Anal. Calcd. for $C_{10}H_8ON_2Br$: C, 36.2; H, 2.43. Found: C, 36.6; H, 2.69.

The acetyl derivative (m.p. 135–136.5°) was obtained by treatment with acetic anhydride.

The Action of Hydrobromic Acid on 5,7-Dibromo-6-methoxy-8-aminoquinoline in the Presence of Phenol.—5,7-Dibromo-6-methoxy-8-aminoquinoline (1.2 g.) and phenol (*ca.* 0.3 g.) were placed in a flask with hydrobromic acid (20%, 70 ml.) and heated under reflux for 1.5 hours. The reaction mixture was cooled and the orange solid was removed by filtration. (The filtrate contained the phenolic substances.) The orange solid was treated with alkali to convert the hydrobromide to the free base, which was washed with water and crystallized from ethanol. 6-Methoxy-7-bromo-8-aminoquinoline (0.4 g., m.p. 113–114°) was obtained.

The filtrate containing the phenolic substances was extracted with ether. The ether extract gave a small amount of an oil, which was dissolved in sodium hydroxide and treated with 2,4-dinitrochlorobenzene. *o*-Bromophenyl 2,4-dinitrophenyl ether (m.p. 84–85.5°) was obtained.

The Transformation of 5-Bromo-6-methoxy-8-aminoquinoline into 6-Methoxy-7-bromo-8-aminoquinoline in the Presence of Phenol.—A solution of phenol (4.7 g.) in hydrobromic acid (10%, 200 ml.) was placed in a 3-neck flask fitted with stirrer and reflux condenser. The solution was heated to boiling and then 5-bromo-6-methoxy-8-aminoquinoline (15 g.) was added in small portions over a period of 1.75 hours. The solution became deep red. After the addition of the quinoline was complete, refluxing was continued for another one-half hour. During this time, a large quantity of yellow needles separated. The mixture was then cooled and filtered. (The filtrate contained the phenolic substances.) These yellow needles were treated with sodium hydroxide (10%, 270 ml.) to produce the free base. (Additional phenolic material can be recovered from the alkaline filtrate.) Repeated crystallization of the free base from alcohol yielded 6-methoxy-7-bromo-8-aminoquinoline (m.p. 112–14°, 4.1 g., 32% theory).

The phenol containing filtrate was extracted with ether. This ether extract possesses the characteristic odor of halogenated phenols. Two derivatives were prepared from this phenolic fraction, *o*-bromophenyl 2,4-dinitrophenyl ether (m.p. 84–85°) and *p*-bromophenoxyacetic acid (m.p. 154–55°). A mixture of *o*- and *p*-bromophenol was therefore produced in this experiment.

MINNEAPOLIS, MINNESOTA RECEIVED DECEMBER 26, 1951

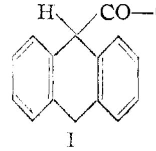
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Reaction of α-Haloketones with Bases

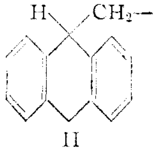
BY WILLIAM G. DAUBEN, CLAUDE F. HISKEY[1] AND MERRILL A. MUHS

It was found that when benzhydryl chloromethyl or bromomethyl ketone was allowed to react with diethylamine only the displacement product was obtained. When the base was alcoholic sodium methoxide, however, rearrangement to methyl 3,3-diphenylpropionate occurred. The reaction of the corresponding 4,4′-dinitrobenzhydryl chloromethyl ketone with sodium methoxide yielded only the cleavage product, 4,4′-dinitrodiphenylmethane. Desyl chloride under the same conditions was transformed into benzoin methyl ether and not the oxirane as previous workers had reported.

