from rearrangement. In most runs, recovered half ester was determined by chromatographing on silicone the material recovered from the carbonate solution, but these data are not recorded in Table II.

Organocadmium reactions in presence of ferric chloride (Table III). The cadmium reagent was prepared (nitrogen atmosphere) from butyl bromide, by way of the Grignard reagent, in a usual manner[18] except that no ether was distilled from the solution. After a negative Gilman test had been obtained, there was added 5 ml. of toluene, the stirred reaction mixture was cooled to the desired reaction temperature, and the ether-toluene solution of ferric chloride was added. Immediately after the ferric chloride had been added, a toluene solution of the ester acid chloride was added during about 2 min. or as rapidly as was consistent with keeping the reaction temperature within the limit of ±2°. At the end of the reaction period, ice and sulfuric acid were added, the reaction mixture was worked up, and the products were determined by gas chromatography in the manner described for the Grignard reactions.

Reaction III-17 was carried out as usual for 45 min. at −10°, then it was heated under reflux for 15 min. as the condenser outlet was attached to a trap cooled in Dry Ice and acetone. No volatile products were collected in the trap. In addition to the analysis for the usual products by gas chromatography at high temperature, injections were also made at 48° in order to allow determination of butyl chloride. In a 2-m. silicone column, at a flow rate of 30 ml./min., retention time of butyl chloride from the reaction mixture was 10:48. Retention times of several of the compounds run for comparison in assigning the 10:48 peak were: ethanol, 3:18; butyl chloride, 10:30; butanol, 15:45; *n*-heptane, 16:48; butyl bromide, 20:06.

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[18] J. Cason and F. S. Prout, *Org. Syntheses*, **28**, 75 (1948).

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

Action of Grignard Reagents. XXI. Action of Organomagnesium Compounds on 4-Arylazo and of Lithium Aluminum Hydride on 4-Arylidene Derivatives of 1-Phenyl-3-methyl-5-pyrazolone

AHMED MUSTAFA, W. ASKER, AHMED FATHY A. SHALABY, AND Z. SELIM

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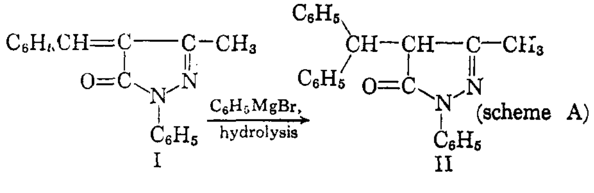
Treatment of 4-arylazo derivatives of 1-phenyl-3-methyl-5-pyrazolone with Grignard reagents does not effect hetero-ring opening and only the carbonyl group of III enters into reaction, followed by elimination of the elements of water on acidification, yielding colored products, believed to be derivatives of 1-phenyl-3-methyl-4-arylazo-5-arylpyrazole (IV). 1,5-Diphenyl-3-methyl-4-phenylazo-5-pyrazole (IVa) now has been obtained by the action of phenylmagnesium bromide on 1-phenyl-3-methyl-4-phenylazo-5-chloropyrazole (IVe), followed by hydrolysis.

Treatment of IVe and of 1-phenyl-3-methyl-4-arylidene-5-pyrazolones (Xa-d) with lithium aluminum hydride effects the formation of 1-phenyl-3-methyl-4-phenylazo-5-pyrazole (IVf) and 1-phenyl-3-methyl-4-arylmethyl-5-pyrazolones (XIa-d) respectively.

Recently, Mustafa and co-workers[1] showed that treatment of 1-phenyl-3-methyl-4-phenylazo-5-pyrazolone (I) with phenylmagnesium bromide, followed by hydrolysis, resulted in the addition of the reagent to the conjugation created by the attachment of an exocyclic double bond in the position 4 of a heterocyclic nitrogen ring having carbonyl function and yielded 1-phenyl-3-methyl-4-diphenylmethyl-5-pyrazolone (II).



(scheme A)

We now have undertaken the investigation of the effect of the introduction of the electron withdrawing group, namely, the phenylazo group in the 4-position of 1-phenyl-3-methyl-5-pyrazolone,[2] on the reactivity of the carbonyl group toward the action of organomagnesium compounds. When the highly colored 1-phenyl-3-methyl-4-arylazo-5-pyrazolones[3] (III) are treated with organomagnesium compounds, colored products of 1-phenyl-3-methyl-4-arylazo-5-arylpyrazoles (IV) are obtained (scheme B).

The assigned structure for the Grignard products (IVa-d) is inferred from: (1) the fact that they are colored,[4] (2) the identity of IVa with the product obtained by treating IVe with phenylmagnesium bromide, and (3) agreement of the ultimate analyses with those expected.

