
Vc	VIIc	141	82	$C_{21}H_{22}N_4O$	72.83	72.25	6.36	6.10	16.18	16.22
Vd	VIId	130	77	$C_{24}H_{22}N_4O$	75.39	75.11	5.76	5.77	14.66	14.44

TABLE IV

1-ARYL-5-PHENYL-3-ARYLTHIOCARBOXY-1*H*-1,2,4-TRIAZOLES (VIII)

4-Arylazos derivative	Product	M.P.[a]	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Sulfur, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
Va	VIIIa	146	41	$C_{21}H_{15}N_3OS$	70.58	70.86	4.20	4.48	11.76	11.47	8.96	8.53
Va	VIIIb	195	62	$C_{22}H_{17}N_3OS$	71.15	71.25	4.58	4.45	11.32	11.05	8.62	8.90
Vb	VIIIc	181	55	$C_{23}H_{19}N_3OS$	71.68	71.24	4.93	4.81	10.90	10.81	8.31	8.04
Vc	VIIId	177	41	$C_{23}H_{19}N_3O_3$	71.68	70.81	4.93	4.90	10.90	10.71	8.31	8.07
Vd	VIIIe	183	46	$C_{26}H_{19}N_3OS$	74.10	74.07	4.51	4.42	9.97	9.70	7.60	7.34

[a] Melting points are uncorrected. [b] Orange-yellow crystals. [c] Brown-red needles.

ether (b.p. 60–80°) and the resulting solid (VId) was crystallized from ethanol, m.p. 180°.

The products VId-h listed in Table II were thus prepared. In general, they are soluble in hot benzene and chloroform, but are sparingly soluble in petroleum ether, and give a deep red color with sulfuric acid.

Action of phenylmagnesium bromide on 1,5-diphenyl-3-carbomethoxy-1H-1,2,4-triazole (VIb). A solution of 1 g. of VIb[2] in 40 ml. of dry benzene was treated with phenylmagnesium bromide as described above. The ether-benzene solution was evaporated and the solid residue was crystallized from hot alcohol as colorless crystals (*ca.* 0.61 g.), m.p. 180°, identified as VId.

Reaction of 4-arylazo-2-phenyloxazoline-5-ones (Va-d) *with piperidine.* A 0.5-g. sample of Va[2] was added to 0.5 ml. of freshly distilled piperidine. An exothermic reaction took place; after shaking for 15 min. a clear solution was obtained which was kept at room temperature overnight. It was triturated several times with hot petroleum ether and the solid so obtained was crystallized from dilute ethyl alcohol. The products VIIa-d listed in Table III were prepared similarly. In general, they form colorless crystals, sparingly soluble in petroleum ether but readily soluble in hot benzene and alcohol. They are insoluble in aqueous sodium hydroxide.

Reaction of 1,5-diphenyl-3-carbpiperide-1H-1,2,4-triazole (VIIa) *with methanolic potassium hydroxide.* A solution of 0.5 g. of VIIa in 10 ml. of methanol containing 1 ml. of 20% aqueous potassium hydroxide solution was refluxed for 1 hr. The cooled reaction mixture was poured into ice-cold water, and was made neutral to litmus with hydrochloric acid. The collected solid was crystallized from hot dilute ethyl alcohol as colorless needles (*ca.* 0.35 g.) m.p. 181°C. identified as 1,5-diphenyl-3-carboxy-1*H*-1,2,4-triazole (VIa).[2]

Aromatic thiols. A mixture of 1 g. of each of Va-d and 1 g. of the appropriate thiol was heated at 110° (oil bath) for 1.5 hr. or on a boiling steam bath for 3 hr. The resulting solution was cooled, triturated with petroleum ether several times and the residue crystallized from ethanol.

The arylthio esters of 1-aryl-5-phenyl-3-carboxy-1*H*-1,2,4-triazoles (VIIIa-e) listed in Table IV are colorless, soluble in benzene, hot alcohol, sparingly soluble in petroleum ether.

Reaction of 1,5-diphenyl-3-phenylthiocarboxy-1H-1,2,4-triazole VIIIa *with methanolic potassium hydroxide.* Similar treatment of 0.5 g. of VIIIa with methanolic potassium

hydroxide, as described in the case of VIIa, resulted in the formation of 0.31 g. of colorless crystals of 1,5-diphenyl-4-carboxy-1*H*-1,2,4-triazole (VIa).[2] Extraction of the reaction mixture with aqueous sodium carbonate, followed by extraction with ether and evaporation of the latter gave *p*-thiocresol, identified as *p*-tolylthiobenzoate.

Preparation of 4-arylazo-2-phenyloxazoline-5-ones (Vb-d): 4-Arylazo-2-phenyloxazoline-5-ones (Vb-d) were obtained according to Sawdey[2] as follows: To a solution of 0.2 mole of the appropriate aromatic amine in 200 ml. of glacial acetic acid was added 40 ml. of concd. hydrochloric acid, then, dropwise, 0.23 mole of isoamyl nitrite at room temperature. To the diazonium mixture 30 g. of anhydrous sodium acetate was added. Hippuric acid, 0.25 mole, was heated in 200 ml. of acetic anhydride until a clear solution was obtained. This solution was cooled to room temperature, added slowly with agitation to the diazonium mixture. The mixture was then cooled and the precipitate was collected. The reaction products, listed in Table I are readily crystallized from acetone.

