3-Ethyl-5-chloroacenaphthene. To 16 g. of amalgamated mossy zinc was added a solution of 7 g. of 3-acetyl-5-chloroacenaphthene in 225 ml. of glacial acetic acid and 40 ml. of concd. hydrochloric acid. After the solution had refluxed for 1 hr., an additional 40 ml. of concd. hydrochloric acid was added and refluxing continued for an additional 9 hr. The reduction product was isolated in the usual manner and was obtained in white needles m.p. 43.5–44.5°. The yield was 4.5 g. (68%).

Anal. Calcd. for $C_{14}H_{13}Cl$: C, 77.59; H, 6.05. Found: C, 77.38; H, 6.14.

3-Ethyl-5-bromoacenaphthene. 3-Acetyl-5-bromoacenaphthene was reduced in the same way. The product, m.p. 46.5–47°, was obtained in 63% yield.

Anal. Calcd. for $C_{14}H_{13}Br$: C, 64.37; H, 5.02. Found: C, 64.55; H, 5.28.

Reaction of 2-ethyl-4-bromo-1,8-naphthalic anhydride with phenylmagnesium bromide. A solution of phenylmagnesium bromide in 100 ml. of ether was added to a well stirred suspension of 30 g. (0.098 mol.) of 2-ethyl-4-bromonaphthalic anhydride. The reaction mixture became blood red in color, and was heated with stirring while the ether was removed by distillation. The complex was decomposed with 50 ml. of concd. hydrochloric acid and the solution heated to boiling. The solution was filtered and the aqueous layer separated and discarded. The toluene layer was cooled in the ice box and the solid which separated was collected on a filter. Recrystallization of this crude product (11.5 g. m.p. 155–158°) from toluene raised the melting point to 182.5–183°.

Anal. Calcd. for $C_{20}H_{15}BrO_3$: C, 62.68; H, 3.95; neut. equiv., 383.2. Found: C, 62.88; H, 4.21; neut. equiv., 380.8.

The melting point of this compound varied with the rate of heating. The reported melting point was obtained by heating the block at a rate of about two degrees per minute.

After standing for several days, another 22 g. of solid, m.p. 140–146° neut. equiv. 381.1, separated from the toluene mother liquor. This material, apparently a mixture of the isomeric keto acids, could not be further purified by recrystallization.

2-Benzoyl-4-bromo-N-phenyl-1,8-naphthalimide. 4-Bromo-1,8-naphthalic anhydride (4 g.) and 6 ml. of aniline were heated over a free flame for 30 min. The solid which formed on cooling was washed with 5% hydrochloric acid and warmed briefly with 10% sodium carbonate solution. The crude product (4.4 g., 87% yield) was recrystallized once from glacial acetic acid and then from ethanol to give white crystals, m.p. 230–230.5° with sublimation.

Anal. Calcd. for $C_{18}H_{10}BrNO_2$: C, 61.39; H, 2.96. Found: C, 61.50; H, 3.06.

COLUMBIA, MO.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, CAIRO UNIVERSITY AND THE NATIONAL RESEARCH CENTRE, DOKKI, CAIRO]

Action of Grignard Reagents. XV.[1] Action of Phenylmagnesium Bromide on Substituted 1-Phenyl-4-methylene-3,5-pyrazolidinediones

AHMED MUSTAFA, MOHAMED KIRA, AND (MISS) MAKAREM EL-ESSAWI

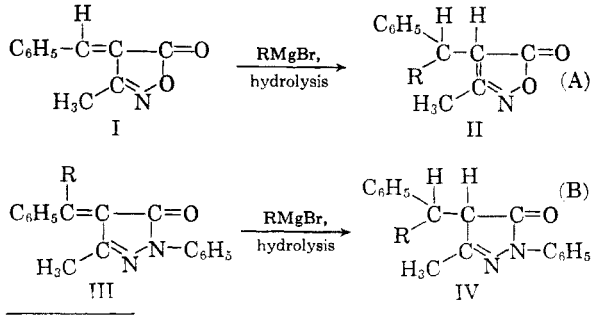
Received July 20, 1959

Phenylmagnesium bromide adds to the exocyclic double bond of the highly colored 1-phenyl-4-benzilidene- and 1-phenyl-4-benzhydrylidene-3,5-pyrazolidinediones (Va–b) to give, after hydrolysis, colorless products believed to have structure VI. Similarly, VIII is obtained by the action of the same reagent on benzylidenemalonic anilide (VII). Syntheses for VIb and VIII are reported.

In extension of the work of one of us[2] on the action of Grignard reagents on heterocyclic compounds, the action of phenylmagnesium bromide on 1-phenyl-4-benzylidene-3,5-pyrazolidinedione (Va) now has been investigated.

