[Contribution from the Department of Chemistry, University of Missouri]

Preparation and Reactions of Some 2-Acylhalo-1,8-naphthalic Anhydrides

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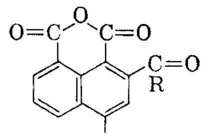
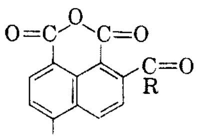
The oxidation of a series of acylhaloacenaphthenes with sodium dichromate in glacial acetic acid gave the corresponding acylhalo-1,8-naphthalic anhydrides in nearly quantitative yields.

4-Bromo-1,8-naphthalic anhydride and 2-ethyl-4-bromo-1,8-naphthalic anhydride each reacted with phenylmagnesium bromide to form a mixture of isomeric keto acids.

In connection with our study of the reactions of some polynuclear aroyl acid chlorides and anhydrides with organometallic compounds,[2] we have prepared a series of acylhalo-1,8-naphthalic anhydrides of types I and II. In view of the recent publication in this area by Richter and Stocker,[3] it seems advisable to record at this time our data relative to these anhydrides.



I



II

Ia. R = C_6H_5; X = Br
Ib. R = C_6H_5; X = Cl
Ic. R = CH_3; X = Br
Id. R = CH_3; X = Cl

IIa. R = C_6H_5; X = Br
IIb. R = C_6H_5; X = Cl

The acylhalonaphthalic anhydrides in Series I and the anhydrides IIa and IIb were readily obtained in nearly quantitative yields by the oxidation of the corresponding acylhaloacenaphthenes with sodium dichromate in glacial acetic acid. No isolatable product was obtained from the oxidation of 3-acetyl-6-chloro- and 3-acetyl-6-bromoacenaphthene.

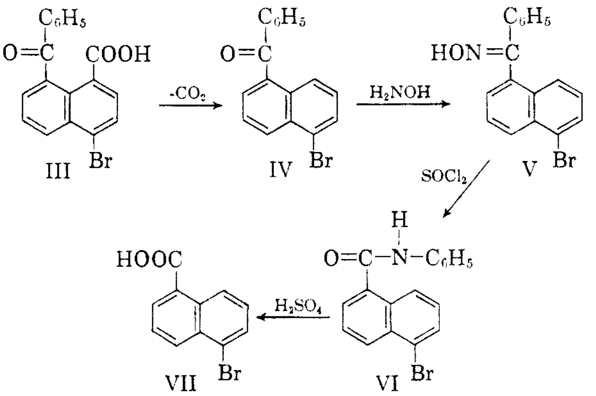
There were noticeable differences in the ease with which the anhydrides were formed. 3-Acetyl-5-bromo- and 3-acetyl-5-chloroacenaphthene were the most readily oxidized and formed the corresponding anhydrides in theoretical yields, even when the reaction time was only ten minutes. The oxidation of the four benzoylhaloacenaphthenes required a reaction time of forty-five minutes to obtain a theoretical yield of anhydride, while 3-ethyl-5-chloro- and 3-ethyl-5-bromoacenaphthene required one hour.

For comparison, 5-bromoacenaphthene and acenaphthene were oxidized under the same conditions. The former required a reaction time of one hour to obtain 4-bromo-1,8-naphthalic anhydride in 93% yield while the latter gave only a 63% yield of 1,8-naphthalic anhydride after a reaction time of an hour and a half and the yield was not increased by longer heating.

The 2-ethyl-4-haloacenaphthenes were prepared by the Clemmensen reduction of the corresponding ketones. The Wolff-Kishner reduction of the ketones gave a tar from which no product was isolated.

As might be expected, the reaction of phenylmagnesium bromide with 4-bromo-1,8-naphthalic anhydride gave a mixture of isomeric keto acids in 93% yield. One isomer, 8-benzoyl-4-bromo-1-naphthoic acid III was isolated in 25% yield by crystallization of the mixture from toluene.

Compound III was not described in the literature and its structure was determined by the reactions illustrated.



When III was decarboxylated, the product IV was found to melt at 95–96°. This value is close to the reported values of 98° and 100.5° for the 1-benzoylbromonaphthalene which Elbs and Steinike[4] and Rospendowski[5] obtained from the bromination of 1-benzoylnaphthalene. The procedure of Rospendowski[5] for this bromination was repeated and the product was shown by a mixed melting point to be identical with IV.

