7-Chloro-3-methyl-6-sulfamyl-4(3H)-quinazolinone (XXI).—A 1.0-g. sample (0.0040 mole) of 4-chloro-5-sulfamylanthranilic acid (XII) was heated at 175–180° with 1.0 ml. of N-methylformamide for 4 hours. The reaction product was cooled, triturated with 5 ml. of methanol, and the resultant off-white crystals were filtered off. The solid was stirred with 5 ml. of 10% sodium bicarbonate to remove traces of starting material and again filtered off. The solid was then dissolved in 5 ml. of 1.0 *N* sodium hydroxide, clarified with activated carbon and precipitated with hydrochloric acid; yield 0.25 g. On a second run the yield was doubled; in the infrared, bands at 6.00, 6.23 μ; in the ultraviolet $\lambda_{\max}$ 282 mμ, ϵ 32,800.

7-Chloro-2,3-dimethyl-6-sulfamyl-4(3H)-quinazolinone (XXII).—A 0.5-g. (0.002 mole) sample of 4-chloro-5-sulfamylanthranilic acid (XII) and 0.5 ml. of N-methylacetamide were heated together at 195–200° for 4 hours. After cooling, the residue was triturated with methanol and 5 ml. of water was added. An oil formed which crystallized in the refrigerator overnight. The solid (0.50 g.) was stirred with 10% sodium bicarbonate and then filtered off to yield 0.15 g. (26%) of light yellow crystals. For further purification, the sample was dissolved in 5 ml. of 1 *N* sodium hydroxide, clarified with activated carbon and precipitated by the addition of hydrochloric acid; m.p. 245°.

7-Chloro-2-isopropyl-6-sulfamyl-4(3H)-quinazolinone (XXIII).—A mixture of 2.5 g. (0.010 mole) of 4-chloro-5-sulfamylanthranilic acid (XII) and 2.5 g. (0.029 mole) of isobutyramide was heated at 190° for 3.5 hours in an open flask. The residue was taken up in hot methanol, concentrated slightly and water was added. A tan solid (1.0 g.) formed and was filtered off. The solid was stirred with bicarbonate to remove starting material and after filtering off again, the solid was taken up in 1.0 *N* sodium hydroxide, clarified with activated carbon and acidified with concentrated hydrochloric acid. The product was then recrystallized from acetone–water to yield 0.20 g. (6.8%) of material, m.p. 280°. A second recrystallization from ethanol yielded white needles, m.p. 290°; in the infrared, bands at 6.01, 6.24 μ; in the ultraviolet, $\lambda_{\max}$ 295 mμ, ϵ 34,400.

7-Chloro-2,4-dihydroxy-6-sulfamylquinazoline (XXIV).—A 0.50-g. (0.0020 mole) sample of 4-chloro-4-sulfamylanthranilic acid (XII) was heated with 0.50 g. (0.0083 mole) of urea at 180° for 3 hours. Ammonia was evolved during this time. Sodium bicarbonate solution (10%) was added to the cooled residue and the mixture was stirred to dissolve unreacted starting material. The remaining crystals (0.30 g.) were filtered off and then recrystallized by dissolving in 5 ml. of 1 *N* sodium hydroxide, clarifying with activated carbon and acidifying with 6 *N* hydrochloric acid; yield 0.15 g. (21%), m.p. 275°. The infrared spectrum showed carbonyl absorptions at 5.75 and 5.85 μ; in the ultraviolet, $\lambda_{\max}$ 264 mμ, ϵ 55,000; $\lambda_{\max}$ 325 mμ, ϵ 15,600.

Urethan can be substituted for urea with the same results.

General Method for the Preparation of the Tetrahydroquinazolinones (Table II) by Hydride Reduction. 7-Chloro-6-sulfamyl-1,2,3,4-tetrahydro-4(3H)-quinazolinone (XXV).—Aluminum chloride (1.03 g., 0.0077 mole) was added to 250 ml. of dry diglyme in an ice-bath. The stirred mixture was then warmed while 2.0 g. (0.0077 mole) of 7-chloro-6-sulfamyl-4(3H)-quinazolinone was added. A solution of 1.4 g. (0.037 mole) of sodium borohydride in 70 ml. of dry diglyme was added dropwise. The orange mixture was kept at 85° for one hour. The flask was cooled in ice and 40 ml. of water was slowly added. Dilute hydrochloric acid was added to obtain a strongly acidic, clear solution which was then concentrated *in vacuo* to dryness. The solid residue was triturated with cold water to yield 0.90 g. of solid melting over a broad range. Recrystallization from 50% aqueous acetone gave 0.65 g. (33%) of pale yellow crystals, m.p. 254–256°.