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U.A.R.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLLEGE OF PHARMACY, UNIVERSITY OF ILLINOIS]

Addition of Thiourea to Acrylonitrile and Acrylamides[1]

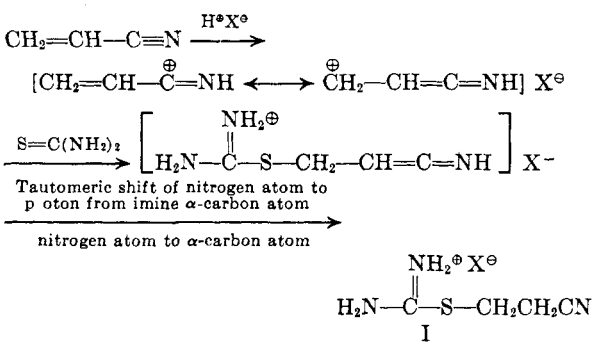
LUDWIG BAUER AND THOMAS L. WELSH

Received August 8, 1960

The addition of salts of thiourea to acrylonitrile and acrylamides is reported. This reaction presents an expeditious route to the synthesis of *S*-(β-cyanoethyl)- and *S*-(β-carboxamidoethyl)isothiuronium salts in excellent yields. Hydrolysis of these salts with ice-cold sodium hydroxide solution afforded β-mercaptopropionitrile and β-mercaptopropionamides.

The recent report[2] on the reaction of thiourea to derivatives of maleic acids, prompts us to report the facile acid-catalyzed addition of thiourea to acrylonitrile and acrylamides. An attempt[3] to add thiourea to acrylonitrile under base-catalyzed conditions at 100° failed, but it is claimed[4] in the patent literature that this addition does occur. However the compound so formed is not characterized. Base-catalyzed additions of several substituted thioureas to acrylonitrile have been reported to yield *N*-(β-cyanoethyl) derivatives. Thus, *N*-phenylthiourea[5] and *N,N'-o*-phenylenethiourea[6] yield *N*-phenyl-*N*-(β-cyanoethyl)thiourea and *N,N'*-di(β-cyanoethyl)-*N,N'*-(*o*-phenylene)-thiourea respectively.

We have found that salts of thiourea *viz.*, the hydrochloride, hydrobromide, or *p*-toluenesulfonate, readily add to acrylonitrile to afford *S*-(β-cyanoethyl)isothiuronium salts (I X = Cl, Br, or p-$CH_3C_6H_4SO_3$). These salts are formed in excellent yield. It is postulated that the mechanism for this reaction is similar to that advanced for the acid-catalyzed addition of thiourea to 2- and 4-vinylpyridine.[7] Protonation of the nitrile nitrogen atom facilitates nucleophilic attack by thiourea at the electrophilic carbon atom at the end of the conjugated system and this reaction path is shown by the following equation:



I

The structure of *S*-(β-cyanoethyl)isothiuronium chloride (I X = Cl) was proved by comparing a sample of it with one obtained from the conventional reaction of β-chloropropionitrile with thiourea.[8] Also, hydrolysis of I with hot concentrated hydrochloric acid yielded *S*-(β-carboxyethyl)isothiuronium chloride which was identical with a specimen prepared by the addition of thiourea hydrochloride to acrylic acid.[9]

We have extended this reaction to the addition of salts of thiourea to acrylamides and obtained *S*-(β-carboxamidoethyl)isothiuronium salts, II, (R = H; X = Cl, Br, or p-$CH_3C_6H_4SO_3$) as expressed by the equation below. Best yields of these salts (II) were procured when the reaction was carried

(1) The authors hereby acknowledge the generous support for this study by a grant from the Surgeon-General, U. S. Army, Contract DA-49-193-MD-2047.

(2) A. N. Arakelian, H. Dunn, Jr., L. L. Grieshammer, and L. E. Coleman, *J. Org. Chem.*, **25**, 485 (1960).

(3) C. D. Hurd and L. L. Gershbein, *J. Am. Chem. Soc.*, **69**, 2329 (1947).

(4) H. A. Bruson, *Org. Reactions*, **5**, 96 (1949); and *Chemistry of Acrylonitrile* (Second Edition) published by American Cyanamid Company, 1959, p. 239, quotes M. W. Harman, U. S. Patent 2,413,917 (1947) [*Chem. Abstr.*, **41**, 2446 (1947)].

(5) O. Bayer, *Angew. Chem.*, **61**, 236 (1949).

(6) A. M. Efros, *J. Gen. Chem.*, (*USSR*), *Eng. Transl.*, **28**, 599 (1958).

(7) L. Bauer and L. A. Gardella, Jr., *J. Org. Chem.*, **26**, 82 (1961).

(8) This salt was mentioned by R. Shapira, D. G. Doherty, and W. T. Burnett, Jr., *Radiation Research*, **7**, 25 (1957) and by private communication from Dr. Doherty.

(9) H. Behringer and P. Zillikens, *Ann.*, **574**, 140 (1951).