When the oxime V was treated with thionyl chloride, a rearrangement product VI was obtained which melted at 218–218.5°. This value agreed closely with the value 216–217° reported by Ruggli and Preuss[6] for the anilide of authentic

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[1] Abstract of a portion of the Ph.D. dissertation of William S. Wagner, 1952.

[2] D. V. Nightingale, W. S. Wagner, and R. H. Wise, *J. Am. Chem. Soc.*, **75**, 4701 (1953).

[3] H. J. Richter and F. B. Stocker, *J. Org. Chem.*, **24**, 214 (1959).

[4] K. Elbs and G. Steinike, *Ber.*, **19**, 1965 (1886).

[5] M. Rospendowski, *Compt. rend.*, **102**, 872 (1886).

[6] P. Ruggli and R. Preuss, *Helv. Chim. Acta*, **24**, 1345 (1941).

TABLE I

SUBSTITUTED 1,8-NAPHTHALIC ANHYDRIDES

1,8-Naphthalic Anhydrides	M.P., °C.	Formula	Calcd.		Found	
			C	H	C	H
2-Acetyl-4-chloro	283.5–284	$C_{14}H_7ClO_4$	61.22	2.57	61.44	2.69
2-Acetyl-4-bromo	275–275.5	$C_{14}H_7BrO_4$	52.69	2.21	52.50	2.47
2-Benzoyl-4-chloro	257.5–258.5	$C_{19}H_9ClO_4$	67.78	2.69	67.99	2.99
2-Benzoyl-5-chloro	215–216	$C_{19}H_9ClO_4$	67.78	2.69	67.40	2.96
2-Benzoyl-4-bromo[a]	250–251	$C_{19}H_9BrO_4$	59.86	2.38	59.65	2.62
2-Benzoyl-5-bromo[a]	250–251	$C_{19}H_9BrO_4$	59.86	2.38	59.62	2.68
2-Ethyl-4-chloro	209–210	$C_{14}H_9ClO_3$	64.48	3.48	64.25	3.52
2-Ethyl-4-bromo	212–213	$C_{14}H_9BrO_3$	55.10	2.97	55.10	3.17

[a] A mixture of these two anhydrides melted at 232°.

5-bromo-1-naphthoic acid. Hydrolysis of VI gave 5-bromo-1-naphthoic acid, m.p. 245–247°. Ekstrand[7] reported a melting point of 246° for this acid. This further established the structure of IV and III.

The reaction of phenylmagnesium bromide with 2-ethyl-4-bromo-1,8-naphthalic anhydride gave a mixture of keto acids from which one isomer was isolated in 21% yield.

EXPERIMENTAL[8]

2-Acetyl-4-chloro-1,8-naphthalic anhydride. The preparation of this anhydride is typical of the preparation of the substituted naphthalic anhydrides and is described in detail. It is essentially the method of Graebe and Hass.[9] The acylhaloacenaphthenes were prepared by the procedure of Nightingale and Brooker.[10]

3-Acetyl-5-chloroacenaphthene (10 g., 0.048 mol.) was dissolved in 120 ml. of glacial acetic acid and to this solution was added 50 g. (0.19 mol.) of sodium dichromate. After the spontaneous reaction had subsided, the solution was refluxed for 10 min. and then poured into 400 ml. of hot water. The precipitated anhydride was separated by filtration and washed with water. The yield of anhydride was practically quantitative. After recrystallization from benzene or ethyl acetate, the compound melted at 283.5–284° with decomposition and sublimation.

The melting points and analyses of the anhydrides are summarized in Table I.

Reaction of phenylmagnesium bromide with 4-bromo-1,8-naphthalic anhydride. The Grignard reagent prepared in the usual manner from 30 g. (0.19 mol.) of bromobenzene in 100 ml. of ether was added rapidly to a well stirred suspension of 48 g. (0.17 mol.) of 4-bromonaphthalic anhydride in 525 ml. of dry toluene. The solution was refluxed for 30 min., then the ether was removed by distillation and the complex was hydrolyzed by the addition of 75 ml. of concd. hydrochloric acid. The solution was filtered to remove a small amount of unchanged anhydride and the acid layer separated and discarded. When the toluene solution was cooled in an ice bath, 16 g. (26%) of crude 8-benzoyl-4-bromo-1-naphthoic acid III, m.p. 184–187°, separated. After recrystallization from toluene, the melting point was 194.5–195.5°.

Anal. Calcd. for $C_{18}H_{11}BrO_3$: C, 60.87; H, 3.12; neut. equiv., 355.2. Found: C, 60.92; H, 3.19; neut. equiv., 353.4.