A 0.20-g. sample was recrystallized in the same manner to yield 0.15 g. of needle crystals, m.p. 256–258°; in the infrared, bands at 6.01, 6.24 μ (a hypsochromic shift of 0.14 μ from the unreduced compound); in the ultraviolet $\lambda_{\max}$ 265 mμ, ϵ 32,000.

PEARL RIVER, N. Y.

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

Action of Grignard Reagents. XVIII. Action of Organomagnesium Compounds on 4-Methyl-2,3-benzoxaz-1-one and on Phthalazones

BY AHMED MUSTAFA, ABDEL HAMID HARHASH AND ABDEL ALLIM SHOEB SALEH

RECEIVED OCTOBER 14, 1959

Treatment of 4-methyl-2,3-benzoxaz-1-one (Id) with Grignard reagents brought about cleavage of the hetero ring with the formation of IId–g. Addition of phenylmagnesium bromide to phthalazone (IIIa), 1-phenylphthalazone (IIIb), 1-phenylthiophthalazone (Xa) or its isomer IXa, and 1-phenyl-3-acetylphthalazone (IIIc), followed by hydrolysis, effects the formation of 1,4-diphenylphthalazine (IV) together with diphenylmethylcarbinol in the case of IIIc. Compound IV now has been obtained either by the action of phenylmagnesium bromide on 1-phenyl-4-chlorophthalazine, which exhibits the reactivity characteristic of chloro heterocyclic compounds containing the group $-\mathrm{N{=}\underset{|}{C}Cl}$ or 1,4-dichlorophthalazine. Phthalazine undergoes 1,2-addition of phenylmagnesium bromide to the C═N, accompanied by autoxidation, to give 1-phenylphthalazine. Treatment of 1,3-diphenylphthalazone (IIIe) with phenyl-, *p*-tolyl-, benzyl- and methylmagnesium halides result in the formation of reaction products, believed to have structures like Va-b and VIa-b, respectively. Similar reaction has been also observed when 1-methyl-3-phenylphthalazone (IIIf) is treated with benzylmagnesium chloride, yielding VIc. The 4-mercaptophthalazine derivatives IXa-c or the corresponding 4-thiophthalazone derivatives Xa–c, as well as the 4-thiophthalazone derivatives XIa–c are obtained by the action of phosphorus pentasulfide on the corresponding phthalazone derivative.

Recently, Mustafa and co-workers[1] have shown that treatment with phenylmagnesium bromide brought about opening of the oxazone ring in the 2,3-benzoxaz-1-ones Ia–c: which yielded the corresponding oximes of 2-formyl- (IIa), 2-benzoyl- (IIb) and 2-(α-naphthoyl)-triphenylcarbinol (IIc), respectively.

We now have extended the study of this reaction and investigated the action of organomagnesium compounds on 4-methyl-2,3-benzoxaz-1-one (Id). Thus, treatment with phenylmagnesium bromide brought about opening of the oxazone ring in Id, which yielded the corresponding oxime of 2-acetyltriphenylcarbinol (IIe). Similarly, the corresponding oximes of 2-acetyldimethylphenylcarbinol (IId), 2-acetyl-di-*p*-tolylphenylcarbinol (IIf) and 2-acetyldibenzylphenylcarbinol (IIg) are obtained by the action of methyl-, *p*-tolyl- and benzylmagnesium halides on Id, respectively. The reactions of phthalazones (III), in general, parallel to a great extent

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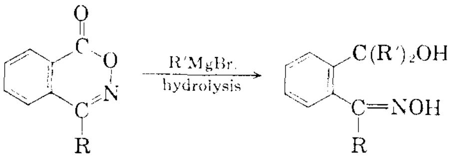
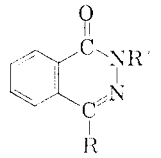
[1] A. Mustafa, W. Asker, M. Kamel, A. F. A. Shalaby and A. E. A. Hassan, THIS JOURNAL, **77**, 1612 (1955).



Ia, R = H
b, R = C_6H_5
c, R = α-$C_{10}H_7$
d, R = CH_3

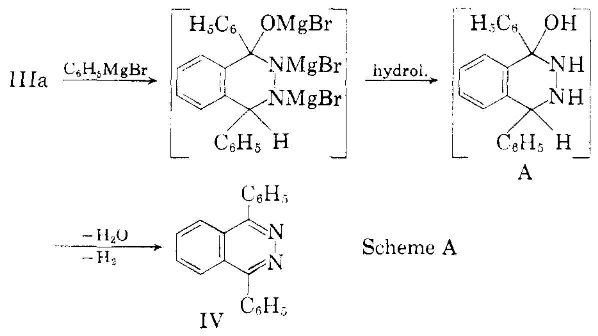
IIa, R = H; R' = C_6H_5
b, R = R' = C_6H_5
c, R = α-$C_{10}H_7$; R' = C_6H_5
d, R = R' = CH_3
e, R = CH_3; R' = C_6H_5
f, R = CH_3; R' = $C_6H_4CH_3$-*p*
g, R = CH_3; R' = $CH_2C_6H_5$

those of the analogous isoquinolones.[2] The action of organomagnesium compounds on III, as far as we are aware, has not yet been investigated. When phthalazone (IIIa) is treated with excess of phenylmagnesium bromide, followed by hydrolysis, 1,4-diphenylphthalazine (IV) is obtained in an almost quantitative yield.