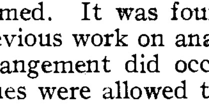
In the course of a recent investigation dealing with the preparation of aryl aminomethyl ketones, May and Mosettig[2] studied the reaction of secondary amines with various aryl halomethyl ketones. When the aryl group was 9,10-dihydro-9-anthryl (I), it was found that in addition to the expected displacement product, an amide was isolated and it was shown to be N,N-dialkyl 9,10-dihydro-9-anthrylacetamide (II). Such a rearrangement of a α-haloketone in the presence of base is well-known[3,4] and, indeed, the rearrangement of benzyl chloromethyl ketone in alkali is quite analogous.[5,6] There is nevertheless one noticeable difference. The rearrangement of the dihydroanthryl compound was initiated by a weak organic base whereas all other rearrangements were brought about by much stronger organic or inorganic bases. Loftfield[4] has recently pointed out that such a result is consistent with his theory in which the ease of removal of the hydrogen atom on the α-carbon not holding the halogen (the α′-hydrogen) greatly influences the course of the reaction. Thus, in the dihydroanthryl case, since the α′-hydrogen atom is activated by two phenyl groups, the rate of its removal is increased and consequently the rearrangement proceeds readily. In line with the foregoing theory, a study of the reaction of the structurally similar benzhydryl halomethyl ketones (III) with amines and alkoxide which had been performed at an earlier date in this Laboratory, is of interest.



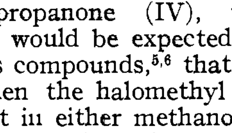
I



II



III



IV

When either benzhydryl chloromethyl or bromomethyl ketone (III) was allowed to react with diethylamine in ether under the conditions of May and Mosettig[2] only the displacement product, 1,1-diphenyl-3-diethylamino-2-propanone (IV), was formed. It was found, as would be expected by previous work on analogous compounds,[5,6] that rearrangement did occur when the halomethyl ketones were allowed to react in either methanol or ether with sodium methoxide and methyl 3,3-diphenylpropionate (V) was obtained.

In order to study the effect of substituents upon the ease of removal of the α′-hydrogen atom and upon the rearrangement reaction 4,4′-dimethoxybenzhydryl and 4,4′-dinitrobenzhydryl chloromethyl ketone (VI) were prepared. When the dimethoxy compound was allowed to react in

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[1] Allied Chemical and Dye Corporation Fellow, 1949–1950.

[2] E. L. May and E. Mosettig, THIS JOURNAL, **70**, 1077 (1948).

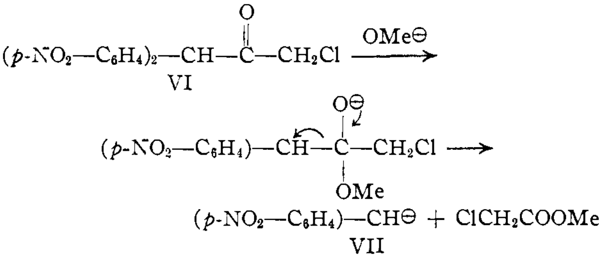
[3] R. Jacquier, *Bull. soc. chim. France*, D-35 (1950).

[4] R. B. Loftfield, THIS JOURNAL, **73**, 4707 (1951).

[5] G. Richard, *Compt. rend.*, **197**, 1432 (1933).

[6] W. D. McPhee and E. Klingsberg, THIS JOURNAL, **66**, 1132 (1944).

ether or methanol with either diethylamine or sodium methoxide only polymerization occurred. The dinitro compound yielded no pure product upon reaction with the amine but in the presence of methanolic sodium hydroxide, 4,4′-dinitrodiphenylmethane (VII) was obtained. Such a result can be rationalized by analogy to the ease with which dinitrodiphenylacetic acid[7] undergoes decarboxylation and might be visualized to proceed as



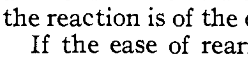
VI

VII

Since rearrangement was not found with any of the foregoing benzhydryl compounds using diethylamine, the unique result in the dihydro anthryl series was reinvestigated using a C^{14}-labeled anthracene derivative. It was found that carbonyl-labeled 9-(ω-bromoaceto)-9,10-dihydroanthracene (I) yielded carboxyl-labeled N,N-diethyl 9,10-dihydro-9-anthrylacetamide (II). Thus, the amide is formed *via* a rearrangement pathway and the reaction is of the expected type.