The wide spectrum of pharmacological action of 3,5-pyrazolidinedione derivatives,[3] has made this class of compounds among the most widely investigated in this field. In view of these activities, a series of new derivatives of 4-methyl-1-phenyl-3,5-pyrazolidinedione (VI) was synthesized.[4]

The addition of organomagnesium compounds to the conjugation created by attachment of an exocyclic double bond in the 4-position of a heterocyclic nitrogen ring having a carbonyl function has been reported in the case of 3-methyl-4-benzylideneisoxazolone (I)[5] and its nitrogen analog, namely,



(1) For part XIV *cf.* A. Mustafa, W. Asker, A. F. A. Shalaby, S. A. Khattab, and Z. E. Selim, *J. Am. Chem. Soc.*, in press.

(2) *Cf.* (a) A. Mustafa, W. Asker, M. Kamel, A. F. A. Shalaby and A. E. Hassan, *J. Am. Chem. Soc.*, **77**, 1612 (1955); (b) A. Mustafa, W. Asker, and O. H. Hishmat, *J. Am. Chem. Soc.*, **77**, 5127 (1955); (c) A. Mustafa, W. Asker, A. F. A. Shalaby and M. E. Sobhy, *J. Org. Chem.*, **23**, 1992 (1958); (d) A. Mustafa and A. H. E. Harhash, *J. Org. Chem.*, **21**, 575 (1956).

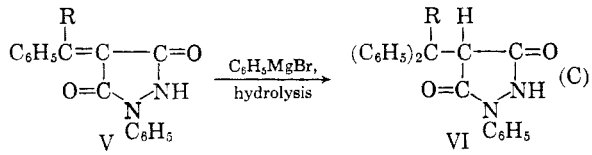
(3) *Cf.* L. Goodman and A. Gilman, *The Pharmacological Basis of Therapeutics*, 2nd ed., The MacMillan Co., New York, 1953, pp. 322–323; Drill (ed.); R. C. Elderfield, *Heterocyclic Compounds*, Vol. 5, John Wiley & Sons, Inc., 1957, pp. 148–149; J. Buchi, J. Ammann, R. Lieberherr, and E. Eichenberger, *Helv. Chim. Acta*, **36**, 75 (1953).

(4) The pharmacological results will be published elsewhere.

(5) L. Panizzi, *Gazz. chim. ital.*, **76**, 44 (1926).

1 - phenyl - 3 - methyl - 4 - benzylidene - 5 - pyrazolone (III) to yield II and IV respectively (*cf.* Scheme A and B).

When the colored Va is treated with excess of phenylmagnesium bromide, followed by hydrolysis, a colorless product, believed to be 1-phenyl-4-diphenylmethyl-3,5-pyrazolidinedione (VIa), is obtained (*cf.* Scheme C). Similarly, treatment of 1-

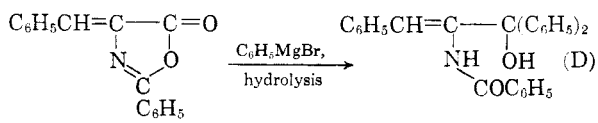


a, R = H; b, R = C_6H_5

phenyl-4-diphenylmethylene-3,5 - pyrazolidinedione (Vb) with phenylmagnesium bromide, followed by hydrolysis, resulted in the formation of 1-phenyl-4-triphenymethyl-3,5-pyrazolidenedione (VIb).

The assigned structure for the Grignard products VIa-b, is inferred from the fact that they are colorless. The melting point and the infrared spectra of VIa are identical with those of the product obtained by the catalytic reduction of Vb. Moreover, the identity of the reaction product obtained by the action of triphenylchloromethane on 1-phenyl-3,5-pyrazolidinedione, an inner hydrazide of malonic acid, in the presence of metallic sodium with VIb is in favor of the given structure.

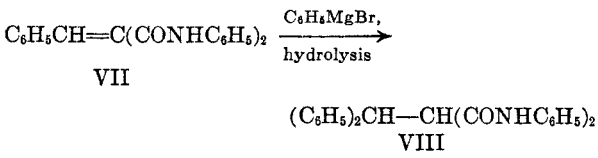
Va-b have the added feature of an α,β-unsaturated carbonyl system and the activity of the exocyclic double bond in position 4 in Va may be compared with the activity of the double bond in I and III. Moreover, the stability of the 5-membered heterocyclic ring in V is in contrast to the ready opening of the oxazolone ring in 2-phenyl-4-benzylidene-2-oxazoline-5-one[2d] (*cf.* Scheme D). We would not like to overlook the



possibility of the tautomeric structures[6] for VI; VIa gives a color reaction with ferric chloride solution.

The action of phenylmagnesium bromide on benzylidenemalondianilide (VII), the open-chain analog of 1,2-diphenyl-4-benzylidene-3,5-pyrazolidinedione (*cf.* Va, N—Ph instead of —NH), now has been investigated. 1,4-Addition[7] of the Grignard reagent takes place and VIII is obtained in good yield (*cf.* Scheme E).