IIIa, R = R' = H
b, R = C_6H_5; R' = H
c, R = C_6H_5; R' = $COCH_3$
d, R = H; R' = C_6H_5
e, R = R' = C_6H_5
f, R = CH_3; R' = C_6H_5
g, R = CH_3; R' = H

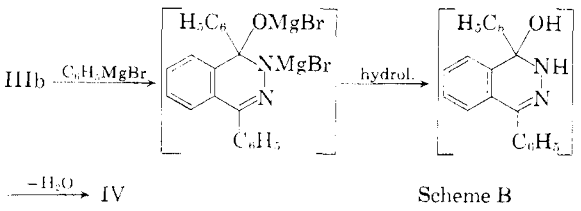
It is believed that the formation of IV proceeds *via* the sequence of reactions indicated in scheme A. 1,2-Addition of the Grignard reagent to the carbonyl group in IIIa simulates the addition of the same reagent to the carbonyl group in N-methylisocarbostyrils to give 1-substituted N-methylisoquinolinium compounds.[3] Moreover, the addition of phenylmagnesium bromide to C=N in IIIa simulates the addition of the same reagent to the carbon–nitrogen double bond in quinoxaline,[4] in N-benzoylphenylhydrazone of benzaldehyde[5] and the arylation of isoquinoline with arylmagnesium halides.[6] The tetrahydro derivative of the type A, formed on hydrolysis, loses hydrogen easily which probably may be attributed to autoxidation.[7]



Scheme A

The finding that phenylmagnesium bromide adds to the C=N *in IIIa prompted us to investigate the* action of the same reagent on phthalazine. Thus, when the latter is treated with the same reagent under the experimental conditions, followed by hydrolysis, 1-phenylphthalazine has been successfully isolated from the reaction mixture. Its structure was inferred from the fact that it is identical with the product obtained by reduction of 1-phenyl-4-chlorophthalazine by hydriodic acid and red phosphorus[8] and the picrate of 1-phenylphthalazine. It gives the correct analytical values calculated for 1-phenylphthalazine. The isolation of 1-phenylphthalazine, and not the dihydro derivative, namely, 1-phenyl-1,2-dihydrophthalazine in this reaction, may be similarly attributed to autoxidation.

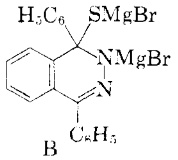
The action of phenylmagnesium bromide on 1-phenylphthalazone (IIIb), followed by hydrolysis, effects the formation of IV (*cf.* Scheme B).



Scheme B

The presence of substituent in position I indicates addition only to the C=O group and not to the C=N group. Compound IIIb appears to be more or less sterically[9] inhibited so far as "normal" addition of Grignard reagent at the carbon–nitrogen double bond is also concerned.

Treatment of the corresponding thio derivative of IIIb, namely 4-mercapto-1-phenylphthalazine (IXa) or its isomer Xa, with phenylmagnesium bromide yields IV; B is an intermediate in this reaction.



B

The behavior of IXa or Xa toward phenylmagnesium bromide simulates the behavior of S-methylated thiohydrazides, *e.g.*, $C_6H_5C(SCH_3)$=NN$(CH_3)C_6H_5$[10] and of thioacylated hydrazones, *e.g.*,

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(2) R. C. Elderfield, "Heterocyclic Compounds," Vol. 6, John Wiley and Sons, Inc., New York, N. Y., 1957, p. 198.

(3) H. Decker and R. Pschorr, *Ber.*, **37**, 3396 (1904); H. Erlenmeyer, H. Baumann and E. Sorkin, *Helv. Chim. Acta*, **31**, 1978 (1948).

(4) F. W. Bergstrom and R. A. Ogg, THIS JOURNAL, **53**, 245 (1931).

(5) P. Grammaticakis, *Compt. rend.*, **208**, 1910 (1939); *C. A.*, **33**, 7287 (1939).

(6) F. W. Bergstrom and S. H. McAllister, THIS JOURNAL, **52**, 2845 (1930); E. Bergmann and W. Rosenthal, *J. prakt. Chem.*, **135**, 267 (1932).