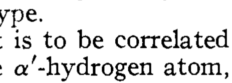
If the ease of rearrangement is to be correlated with the rate of removal of the α'-hydrogen atom, it must be concluded that the benzhydryl compounds ionize more slowly than the 9,10-dihydroanthryl ketone. It would seem plausible that this difference could be due to the more rigid structure of the dihydroanthryl nucleus. Although the substitution of nitro groups in the 4,4′-positions would be expected to increase the ease of removal of the α'-hydrogen, the results obtained do not lend themselves to such an evaluation. The formation of the 4,4′-dinitrodiphenylmethane does suggest an increased electrophilic character of the carbonyl carbon of the ketone. The large stabilization of the dinitrodiphenylmethyl anion, however, may be of equal importance.

The reaction of another phenyl substituted α-haloketone, desyl chloride (VIII), also is of interest. Madelung and Oberwegner[8] have reported that when this chloroketone was allowed to react with methanolic sodium ethoxide,[9] 1-methoxy-1,2-diphenyloxirane (IX) was isolated as an oil. Pyrolysis of this compound was stated to yield diphenylacetylene epoxide (X). Repetition of this work gave a liquid product identical in properties to IX which, upon standing, crystallized and yielded a compound identical with X. The solid product was shown to be benzoin methyl ether (XI). Thus, it would appear that both compounds isolated by Madelung and Oberwegner[8] were benzoin methyl ether in different states of purity. Weiner and Stevens[10] have recently announced that they have arrived at a similar conclusion.

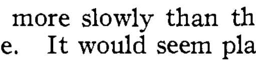


$C_6H_5-CH(Cl)-CO-C_6H_5$

VIII



IX



X

Experimental[11]

1,1-Diphenyl-3-bromopropanone.—A solution of diphenylacetyl chloride[12] (13.3 g., 0.057 mole) in 100 ml. of dry ether was added dropwise with stirring to an ice-cold ethereal solution of diazomethane (prepared from 20 g. of nitrosomethylurea). After the addition was completed, the solution was allowed to stand at ice temperature for an additional 30 minutes and at room temperature for one hour. The excess diazomethane was removed by distillation of the ether and the residue dissolved in 100 ml. of dry ether. A solution of 14 ml. of 48% hydrobromic acid in 14 ml. of ether was added dropwise with stirring to the diazoketone solution. The mixture was processed in the usual manner and bromoketone recrystallized from hot methanol; yield 11.1 g. (67%), m.p. 66–67°.

Anal. Calcd. for $C_{15}H_{13}OBr$: C, 62.30; H, 4.53; Br, 27.64. Found: C, 62.44; H, 4.61; Br, 28.02.

1,1-Diphenyl-3-chloropropanone.—The above procedure was followed using 18.8 g. (0.081 mole) of acid chloride except that hydrochloric acid was employed. The product was recrystallized from hot methanol; yield 12.2 g. (62%), m.p. 70–71°. Lewis, Nierenstein and Rich[13] report a value of 91–92°.

Anal. Calcd. for $C_{15}H_{13}OCl$: C, 73.62; H, 5.35; Cl, 14.49. Found: C, 73.67; H, 5.18; Cl, 14.59.