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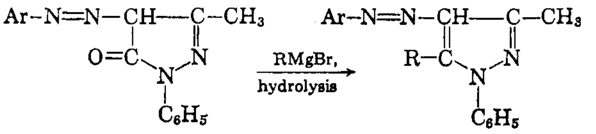
[1] A. Mustafa, W. Asker, A. F. A. Shalaby, S. A. Khattab, and Z. Selim, *J. Amer. Chem. Soc.*, **81**, 6007 (1959).

[2] The effect of the electron-withdrawing groups such as phenylazo in the 4-position, on the ease of replacement of a halogen in position 5 by nucleophilic reagents has been carefully studied with 1-phenyl-3-methyl-4-phenylazo-5-chloropyrazole (*cf.* P. Duquenois and H. Amal, *Bull. soc. chim. France*, (5) **9**, 721 (1942); A. Michaelis and H. Klopstock, *Ann.*, **354**, 102 (1907).

[3] The arylazo-derivatives may have the structure in III or one of the tautomeric structures (*cf.*, K. Auwers and A. Boennecke, *Ann.*, **378**, 218 (1911)).

[4] The colored substituted 1-phenyl-3-methyl-4-arylazo-5-pyrazole, A. Michaelis and R. Leonhardt, *Ber.*, **36**, 3597 (1903).

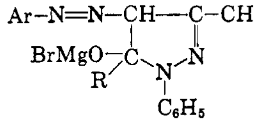


IIIa. Ar = C_6H_5
b. Ar = p-$CH_3C_6H_4$

IVa. Ar = C_6H_5, R = C_6H_5
b. Ar = C_6H_5, R = $C_{10}H_7$—
c. Ar = p-$CH_3C_6H_4$, R = C_6H_5
d. Ar = p-$CH_3C_6H_4$, R = p-$CH_3OC_6H_4$
e. Ar = C_6H_5, R = Cl
f. Ar = C_6H_5, R = H

Scheme B

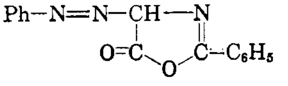
The Grignard reagent adds to the lactam group to give the salt of the intermediate alcohol-ammonia (V), which hydrolyzes and loses the elements of water on acidification. Grignard reagents react less radily with azo and imine bonds than with lactams or amides; therefore, in the 1-phenyl-3-methyl-4-arylazo-5-pyrazolones (III) reaction occurs preferentially with the lactam. The stability of the five-membered ring in III toward



V

the action of organomagnesium compounds has already been shown by Mustafa and co-workers[1] *via* the recovery of 1-phenyl-3-methyl-5-pyrazolone unchanged from the Grignard machine.

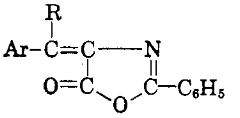
Furthermore, the reactivity of the carbonyl function in III toward the action of phenylmagnesium bromide may parallel the reactivity of the same group in 4-phenylazo-2-phenyloxazolin-5-one (VI) toward the same reagents.[5]



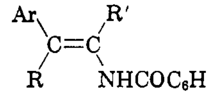
VI

Action of lithium aluminum hydride on; (a) *1-Phenyl-3-methyl-4-phenylazo-5-chloropyrazole* (IVe). We now have found that IVe undergoes hydrogenolysis upon treatment with lithium aluminum hydride with the loss of halogen[2] yielding 1-phenyl-3-methyl-4-benzeneazopyrazole (IVf). A similar observation was reported by Michaelis[4] using a mixture of zinc dust and aqueous sodium hydroxide solution.

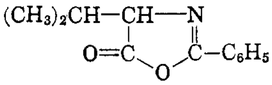
(*b*) *1-Phenyl-3-methyl-4-arylidene-5-pyrazolones* (X). 2-Phenyl-4-arylidene-5(4H)-oxazolones (VII, R = H) undergo reduction with lithium aluminum hydride, at low temperature, with opening of the oxazolone ring to produce substituted benzoylaminocinnamyl alcohols[6] (VIIIa). However, in 2-phenyl-4-isopropylidene-5(4H)-oxazolone (VII, R = Ar = CH_3) the five-membered heterocyclic ring seemed not to be affected, and only the exocycylic carbon-carbon double bond undergoes reduction with the same reagent to yield IX[7] which upon decomposition with ethyl acetate gives the α-benzoylamino ester VIIIb in good yield.[7]



VII

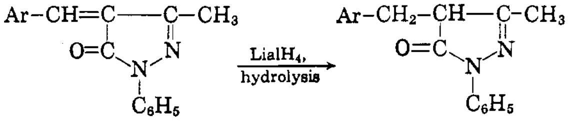


VIIIa. R=H, R′=CH_2OH
b. R=Ar=CH_3, R′=$COOC_2H_5$



IX

We now have found that, in contrast to VII (R = H), the pyrazolone ring in 1-phenyl-3-methyl-4-arylidene-5-pyrazolones (Xa–d), is not affected and only the exocyclic carbon-carbon double bond is reduced with lithium aluminum hydride to give the substituted 1-phenyl-3-methyl-4-arylmethyl-5-pyrazolones (XIa–d) respectively in good yield.