(7) Autoxidation of dihydro derivatives has been reported in the case of symmetrically substituted phenylhydrazines of the type RR'-CHNHNHC$_6$H$_5$, produced by "normal" addition of Grignard reagents to C=N of phenylhydrazones of aromatic aldehydes (*cf.* P. Grammaticakis, *Compt. rend.*, **204**, 1262 (1937); *C. A.*, **31**, 4954 (1937)). It seem also probable that the corresponding halomagnesium intermediates would be similarly oxy-sensitive (*cf.* M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, p. 1213). *Cf.* also the ready loss of hydrogen from the dihydro product obtained by treatment of isoquinoline with phenylmagnesium bromide (ref. 6).

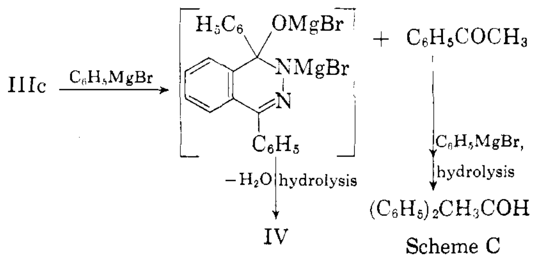
(8) A. Leick, *Ber.*, **38**, 3918 (1905).

(9) The addition of a Grignard reagent at the carbon-nitrogen double bond appears to be more or less sterically inhibited in the case of phenylhydrazones of ketones, *e.g.*, $(C_6H_5)_2C$=NNHC$_6$H$_5$ (P. Grammaticakis, *Compt. rend.*, **223**, 804 (1946); *C. A.*, **41**, 1602 (1947)), the phenylosazone of phenylglyoxal, and of phenylosazone of diphenylglyoxal (P. Grammaticakis, *ibid.*, **208**, 1998 (1939); *C. A.*, **33**, 7285 (1939)), and in the case of 2,3-diphenylquinoxaline (K. Maurer, B. Schiedt and H. Schoeter, *Ber.*, **68**, 1716 (1935)).

(10) H. Wuyts and A. Lacourt, *Bull. soc. chim. Belg.*, **44**, 395 (1935); *C. A.*, **29**, 7951 (1935).

$C_6H_5CSN(CH_3)N{=}CHC_6H_5$[11] toward Grignard reagents.

Treatment of 1-phenyl-3-acetylphthalazone (IIIc) with phenylmagnesium bromide gives IV together with diphenylmethylcarbinol. It is believed that the formation of IV proceeds *via* the sequence of reactions indicated in scheme C.

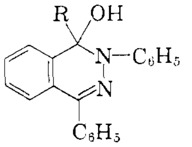


Scheme C

The elimination of the acetyl group by the action of the Grignard reagent is similar to the elimination of the acetyl group in N-acetylphenylhydrazone of benzaldehyde[5] and of the benzoyl group in 1-benzoylbenztriazole[12] by the same reagent.

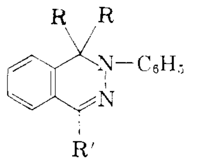
The structure of IV was inferred from the fact that it is obtained on treatment of either 1-chloro-4-phenylphthalazine which exhibits the reactivity characteristic of chloro heterocyclic compounds containing the group —N=CCl or its vinyl analog or 1,4-dichlorophthalazine with phenylmagnesium bromide,[13] and is identical with 1,4-diphenylphthalazine obtained by the action of hydrazine on 1,2-dibenzylbenzene.[14]

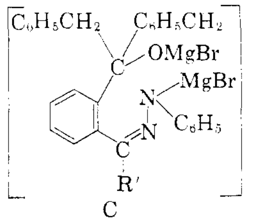
The action of phenylmagnesium bromide and of *p*-tolylmagnesium iodide on 1,3-diphenylphthalazone (IIIe) now has been undertaken. Thus, 4-phenyl-4-hydroxy-(Va) and 4-*p*-tolyl-4-hydroxy-1,3-diphenyl-3,4-dihydrophthalazine (Vb) are obtained, respectively. Compound Va turns red on exposure to light and air.[15] The phenomenon is reversible. The inactivity of the C=N in IIIe toward the action of Grignard reagent simulates the behavior of IIIb toward the same reagent.[9]



Va, R = C_6H_5
b, R = $C_6H_4CH_3$-*p*

On the other hand, treatment of IIIe with benzylmagnesium chloride and with methylmagnesium iodide results in the formation of reaction products for which structure VIa and VIb are proposed, respectively; (C) is a likely intermediate in this reaction.