1,1-Diphenyl-3-diethylaminopropanone Hydrochloride.—A mixture of 3.7 g. (0.013 mole) of 1,1-diphenyl-3-bromopropanone, 4 ml. of diethylamine and 32 ml. of dry ether was shaken for one hour. A white solid precipitated during the reaction. After standing for 72 hours, the mixture was diluted with 20 ml. of petroleum ether (b.p. 30–60°) and cooled in ice. The diethylamine hydrobromide (0.4 g.) was filtered. The filtrate was washed with water and dried over anhydrous sodium sulfate. Dry gaseous hydrogen chloride was bubbled into the filtrate and a gummy, orange solid precipitated. Recrystallization of the solid from hot ether–ethanol gave 1.4 g. (35%) of hydrochloride as white needles, m.p. 182–186°.

Anal. Calcd. for $C_{19}H_{24}ONCl$: C, 71.79; H, 7.61; N, 4.41; Cl, 11.18. Found: C, 71.91; H, 7.50; N, 4.40; Cl, 11.21.

The reaction was repeated using 3.15 g. (0.013 mole) of 1,1-diphenyl-3-chloropropanone. Diethylamine hydrochloride (0.75 g.) was isolated. The reaction mixture was processed as above and the 1,1-diphenyl-3-diethylaminopropanone hydrochloride isolated in 16% yield (0.50 g.), m.p. 184–186°, no depression upon admixture with the material prepared from the bromoketone. A small amount (0.7 g.) of the starting chloroketone was recovered.

Methyl 3,3-Diphenylpropionate (a) In Methanol.—Sodium (0.91 g., 0.04 mole) was added to 30 ml. of anhydrous methanol. A solution of 8.0 g. (0.032 mole) of 1,1-diphenyl-3-chloropropanone in 45 ml. of anhydrous methanol was added dropwise with stirring to the refluxing methoxide solution. The reaction mixture was heated for an additional hour at the end of which time it was dark brown in color and

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[7] L. Haskelberg and D. Lavie, THIS JOURNAL, **71**, 2580 (1949).

[8] W. Madelung and M. E. Oberwegner, *Ann.*, **490**, 201 (1931).

[9] Richard[5] has reported that desyl chloride rearranges to diphenylacetic acid when allowed to react with potassium in ether. This reaction has been repeated using sodium methoxide as the base and the only acidic product isolated was benzilic acid. Roger and McGregor (*J. Chem. Soc.*, 1850 (1934)) also obtained only benzilic acid with potassium hydroxide in toluene.

[10] N. Weiner and C. L. Stevens, Abstracts of the XIIth International Congress of Pure and Applied Chemistry, New York, Sept., 1951, p. 404.

[11] Analyses by the Microanalytical Laboratory of the University of California. All melting points are corrected and all boiling points are uncorrected.

[12] A. Bistrzycki and H. Landtwing, *Ber.*, **41**, 686 (1908).

[13] H. H. Lewis, M. Nierenstein and E. M. Rich, THIS JOURNAL **47**, 1728 (1925).

a white solid had precipitated. The bulk of the methanol was removed under reduced pressure and the residue diluted with water and ether. The aqueous layer was extracted three times with ether and the combined ether fraction dried. The ether was removed and the product distilled, b.p. 168–170° (5 mm.). The distillate crystallized upon standing to give a white solid; m.p. 43–45° (lit.[14] 48°), yield 6.0 g. (77%). The aqueous layer from the reaction was acidified, the solid acid collected and recrystallized from aqueous methanol, yield 0.30 g. (3.5%), m.p. 154–155° (lit.[15] 154–155°), no depression upon admixture with an authentic sample.

The ester (12.0 g., 0.05 mole) was saponified with 11.0 g. (0.2 mole) of potassium hydroxide in 100 ml. of water and 5 ml. of methanol. The acid was recrystallized from aqueous ethanol, yield 10.5 g. (93%), m.p. 154–155°, no depression upon admixture with an authentic sample.

The reaction was repeated using 8.0 g. (0.035 mole) of 1,1-diphenyl-3-bromopropanone and 4.8 g. (71%) of the ester (m.p. 43–45°) was obtained. The aqueous layer yielded 0.35 g. (5.6%) of acid, m.p. 154–155°.