The assigned structure for VIII is inferred from the fact that it is proved to be identical with the product, obtained by the action of aniline on ethyl benzylidenemalonate which was prepared by the condensation of diphenylbromomethane with ethyl malonate in the presence of metallic sodium.



EXPERIMENTAL

1-Phenyl-4-diphenylmethylene-3,5-pyrazolidinedione (Vb). A mixture of 3 g. of 1-phenyl-3,5-pyrazolidinedione[8] and 10 g. of benzophenone was heated at 170° (bath temperature) for 6 hr. The cooled reaction mixture was triturated with ether and the solid so obtained was filtered off and crystallized from ethyl alcohol (*ca.* 1.5 g.). Vb forms deep red crystals and melts at 204° (dec.).

Anal. Calcd. for $C_{22}H_{16}N_2O_2$: N, 8.23. Found: N, 8.49.

Action of Grignard reagents on Va-b. The following illustrates the general procedure; 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 suspension of Va[8] in 30 ml. of dry ether. The red color of Va readily disappeared. The reaction mixture was refluxed (steam bath) for 8 hr., set aside at room temperature overnight, and then treated with a cold saturated aqueous ammonium chloride solution and extracted with an ether-benzene mixture. The ethereal benzene layer was extracted with a cold aqueous sodium hydroxide solution (100 ml.; 5%). The aqueous alkaline solution was acidified with cold dilute hydrochloric acid and the solid that separated was extracted with cold chloroform (*ca.* 50 ml.) and was dried over anhydrous sodium sulfate. The chloroform extract, on evaporation deposited pale yellow crystals. 1-Phenyl-4-diphenylmethyl-3,5-pyrazolidinedione (VIa) was obtained as colorless crystals (0.8 g.) from ethyl alcohol; m.p. 200° (dec.).

Anal. Calcd. for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.71; H, 5.35; N, 8.47.

An alcoholic solution of Va gives a red color upon treatment with an alcoholic solution of ferric chloride.

1-Phenyl-4-triphenylmethyl-3,5-pyrazolidinedione (VIb) was obtained by the action of phenylmagnesium bromide on 1 g. of Vb, as described above, as colorless crystals from a chloroform ethyl alcohol mixture (*ca.* 0.78 g.), m.p. 234° (dec.).

Anal. Calcd. for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.81; H, 5.53; N, 6.69.

It gives a red color when its alcoholic solution is treated with an alcoholic solution of ferric chloride.

Catalytic hydrogenation of Vb. A mixture of 0.2 g. of 5% palladium on calcium carbonate[9] in 50 ml. of absolute ethyl alcohol was shaken in a hydrogen atmosphere for 15 min. to reduce the palladium hydroxide, then 1 g. of Vb in 50 ml. of absolute ethyl alcohol was added. The hydrogenation

(6) For the possibility of tautomerization of a number of substituted 3,5-pyrazolidinediones (*cf.* A. Michaelis, H. Rohmer, *Ber.*, **31**, 2907, 3003, 3193 (1898); S. Imanishi, *J. Chem. Phys.*, **18**, 1307 (1950); R. C. Elderfield, *Heterocyclic Compounds*, Vol. 5, John Wiley & Sons, 1957, p. 148).

(7) Similar 1,4-additions have been reported in the case of ethyl benzylidenemalonate (E. P. Kohler, *Am. Chem. J.*, **34**, 132 (1906); Reynolds, *Am. Chem. J.*, **44**, 305 (1910); M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, Inc., New York, 1954, p. 563) and in the case of *N,N*-disubstituted cinnamides (*cf.* E. P. Kohler, *Am. Chem. J.*, **33**, 21 (1905); N. Maxim and N. Ioanid, *Bull. soc. chim. Romania*, **10**, 29 (1928); *Chem. Abstr.*, **22**, 4114 (1928).

(8) A. Michaelis and R. Burmeiser, *Ber.*, **25**, 1502 (1892).

(9) R. Mozingo, *Org. Syntheses*, **III**, 685 (1955), John Wiley & Sons, Inc., New York.

was continued until the red color was completely discharged (*ca.* 20 min.). The alcoholic solution was separated by filtration and on concentration and cooling, it deposited colorless crystals (*ca.* 0.82 g.).

Anal. Calcd. for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.04; H, 5.26; N, 8.46.

They were identified as 1-phenyl-4-diphenylmethyl-3,5-pyrazolidinedione (VIa). Determination of the melting point and mixed m.p. with a sample of VIa, obtained as above, gave no depression; similarly the infrared spectra of both samples were found to be identical.