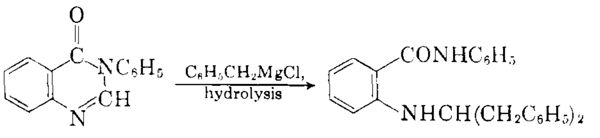


C

VIa, R = $CH_2C_6H_5$; R′ = C_6H_5
b, R = CH_3; R′ = C_6H_5
c, R = $CH_2C_6H_5$; R′ = CH_3

The unusual reaction of IIIe with benzylmagnesium chloride simulates the unusual reaction of 3-phenyl-4-quinazolone (VII) with the same reagent to yield N-(β,β′-diphenylisopropyl)-anthranilide (VIII).[15] Moreover, the 1,2-addition of phenylmagnesium bromide to the carbonyl group in IIIe to yield Va parallels the 1,2-addition of the same reagent to the carbonyl group in 2-methyl-3-phenyl-4-quinazolone,[16] and in 1,2-dimethyl-4-quinazolone.[17]

Compound VIa gives the correct analytical values. The fact that it is colorless may eliminate the possibility of the formation of 4-benzylidene-1,3-diphenyl-3,4-dihydrophthalazine, *via* the 1,2-addition of one mole of benzylmagnesium chloride to the carbonyl group, followed by dehydration after hydrolysis.[18]



VII VIII

A similar reaction now has also been observed when IIIf is treated with benzylmagnesium chloride followed by hydrolysis, to yield VIc.

We would like to report that we are now not in a position to establish the proposed structure VI beyond any doubt; this is under further investigation.

Treatment of 2-phenyl-4-hydroxyphthalazone with phosphorus pentasulfide in xylene to give the expected 2-phenyl-4-mercaptothiophthalazone together with the corresponding diphthalazinyl sulfide has been recently reported.[19] We now have found that treatment of IIIa-b and IIIg with the same reagent effects the formation of the 4-mercaptophthalazine derivatives IXa–c[20] or the corresponding 4-thiophthalazone derivatives Xa–c, respectively.

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(11) H. Wuyts and A. Lacourt, *Bull. soc. chim. Belg.*, **45**, 445 (1936); *C. A.*, **30**, 8212 (1936).

(12) A. Mustafa, W. Asker and O. H. Hishmat, THIS JOURNAL, **77**, 5127 (1955).

(13) For the reactivity of the chlorine atom attached to C=N in heterocyclic compounds, *cf.* the action of Grignard reagents on 2,3-dichloroquinoxaline (R. A. Ogg and F. W. Bergstrom, THIS JOURNAL, **53**, 1846 (1931)) and on 1-chlorosultim (A. Mustafa and M. K. Hilmy, *J. Chem. Soc.*, 1339 (1952)).

(14) A. Guyot and J. Catel, *Compt. rend.*, **140**, 1348 (1905).

(15) *Cf.* the behavior of the N-acetyl derivatives of 3-aminoaryl-1-ketophthalazine which are usually colorless compounds, frequently turning blue on exposure to light and air (J. C. E. Simpson, "Condensed Pyridazine and Pyrazine Rings," Interscience Publishers, Inc., New York, N. Y., 1953, p. 126.

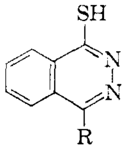
(16) C. F. Koelsch, THIS JOURNAL, **67**, 1718 (1954).

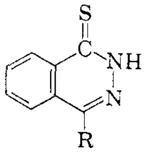
(17) F. M. Hammer, I. M. Heilbron, J. H. Reade and H. N. Walls, *J. Chem. Soc.*, 251 (1932).

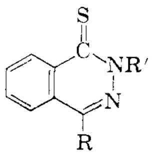
(18) 1-Methoxy-3-aryl-4-methylene-3,4-dihydrophthalazines are colored compounds (*cf.* C. I. Brodrick, A. T. Peters and F. M. Rowe, *J. Chem. Soc.*, 1026 (1948); A. T. Peters, G. T. Pringle and F. M. Rowe, *ibid.*, 597 (1948)).

(19) D. J. Drain and D. E. Seymour, *ibid.*, 852 (1955).

(20) *Cf.* the formation of 1-mercaptophthalazines by treatment of phthalazones with phosphorus pentasulfide (P. T. Paul, to United States Rubber Co., U. S. Patent, 2,382,769 (Aug. 14, 1945)); *C. A.*, **40**, 2032 (1946); R. C. Elderfield, ref. 2, p. 203.







IXa, R = H
b, R = C_6H_5
c, R = CH_3

XIa, R = H; R' = C_6H_5
b, R = R' = C_6H_5
c, R = CH_3; R' = C_6H_5

The mercapto derivatives are readily soluble in aqueous sodium hydroxide solution. On the other hand, treatment of 3-phenyl substituted phthalazones IIId–f with the same reagent results in the formation of the corresponding 4-thiophthalazone derivatives XIa–c,[19] respectively.

Experimental

Action of Grignard Reagents on Id.—The following illustrates the procedure. *To an ethereal solution of phenylmagnesium bromide* (prepared from 0.9 g. of magnesium, 8.0 g. of bromobenzene and 40 ml. of dry ether) was added a solution of 1 g. of Id[21] in 30 ml. of benzene. The reaction mixture was refluxed (steam-bath) for 2 hours, set aside at room temperature overnight, and then decomposed with a cold, saturated solution of ammonium chloride. The reaction mixture was extracted with ether; the ethereal layer was dried over anhydrous sodium sulfate and then allowed to evaporate slowly.