(b) **In Ether.**—Dry sodium methoxide, prepared from 30 ml. of anhydrous methanol and 1.08 g. (0.047 mole) of sodium, was suspended in 100 ml. of anhydrous ether. A solution of 9.2 g. (0.038) of 1,1-diphenyl-3-chloropropanone in 100 ml. of ether was added slowly and the resulting mixture refluxed for three hours. The reaction mixture was processed as described above and 3.9 g. of ester (43%), m.p. 43–45°, was obtained. The aqueous layer yielded 0.6 g. (7%) of acid, m.p. 153–155°.

Upon repeating with 9.1 g. (0.032 mole) of 1,1-diphenyl-3-bromopropanone in 180 ml. of ether, the yield of ester (m.p. 44–46°) was 2.4 g. (31%).

4,4'-Dimethoxybenzhydryl Chloromethyl Ketone.—Di-*p*-anisylacetyl chloride[16] (m.p. 61.3–63.3°) was allowed to react with excess diazomethane in the usual manner and the resulting diazoketone converted to the chloroketone with concentrated hydrochloric acid. The crude product was recrystallized from 60 ml. of methanol; yield 10.0 g. (82.5%), m.p. 69.3–70.3°.

Anal. Calcd. for $C_{17}H_{17}O_3Cl$: Cl, 11.63. Found: Cl, 11.60.

4,4'-Dinitrobenzohydryl Chloromethyl Ketone.—A solution of 15.5 g. (0.047 mole, m.p. 140–143°) of 4,4'-dinitrodiphenylacetyl chloride[7] in 100 ml. of dry methylene dichloride was allowed to react with an excess of diazomethane and the resulting diazoketone transformed to the chloroketone with concentrated hydrochloric acid. The product was recrystallized from methanol; m.p. 130.6–132.5°, yield 12.7 g. (80%).

Anal. Calcd. for $C_{15}H_{11}O_5N_2Cl$: Cl, 10.59. Found: Cl, 10.33.

4,4'-Dinitrodiphenylmethane.—4,4'-Dinitrobenzhydryl chloromethyl ketone (3.0 g., 0.009 mole) was dissolved in a solution of 0.21 g. (0.009 mole) of sodium and 250 ml. of dry methanol. The resulting dark purple mixture was refluxed for 30 minutes, the bulk of the methanol distilled and the residue diluted with water. The greenish-yellow solid was filtered and recrystallized from ethyl acetate to yield 1.72 g. (71.7%) of 4,4'-dinitrodiphenylmethane, m.p. 187.4–188.4° (lit.[7] 187°).

Anal. Calcd. for $C_{13}H_{10}O_4N_2$: C, 60.46; H, 3.94; N, 10.83. Found: C, 60.77; H, 3.91; N, 10.76.

Cuprous Cyanide-C^{14}.—The compound was prepared following the procedure of Barber[17] employing sodium cyanide-C^{14} (8.8 g., 0.18 mole), containing approximately 0.5 millicurie, copper sulfate (45 g., 0.18 mole) and sodium metabisulfite (12.8 g., 0.067 mole); yield 12.8 g. (79.6%).

Cyano-labeled 9-Cyanoanthracene.—The reaction was conducted following a modified procedure of Bachmann and Kloetzel.[18] From 12.8 g. (0.142 mole) of dry cuprous cyanide-C^{14} and 32.4 g. (0.127 mole) of 9-bromoanthracene, there was obtained 26.6 g. (92.4%) of 9-cyanoanthracene, m.p. 172–173°, *specific activity* × 15: 2720 cts./min./mg. barium carbonate.[19]

Carboxyl-labeled 9,10-Dihydro-9-anthrylacetic Acid.—This compound was prepared from the above labeled 9-cyanoanthracene following the procedure of May and Mosettig[2] except that in the preparation of the intermediate diazoketone, methylene chloride was used as solvent. The over-all yield was 12.4% and the acid melts 171–172°[2] (reported 168–169.5°). The *specific activities* of all of the compounds prepared were 2760 ± 40 cts./min./mg. barium carbonate.