X XI

X XI

a. Ar = C_6H_5
b. Ar = p-$CH_3C_6H_4$
c. Ar = p-$CH_3OC_6H_4$
d. Ar = o-ClC_6H_4

The assigned structure for the products (XIa–d). is inferred from the fact that they are colorless. XIa is identical with the product obtained by the catalytic reduction of Xa. The stability of the heterocyclic ring in 1-phenyl-3-methyl-5-pyrazolone has been conferred from its recovery unchanged when treated with lithium aluminum hydride under the same experimental conditions.

There is a formal analogy between the behavior of X toward the action of lithium aluminum hydride and that of organomagnesium compounds.[1]

EXPERIMENTAL

Action of phenylmagnesium bromide on 1-phenyl-3-methyl-4-phenylazo-5-pyrazolone (IIIa). A solution of 2 g. of IIIa[8] in 50 ml. of dry benzene was added to phenylmagnesium bromide (prepared from 1.8 g. of magnesium and 18 g. of bromobenzene in 50 ml. of dry ether). The reaction mixture was refluxed on a steam bath for 3 hr. and left at room temperature. Then it was decomposed by 200 ml. of cold saturated aqueous ammonium chloride solution and extracted with ether. The ethereal layer was dried over

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(5) Private communication by Dr. W. Asker, submitted for publication in *J. Org. Chem.*

(6) E. Baltazzi and R. Robinson, *Chem. & Ind.*, 541 (1953).

(7) E. Baltazzi and R. Robinson, *Chem. & Ind.*, 868 (1953).

(8) L. Knorr, *Ann.*, **238**, 183 (1887).

TABLE I

ACTION OF LITHIUM ALUMINUM HYDRIDE ON 1-PHENYL-3-METHYL-4-ARYLIDENE-5-PYRAZOLONES (X)

Pyrazolones (X)	Products (XI)	M.P.[a]	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
Xa	XIa	137	88	$C_{17}H_{16}N_2O$	77.27	77.18	6.06	5.99	10.60	10.57		
Xb	XIb	160	91	$C_{18}H_{18}N_2O$	77.69	77.71	6.47	6.40	10.07	10.12		
Xc	XIc	163	79	$C_{18}H_{18}N_2O_2$	73.46	73.50	6.12	6.09	9.52	9.48		
Xd	XId	157	84	$C_{17}H_{15}N_2OCl$	68.34	68.32	5.02	5.00	9.38	9.41	11.89	11.82

[a] Melting points are uncorrected.

anhydrous sodium sulfate and evaporated. The dark solid residue was washed with petroleum ether (b.p. 40–60°, 30 ml.) and was crystallized from ethyl alcohol as orange yellow crystals of IVa, m.p. 132°, yield, 1.3 g.

Anal. Calcd. for $C_{22}H_{18}N_4$: C, 78.10; H, 5.32; N, 16.56. Found: C, 78.22; H, 5.40; N, 16.51.

Action of phenylmagnesium bromide on 1-phenyl-3-methyl-4-phenylazo-5-chloropyrazole (IVe). To an ethereal solution of phenylmagnesium bromide (prepared from 0.9 g. of magnesium, 8 g. of bromobenzene, and 40 ml. of dry ether) was added a solution of 1 g. of IVe[4] in 30 ml. of dry benzene. The reaction mixture was refluxed on a water bath for 3 hr., kept overnight at room temperature, then decomposed with a cold saturated solution of ammonium chloride. The reaction mixture was extracted with ether, then the ethereal layer was dried and evaporated slowly. The solid residue was washed with 25 ml. of petroleum ether (b.p. 40–60°) and then crystallized from ethyl alcohol and identified as IVa (m.p. and mixed m.p. determinations).

Action of α-napthylmagnesium bromide on IIIa. To an ethereal solution of α-naphthylmagnesium bromide (prepared from 1.2 g. of magnesium, 10 g. of freshly distilled α-bromonaphthalene and 50 ml. of dry ether) was added 1 g. of IIIa and 50 ml. of dry benzene. The reaction mixture was refluxed on water bath for 2 hr. and left aside overnight at room temperature. Then, it was worked up in the usual manner. The solid residue was washed with 10 ml. of ethyl alcohol and crystallized from alcohol as orange crystals of IVb, m.p. 168°; yield, 0.7 g.