Action of triphenylchloromethane on 1-phenyl-3,5-pyrazolidinedione. To a solution of 0.23 g. of metallic sodium in 10 ml. of absolute ethyl alcohol was added a solution of 1.78 g. of 1-phenyl-3,5-pyrazolidinedione[8] in 15 ml. of absolute ethyl alcohol. The stirred reaction mixture was treated, at room temperature, with a solution of 2.28 g. of triphenylchloromethane in 15 ml. of absolute ethyl alcohol. It was left overnight and then refluxed (steam bath) for 1 hr. to effect completion of the reaction. The cooled reaction mixture was poured into ice cold water and the solid that separated was filtered off, washed with water, and crystallized from a chloroform–ethyl alcohol mixture (*ca.* 1.9 g.), m.p. 234° (dec.).

Anal. Calcd. for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.32; H, 5.84; N, 7.24.

The reaction product proved to be identical with VIb; (melting point and mixed melting point determination with a sample of VIb obtained as above).

Action of phenylmagnesium bromide on VII. One gram of VII was treated with phenylmagnesium bromide as described in the case of V. The reaction product (VIII) was obtained from ethyl alcohol and/or from acetone in colorless crystals (*ca.* 0.78 g.), m.p. 285°.

Anal. Calcd. for $C_{28}H_{24}N_2O_2$: C, 79.97; H, 5.75. Found: C, 79.92; H, 5.93.

Action of aniline on ethyl diphenylmethylmalonate. Ethyl diphenylmethylmalonate was prepared after the procedure described for the preparation of ethyl *n*-butylmalonate,[10] and was obtained as colorless crystals from petroleum ether (b.p. 50–80°) (52% yield), m.p. 55°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.44; H, 6.15. Found: C, 73.53; H, 6.45.

A mixture of 2 g. of ethyl diphenylmethylmalonate and 6 g. of freshly distilled aniline was refluxed (oil bath) for 7 hr. The cooled reaction mixture was treated with ether and the separated solid was filtered off, washed with ether, and crystallized from ethyl alcohol. Colorless needles (*ca.* 1.9 g.), m.p. 285°.

Anal. Calcd. for $C_{28}H_{24}N_2O_2$: C, 79.97; H, 5.75. Found: C, 80.26; H, 5.58.

It proved to be identical with VIII (m.p. and mixed m.p. determinations).

GIZA, CAIRO
U. A. R.

(10) *Cf. Org. Syntheses*, I, 250 (1948).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF ABERDEEN]

Studies in the Juglone Series. IV. The Addition of Aniline and Toluene-*p*-thiol to 5-Substituted 1,4-Naphthoquinones

J. W. MACLEOD AND R. H. THOMSON

Received August 5, 1959

The structures previously assigned to the products of addition of toluene-*p*-thiol to juglone and juglone acetate have been confirmed. Addition of both aniline and toluene-*p*-thiol to 5-methoxy-, 5-methyl-, 5-acetamido- and 5-chloro-1,4-naphthoquinones takes place predominantly at position 3.

In Part III[1] of this series it was reported that addition of toluene-*p*-thiol and thioglycolic acid to juglone occurred predominantly at position 3, whereas addition to juglone acetate occurred mainly at position 2. The 3-substituted juglones were also prepared by reaction of 3-chlorojuglone with the appropriate thiol in the presence of pyridine; in addition 2-*p*-tolythiojuglone was obtained, in small yield [together with a second product, now identified as 2,3-di(*p*-tolythio)juglone] by reaction of 2-chlorojuglone with toluene-*p*-thiol in the presence of pyridine. These reactions were considered to establish the structures of the addition products. However, the thioglycolic acid reactions were recently reexamined by Rothman[2] who concluded that addition to juglone occurred predominantly at position 2, while addition to juglone acetate occurred mainly at position 3. These results are opposite to those found earlier by one of us,[1] and, at first sight appear to be very satisfactory insofar as they bring thioglycolic acid and, by implication, toluene-*p*-thiol, into line with other nucleophilic additions in the juglone series, and the radical addition mechanism proposed[1] becomes unnecessary. Unfortunately, Rothman's experimental evidence is not entirely convincing. His method of orientation consisted in catalytic reduction of each juglone-thioglycolic acid, followed by condensation of the carboxyl group with the neighboring quinol hydroxyl group. This gave two isomeric lactones (which can be regarded as substituted naphthalene-1,5- and 4,5- diols) which were distinguished by their relative abilities to increase the acidity of a boric acid solution. As one of the lactones was amorphous (and no analysis was reported) the results are in some doubt, and further verification is therefore desirable. We have confirmed (by comparison of their ethyl esters) that the compound obtained by addition of thioglycolic acid to juglone is identical with that formed by reaction

(1) R. H. Thomson, *J. Org. Chem.*, 16, 1082 (1951).
(2) F. G. Rothman, *J. Org. Chem.*, 23, 1049 (1958).