The oily residue was washed several times with hot petroleum ether (b.p. 40–60°) and recrystallized from alcohol to give *ca.* 0.72 g. of colorless crystals of the oxime of 2-acetylphenyldiphenylcarbinol (IIe), m.p. 182°. The oxime gives a yellow color with sulfuric acid.

Anal. Calcd. for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.13; H, 5.78; N, 4.35.

The oxime of 2-acetylphenyldimethylcarbinol (IId) forms colorless crystals from benzene–petroleum ether mixture; m.p. 98°, yield 0.69 g.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.39; H, 7.75; N, 7.25. Found: C, 68.18; H, 7.62; N, 7.05.

The oxime of 2-acetylphenyl-di-(*p*-tolyl)-carbinol (IIf) is obtained as colorless crystals (*ca.* 0.72 g.) from benzene; m.p. 194°.

Anal. Calcd. for $C_{23}H_{23}NO_2$: C, 80.00; H, 6.64; N, 4.06. Found: C, 79.85; H, 6.52; N, 3.99.

The oxime of 2-acetylphenyldibenzylcarbinol (IIg) gives *ca.* 0.52 g. of colorless crystals from benzene–petroleum ether; m.p. 146°.

Anal. Calcd. for $C_{23}H_{23}NO_2$: C, 80.00; H, 6.64; N, 4.06. Found: C, 79.81; H, 6.38; N, 3.89.

The above carbinol derivatives IId–g are easily soluble in hot benzene, alcohol, chloroform, but they are difficultly soluble in petroleum ether.

Action of Phenylmagnesium Bromide on. (a) **IIIa.**—One gram of IIIa[22] was treated with phenylmagnesium bromide as mentioned above. The ether was evaporated and the reaction mixture was heated for 6 hours (steam-bath), set aside at room temperature overnight, and then decomposed with a cold, saturated aqueous ammonium chloride solution. The oily residue, so obtained upon evaporation of the ethereal extract, was washed several times with hot petroleum ether (b.p. 50–60°) and recrystallized from benzene to give *ca.* 1.1 g. of colorless crystals of 1,4-diphenylphthalazine (IV), m.p. 194°. It gives a yellow color with sulfuric acid.

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.88; H, 4.78; N, 9.75.

(b) **IIIb.**—Similarly, treatment of 1.5 g. of IIIb[22] with phenylmagnesium bromide under the same experimental conditions, with the exception of 3 hours for the time period of the reflux of the reaction mixture, gives *ca.* 0.9 g. of IV. Identification was carried out by m.p. and mixed m.p. determination.

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.78; H, 4.82; N, 9.83.

(c) **IIIc.**—A solution of 1.5 g. of IIIc[22] in 40 ml. of benzene was treated with phenylmagnesium bromide and the reaction mixture was worked up as described in the case of IIIb. The oily residue was washed several times with hot petroleum ether and recrystallized from benzene to give *ca.* 0.6 g. of IV (m.p. and mixed m.p.).

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.77; H, 4.81; N, 9.64.

The colorless crystals, so obtained by concentration of the petroleum ether washings, followed by cooling, proved to be diphenylmethylcarbinol, m.p. 82–83° (m.p. and mixed m.p.).[23]

(d) (**IXb**) **or Xb.**—One gram of IXb or Xb was treated with phenylmagnesium bromide in the usual manner. The reaction mixture, after working up, gave colorless crystals of IV (*ca.* 0.7 g.) from benzene; m.p. 194°, identified as IV by m.p. and mixed m.p. determinations.

(e) **Halogen-substituted Phthalazines.**—Treatment of 1 g. of each of 1-chloro-4-phenylphthalazine[8] and 1,4-dichlorophthalazine[24] with phenylmagnesium bromide was carried out in the usual manner. The reaction mixture was refluxed for 3 hours, kept aside at room temperature overnight. It was worked up, as described for IIIb, and the solid, so obtained upon triturating the oily residue, was crystallized from benzene; m.p. 194°. It was identified as IV (m.p. and mixed m.p.); yield 62, 75%, respectively.

Action of Phenylmagnesium Bromide on Phthalazine.—Phthalazine was prepared by the following modification of the procedure described by Gabriel and Pinkus.[25] To a solution of 5 g. of *o*-phthaldehyde in 1500 ml. of hot water, 2 g. of hydrazine sulfate and 200 ml. of normal sodium hydroxide solution were added. The reaction mixture was concentrated to *ca.* 50 ml., saturated with sodium hydroxide and extracted with benzene. The solid (*ca.* 3.5 g.), so obtained upon evaporation of the benzene extract, was crystallized from ether as pale-yellow crystals, m.p. 91°.