Anal. Calcd. for $C_{26}H_{20}N_4$: C, 80.41; H, 5.15; N, 14.43. Found: C, 80.35; H, 5.20; N, 14.39.

Action of phenylmagnesium bromide on IIIb. A solution of 1.5 g. of IIIb[9] in 40 ml. of dry ether was added to an ethereal solution of phenylmagnesium bromide. The reaction mixture was refluxed for 2.5 hr. on a steam bath and left overnight at room temperature. Then, it was worked up in the usual manner. The solid residue was crystallized from ethyl alcohol as orange crystals of IVc, m.p. 158–159°; yield, 1.1 g.

Anal. Calcd. for $C_{23}H_{20}N_4$: C, 78.40; H, 5.68; N, 15.90. Found: C, 78.45; H, 5.72; N, 15.82.

Action of p-anisylmagnesium bromide on IIIb. A solution of 1.2 g. IIIb in 40 ml. of dry benzene was added to an ethereal solution of *p*-anisylmagnesium bromide (prepared from 0.9 g. of magnesium and 9.5 g. of *p*-bromoanisole in 45 ml. of dry ether). The reaction mixture was refluxed for 3 hr. on a steam-bath, left overnight at room temperature. Then it was worked up in the usual manner. The solid substance was crystallized from ethyl alcohol as orange yellow crystals IVd, m.p. 169–170°; yield, 0.9 g.

Anal. Calcd. for $C_{24}H_{22}N_4O$: C, 75.39; H, 5.75; N, 14.65. Found: C, 75.42; H, 5.71; N, 14.69.

Action of lithium aluminum hydride on IVe. Solvents dried over sodium were used. To 0.7 g. of lithium aluminum hydride (New Metals and Chemicals, Ltd. London) was added 50 ml. of dry ether. After being refluxed for 15 min., a benzene solution (30 ml.) containing 1 g. of IVe was added. The reaction mixture was refluxed for 2 hr. and kept overnight at room temperature. The reaction mixture was poured gradually into a cold saturated solution of ammonium chloride; it was extracted with ether and the ethereal layer was dried over anhydrous sodium sulfate and evaporated. The solid residue was crystallized from ethyl alcohol as pale brown crystals of IVf, m.p. 125°; yield, 0.85 g. (not depressed when admixed with an authentic sample[4]).

Anal. Calcd. for $C_{16}H_{14}N_4$: C, 73.28; H, 5.34; N, 21.37. Found: C, 73.32; H, 5.33; N, 21.34.

Action of lithium aluminum hydride on 1-phenyl-3-methyl-4-arylidene-5-pyrazolones. General procedure. A mixture of 1 g. of lithium aluminum hydride in 50 ml. of dry ether was refluxed for 15 min. on a water bath. To this mixture was added 0.01 mole of the appropriate pyrazolones (X)[1] suspended in ether. The reaction mixture was refluxed for 3 hr. until the deep red color faded completely and the ethereal solution became colorless. It was kept overnight at room temperature, decomposed with a cold saturated solution of ammonium chloride and a few milliliters of concentrated hydrochloric acid. It was extracted with ether and the ethereal layer was dried over anhydrous sodium sulfate and evaporated. The colorless crystals were recrystallized from ethyl alcohol (*cf.* Table I).

The products are insoluble in petroleum ether (b.p. 40–60°) but they are soluble in aqueous sodium hydroxide solution (10%). Their alcoholic solutions give no color when treated with ferric chloride. They give no color with concentrated sulfuric acid.

Catalytic hydrogenation of Xa. A mixture of 1 g. of 5% palladium on barium sulfate[10] in 15 ml. of absolute ethyl alcohol was exposed to nascent hydrogen until it acquired a black coat, then 1 g. of Xa was dissolved in 20 ml. of absolute ethyl alcohol and added to it. The reaction mixture was exposed to the current of hydrogen under reduced pressure for 2 hr. until the red color of the solution disappeared. The alcoholic solution was separated by filtration and on evaporation a colorless residue was left. It was recrystallized from ethyl alcohol into colorless crystals and identified as XIa (melting point and mixed melting point determinations).

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(9) A. Michaelis, R. Leonhardt, and K. Wohle, *Ann.*, **338**, 205 (1905).

(10) *Organic Syntheses;* **Coll. Vol. III**, Wiley, New York, N. Y., 1955, p. 685.