Decarboxylation and Dehydrogenation of Carboxyl-labeled 9,10-Dihydro-9-anthrylacetic Acid.—A mixture of 0.3 g. (1.3 mmoles) of the acid, 0.3 g. of copper chromite catalyst and 5 ml. of quinoline was heated under reflux for one hour. The reaction mixture was flushed continuously with nitrogen and after the heating, the aeration was continued for one hour at room temperature. The evolved carbon dioxide was collected in 50 ml. of 0.14 *M* barium hydroxide solution. The barium carbonate was processed in the usual manner; yield 130 mg. (68.4% based upon recovered acid), *specific activity:* 2850 cts./min./mg. barium carbonate.

The reaction mixture was diluted with 3 *N* hydrochloric acid and the insoluble material separated by centrifugation. The solids were extracted with warm benzene, the benzene evaporated and this residue digested with excess dilute sodium carbonate solution. From the carbonate solution, 0.07 g. of starting acid was recovered, m.p. 168–169°. The carbonate insoluble material was fractionally crystallized from aqueous methanol and yielded 9-methylanthracene, m.p. 75–77° (reported[20] 81.5°) which was devoid of radioactivity.

Radioactivity Determination.—The procedure of Dauben, Reid and Yankwich[21] was employed for sample preparation and counting.

Reaction of Desyl Chloride with Sodium Methoxide in Methanol.—The reaction was conducted essentially as described by Madelung and Oberwegner.[8] A methanol solution of desyl chloride (23 g., 0.1 mole) was added dropwise with stirring to a solution of 2.5 g. (0.11 mole) of sodium in 125 ml. of anhydrous methanol and the resulting mixture allowed to stand for three hours at room temperature. The solution was diluted with one liter of water and the product extracted with ether. Distillation of the dried ethereal extract gave 16.9 g. of a yellow viscous oil, b.p. 179.5–180.5° (9.5 mm.), $n^{26}D$ 1.5790. On standing at zero degrees for several hours, the oil solidified and the resulting yellow solid (m.p. 38–45°) was recrystallized from petroleum ether (b.p. 30–60°) to yield 12.6 g. (56%) of benzoin methyl ether, m.p. 46.4–47.7° (lit.[22] 49–50°). The presence of a carbonyl group was demonstrated by absorption bands at 5.95, 6.25 and 6.33 μ.[23]

BERKELEY 4, CALIFORNIA RECEIVED NOVEMBER 17, 1951

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[14] D. Vorländer, E. Rack and W. Leister, *Ber.*, **56**, 1131 (1923).

[15] J. F. Eijkman, *Chem. Weekblad*, **5**, 655 (1908).

[16] A. Biztrzycki, J. Paulus and R. Perrin, *Ber.*, **44**, 2596 (1911).

[17] H. J. Barber, *J. Chem. Soc.*, 79 (1943).

[18] W. E. Bachmann and M. C. Kloetzel, *J. Org. Chem.*, **3**, 55 (1938).

[19] This value and those reported for subsequent compounds was obtained by combustion of a micro-sample of the compounds, precipitation of the carbon dioxide as barium carbonate and counting the barium carbonate. To correct for the dilution of the activity in the compound, the observed specific activity was multiplied by the number of carbon atoms in the compound.

[20] A. Sieglitz and R. Marz, *Ber.*, **56**, 1619 (1923).

[21] W. G. Dauben, J. C. Reid and P. E. Yankwich, *Anal. Chem.*, **19**, 828 (1947).

[22] E. Fischer, *Ber.*, **26**, 4212 (1893).

[23] R. S. Rasmussen, D. D. Tunnicliff and R. R. Brattain, THIS JOURNAL, **71**, 1068 (1949).