One gram of phthalazine was treated with phenylmagnesium bromide as described for IIIb. The oily residue, obtained upon evaporation of the ethereal solution, was washed several times with petroleum ether (b.p. 50–60°) and was crystallized from benzene–ether; m.p. 144°, yield *ca.* 0.7 g. It is identical with an authentic sample of 1-phenylphthalazine (m.p. and mixed m.p.).[8]

Anal. Calcd. for $C_{14}H_{10}N_2$: C, 81.55; H, 4.85; N, 13.59. Found: C, 81.47; H, 4.79; N, 13.50.

It forms yellow picrate from alcohol; m.p. 180° (m.p. and mixed m.p.).[8]

Action of Grignard Reagents on IIIe. (a) **Phenylmagnesium Bromide.**—To a solution of phenylmagnesium bromide was added a solution of 1 g. of IIIe[26] in 30 ml. of dry benzene. The reaction mixture was worked up as mentioned above. The oily residue, so obtained upon evaporation of the ethereal extract, was solidified upon washing with petroleum ether (b.p. 50–60°). Compound Va was obtained as colorless crystals from alcohol; m.p. 182°, yield *ca.* 0.7 g., Va is easily soluble in chloroform, difficultly soluble in cold ethyl alcohol, and insoluble in aqueous sodium hydroxide solution; it gives a yellow color with sulfuric acid.

Anal. Calcd. for $C_{26}H_{20}N_2O$: C, 79.59; H, 5.10; N, 7.14. Found: C, 79.45; H, 4.96; N, 7.09.

When a colorless benzene solution of Va is exposed to air and light, it acquires a red color which disappears on keeping it in dark. The phenomenon is reversible. It was also observed that similar reversible phenomenon could occur when thin layers of the colorless solid Va are exposed to air and sunlight and then kept aside in dark.

(b) ***p*-Tolylmagnesium Iodide.**—A solution of 1.5 g. of IIIe in 30 ml. of dry benzene was added to a solution of *p*-tolylmagnesium iodide (prepared from 0.8 g. of magnesium and 7.5 g. of *p*-iodotoluene in 40 ml. of dry ether). The reaction mixture was worked up in the usual manner and the solid was crystallized from acetone; m.p. 184°, yield *ca.* 77%; Vb is readily soluble in chloroform, but difficultly soluble in cold benzene and alcohol, and is insoluble in aqueous sodium hydroxide solution; it gives a yellow color with sulfuric acid.

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[22] R. von Rothenburg, *J. prakt. Chem.*, **51**, 140 (1895).

[23] A. Klages, *Ber.*, **35**, 2646 (1902).

[24] H. D. K. Drew and H. H. Hatt, *J. Chem. Soc.*, 16 (1937).

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[26] W. Roser, *ibid.*, **18**, 802 (1885).

TABLE I

REACTION PRODUCTS OBTAINED WITH PHOSPHORUS PENTASULFIDE

Phthala-zone	Reaction product	M.p.,[a] °C.	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Sulfur, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
IIIa	IXa or Xa	174	74	$C_8H_6N_2S$	59.26	59.21	3.70	3.59	17.28	17.18	19.75	19.56
IIIb	IXb or Xb	202	78	$C_{14}H_{10}N_2S$	70.59	70.46	4.20	4.00	11.76	11.70	13.44	13.37
IIId[b]	XIa	138	81	$C_{14}H_{10}N_2S$	70.59	70.50	4.20	4.12	11.76	11.69	13.44	13.50
IIIe	XIb	177	67	$C_{20}H_{14}N_2S$	76.43	76.22	4.46	4.39	8.92	8.86	10.19	10.08
IIIf	XIc	150	73	$C_{15}H_{12}N_2S$	71.43	71.31	4.76	4.59	11.11	10.95	12.70	12.61
IIIg[c]	IXc or Xc	238	81	$C_9H_8N_2S$	61.36	61.11	4.55	4.50	15.91	15.68	18.18	18.09

[a] All melting points are uncorrected. [b] P. C. Mitter and J. N. Sen, *J. Chem. Soc.*, 1145 (1919). [c] F. M. Rowe and A. T. Peters, *ibid.*, 1331 (1933).

Anal. Calcd. for $C_{27}H_{22}N_2O$: C, 79.80; H, 5.42; N, 6.89. Found: C, 79.68; H, 5.29; N, 6.67.