The toluene filtrate was extracted with sodium carbonate solution. When the aqueous extract was acidified, a total of 41 g. (67%) of crude keto acid m.p. 140–146°, was obtained. After recrystallization from toluene, the melting point of this material was 140–141°, and the neutral equivalent was 352.4. A series of mixture melting points of this product with pure 8-benzoyl-4-bromo-1-naphthoic acid indicated that it may be a eutectic mixture of the two isomeric acids possible from this reaction.

Decarboxylation of III. A mixture of 4 g. of III and 4 g. of copper oxide was heated in a distilling flask at 200–250° until gas was no longer evolved. Distillation of the reaction mixture yielded 1 g. of ketone IV, m.p. 95–96°.

Authentic IV was synthesized by the bromination of 1-naphthyl phenyl ketone by the procedure of Rospendowski.[5] It melted at 95–96°, the recorded value, and did not depress the melting point of ketone IV obtained from the decarboxylation of III.

Preparation and rearrangement of the oxime (V) *of* IV. The ketone (6.5 g., 0.021 mol.) was dissolved in 125 ml. of ethanol with 8 g. (0.12 mol.) of hydroxylamine by heating on a steam bath. To the refluxing solution was added 10 g. (0.25 mol.) of sodium acetate at such a rate that the reaction did not become violent. The solution was refluxed an additional 1.5 hr. and poured into water. The oxime separated as a pasty solid which could not be recrystallized from ethanol. The solvent-free product was rearranged to the acylated amine without further purification.

The procedure was an adaptation of the method of Huntress and Walter[11] for the rearrangement of phenyl 2-pyridyl ketoxime with thionyl chloride.

To a solution of crude V from 6.5 g. of IV in 50 ml. of chloroform was added slowly 3.3 g. (0.028 mol.) of thionyl chloride. The chloroform was removed by distillation on a steam bath and the residue recrystallized from ethanol. The white crystals of 1-benzoylamino-5-bromonaphthalene VI melted at 218–218.5°, the literature value.[6] This sample of VI did not depress the melting of authentic VI. A mixture melting point of VI with an authentic sample of the isomeric 1-benzoylamino-4-bromonaphthalene (m.p. 237.5–238°) was 180–210°.

Authentic 1-benzoylamino-4-bromonaphthalene (m.p. 237.5–238°) was prepared by benzoylation of 4-bromo-1-naphthylamine.[12]

Anal. Calcd. for $C_{17}H_{12}BrNO$: C, 62.60; H, 3.71. Found: C, 62.51; H, 3.96.

Hydrolysis of VI by means of 60% sulfuric acid yielded 5-bromo-1-naphthoic acid, m.p. 245–247°, literature value[7] 246°.

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(7) A. Ekstrand, *J. prakt. Chem.*, (2), 38, 155 (1910).

(8) The carbon and hydrogen analyses were performed by Mr. P. D. Strickler, Mr. D. W. Rosenburg, and Mr. Y. C. Lee. All melting points and boiling points are uncorrected.

(9) C. Graebe and P. Hass, *Ann.*, **237**, 91 (1903).

(10) D. V. Nightingale and R. M. Brooker, *J. Am. Chem. Soc.*, **72**, 5539 (1950).

(11) E. Huntress and H. Walter, *J. Am. Chem. Soc.*, **68**, 2487 (1946).

(12) L. F. Fieser and V. Desreux, *J. Am. Chem. Soc.*, **60**, 2255 (1938).

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

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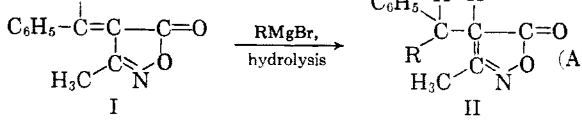
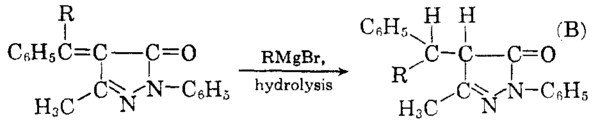
Phenylmagnesium bromide adds to the exocyclic double bond of the highly colored 1-phenyl-4-benzilidene- and 1-phenyl-4-benzhydrylidene-3,5-pyrazolidinediones (Va–b) to give, after hydrolysis, colorless products believed to have structure VI. Similarly, VIII is obtained by the action of the same reagent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


I II (A)


III IV (B)

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(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).