(c) **Benzylmagnesium Chloride.**—To a solution of benzylmagnesium chloride (prepared from 0.8 g. of magnesium, 5.5 g. of benzyl chloride and 50 ml. of dry ether) was added a solution of 1.5 g. of IIIe in 40 ml. of benzene. The reaction mixture was worked up in the usual manner. The oily product was solidified after washing with petroleum ether (b.p. 50–60°). Compound VIa was obtained as colorless crystals from benzene; m.p. 182°, yield *ca.* 0.9 g. VIa is readily soluble in chloroform, difficultly soluble in cold benzene and alcohol, and is insoluble in aqueous sodium hydroxide solution; it gives a green color with sulfuric acid.

Anal. Calcd. for $C_{34}H_{28}N_2$: C, 87.93; H, 6.03; N, 6.03. Found: C, 87.68; H, 5.96; N, 5.92.

(d) **Methylmagnesium Iodide.**—To an ethereal solution of methylmagnesium iodide (prepared from 1 g. of magnesium, 7 g. of methyl iodide and 40 ml. of dry ether) was added a solution of 1 g. of IIIe in 30 ml. of dry benzene. The reaction mixture was worked up in the usual manner and the solid was crystallized from alcohol as colorless crystals, m.p. 139°, yield *ca.* 0.68 g.; VIb is easily soluble in chloroform, difficultly soluble in cold benzene and alcohol, and insoluble in aqueous sodium hydroxide solution; it gives a yellowish-green color with sulfuric acid.

Anal. Calcd. for $C_{22}H_{20}N_2$: C, 84.62; H, 6.41; N, 8.97. Found: C, 84.58; H, 6.35; N, 8.67.

Action of Benzylmagnesium Chloride on IIIf.—A solution of 1.5 g. of IIIf[26] in 40 ml. of benzene was treated with benzylmagnesium chloride, as described above. The solid residue, obtained by evaporation of the ether extract, was crystallized from benzene as colorless crystals, m.p. 162°, yield *ca.* 0.9 g.; VIc is easily soluble in hot chloroform, difficultly soluble in cold ethyl alcohol, and insoluble in aqueous sodium hydroxide solution; it gives a yellow color with sulfuric acid.

Anal. Calcd. for $C_{29}H_{26}N_2$: C, 86.31; H, 6.47; N, 6.97. Found: C, 86.25; H, 6.29; N, 6.75.

Action of Phosphorus Pentasulfide on Phthalazones. *General Procedure.*—To a solution of 1 g. of each of IIIa-b, IIId-g in 40 ml. of dry benzene, except in the case of IIIa in 40 ml. of dry toluene, was added 1 g. of phosphorus pentasulfide. The reaction mixture was refluxed for 6 hours. It was cooled, filtered off and concentrated. The yellow solid, so obtained, was crystallized from benzene–petroleum ether.

The reaction products, listed in Table I, are easily soluble in hot benzene, but difficultly soluble in cold alcohol and petroleum ether. The products obtained from IIIa-b and IIIg are easily soluble in aqueous sodium hydroxide solution (10%).

GIZA, CAIRO, EGYPT (U.A.R.)

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, URBANA, ILL.]

The Action of Sulfur on Indole

BY WAYNE CARPENTER,[1] M. S. GRANT[2] AND H. R. SNYDER

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The substance earlier obtained by heating indole with sulfur in a sealed tube and formulated as a bis-disulfide (II or III) is much more readily obtained by reaction in dimethylformamide. Its reactions, which are studied for the first time, are more readily interpreted on the basis of the 3,3′-diindolyltetrasulfide structure V.

By heating indole with sulfur in sealed tubes under various conditions, earlier investigators have obtained a number of products. Among the structures which have been proposed for the different compounds isolated are those shown by formulas I, II, III and IV. Formula I was assigned by Raffa[3] to a green substance obtained by heating (190–200°) indole with three equivalents of sulfur for forty-eight hours. From a different mixture (about 0.6 equivalent of sulfur) and under different conditions (150–160°, fifty-two hours), Szperl[4] obtained two other compounds, one of which he believed to be a bis-disulfide (II or III); the other product, a white, fluorescent, sulfur-free substance ($C_{16}H_{12}N_2$, m.p. 264°) was not assigned a structure. However, it may be identical with a product obtained earlier in a similar reaction by Oddo[5] and shown to be 3,3′-diindolyl (IV, m.p. 286°), which had been prepared still earlier by an unequivocal method by Gabriel, Gerhard and Walter.[6] Still another white crystalline product (m.p. 326°) had been reported by Madelung and Tencer[7] from an equimolar mixture of indole and sulfur heated two hours at 180–190°. None of the compounds appears to have been obtained in good yield.

In the present work it was found that by heating indole and sulfur in dimethylformamide quite good

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(2) Postdoctorate Research Associate.

(3) L. Raffa, *Gazz. chim. ital.*, **72**, 549 (1942).

(4) Ludwik Szperl, *Roczniki Chem.*, **18**, 804 (1938).

(5) B. Oddo and L. Raffa, *Gazz. chim. ital.*, **69**, 562 (1933).

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