[CONTRIBUTION FROM THE WILLIAM H. NICHOLS LABORATORY, NEW YORK UNIVERSITY]

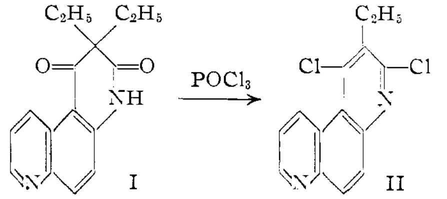
The Preparation of α,α-Dialkylacetoacetanilides and Their Reaction with Sulfuric Acid[1]

BY A. LANGLEY SEARLES AND RICHARD J. KELLY

RECEIVED NOVEMBER 12, 1955

α,α-Dialkylacetoacetanilides have been prepared by the alkylation of mono-α-alkylacetoacetanilides. The reactions of the former compounds with aqueous and concentrated sulfuric acid have been studied. With two exceptions, the chief products of these reactions have been shown to be 3-substituted-4-methylcarbostyrils, formed by elimination of an alkyl group. A mechanism has been suggested which correlates these eliminations with the stabilities of the derivable carbonium ions and the creation of additional conjugation in the system.

It has been observed that 2,2-diethyl-1,3-diketo-1,2,3,4-tetrahydro-4,7-phenanthroline (I) (formed by the condensation of 6-aminoquinoline and ethyl diethylmalonate in a manner recently described)[2] is converted into 1,3-dichloro-2-ethyl-4,7-phenanthroline (II) upon treatment with phosphorus oxychloride.[3] The unexpected loss of an ethyl group during this reaction led us to consider related, simpler systems containing the –NH–CO–CR$_2$–CO– grouping where similar dealkylations might occur and be more easily studied.



Contrary to reported findings[4] we found that one such system, $(C_6H_5NHCO)_2CR_2$, could not be prepared from aniline and ethyl dialkylmalonates[5]; and, having then been obtained from aniline and a dialkylmalonyl chloride,[6] could not be cyclized to quinoline derivatives either with or without dealkylation. Diethylmalonanilide, for example, was not transformed into 3,3-diethyl-2,4-diketo-1,2,3,4-tetrahydroquinoline as claimed by Baumgarten and Kargel,[4] whether distilled at atmospheric pressure or a variety of reduced pressures.

Fruitful results, however, were obtained with α,α-dialkylacetoacetanilides (IV). These compounds were conveniently prepared in good (54–93%) yields by alkylation of the readily available mono-α-alkyl precursors (III),[7,8] frequently according to variations of methods previously described[8,9]; none of the difficulties noted by earlier workers in performing a second alkylation on this type of compound[10] were encountered. The variations in procedure consisted of using both sodium and the alkyl halide in slight excess of the stoichiometric quantities.

$$\underset{\text{III}}{C_6H_5NHCOCHRCOCH_3} \xrightarrow[\text{then } R'X]{NaOC_2H_5,} \underset{\text{IV}}{C_6H_5NHCOCRR'COCH_3}$$

In this fashion the reaction was completed in a shorter time and (presumably through repressed alcoholysis and cleavage of the β-ketoanilide) the yield of dialkylated product increased.

Finally, in order to establish the fact that the second alkyl group was introduced into the molecule in the same position as the first, one of the dialkylated products was synthesized in two ways. First α-acetylpropionanilide (III, R = CH_3) was ethylated. In an independent preparation a methyl group was introduced into α-acetylbutyranilide (III, R = C_2H_5). The product from each reaction proved to be the same compound (mixed m.p.).

TABLE I

ALKYLATIONS OF SUBSTITUTED ACETOACETANILIDES[a]

α-Group present	α-Group introduced	Yield, %	M.p., °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
Methyl	Methyl	85	87.5–88	$C_{12}H_{15}NO_2$	6.83	6.81
Methyl	Ethyl	85	66–67.5	$C_{13}H_{17}NO_2$	6.40	6.28
Methyl	Propyl	54[b]	55.5–57.5	$C_{14}H_{19}NO_2$	6.01	6.09
Methyl	Butyl	63	70.5–72	$C_{15}H_{21}NO_2$	5.67	5.69
Methyl	Benzyl	93[c]	121–123	$C_{18}H_{19}NO_2$	4.98	4.88
Ethyl	Methyl	83	66–67.5	$C_{13}H_{17}NO_2$	6.40	6.28
Ethyl	Ethyl	81	85–87	$C_{14}H_{19}NO_2$	6.01	6.10
Ethyl	Propyl	79	73.5–75	$C_{15}H_{21}NO_2$	5.67	5.59
Ethyl	Isopropyl	81	177–179[d,e]	$C_{15}H_{21}NO_2$[f]	5.67	5.34
Ethyl	Butyl	75	69.5–71.5	$C_{16}H_{23}NO_2$	5.36	5.46
Ethyl	Benzyl	93[c]	101–102	$C_{19}H_{21}NO_2$[g]	4.85	4.73
Propyl	Propyl	80[b]	71	$C_{16}H_{23}NO_2$	5.36	5.45
Propyl	Isopropyl	82	197–201[d]	$C_{16}H_{23}NO_2$[h]	5.36	5.20
Butyl	Isopropyl	84	200–204[d]	$C_{17}H_{25}NO_2$[i]	5.09	5.01
Benzyl	Benzyl	73[j]	117	$C_{24}H_{23}NO_2$[k]	3.91	3.61

[a] Unless otherwise indicated, all solid products characterized here were crystallized from aqueous ethanol, whence they separated as white or transparent needles. [b] White platelets from low boiling petroleum ether. [c] White needles for methanol. [d] B.p. at 2 mm. [e] Becomes semi-solid on long standing at room temperature. [f] The 2,4-dinitrophenylhydrazone forms bright yellow needles, m.p. 218–219°. [g] Also: carbon 77.3% calcd., 77.5% found; hydrogen 7.17% calcd., 7.09% found. [h] The 2,4-dinitrophenylhydrazone forms orange-yellow needles, m.p. 210–211°. [i] The 2,4-dinitrophenylhydrazone forms orange-yellow needles, m.p. 219–222°. [j] Transparent, hexagonal plates from methanol. [k] Also: carbon 80.6%, calcd., 80.8%, found; hydrogen, 6.49% calcd., 6.69% found.

When compounds of type IV were heated with sulfuric acid they underwent ring closure with concomitant loss of an α-alkyl group to give 3-alkyl-4-methylcarbostyrils (V). This was observed to take

---

[1] From a dissertation submitted by Richard J. Kelly in partial fulfillment of the requirements for the degree of Doctor of Philosophy, New York University, 1954.

[2] A. L. Searles and R. M. Warren, *J. Org. Chem.*, **18**, 1317 (1953).

[3] R. M. Warren, Ph.D. thesis, New York University, 1951, p. 19.

[4] P. Baumgarten and W. Kargel, *Ber.*, **60**, 832 (1927).

[5] Similar observations concerning the reaction of 2-aminopyridine with dialkylmalonates are extant: A. E. Chichibabin, *ibid.*, **57**, 1168 (1924), and *Uspekhi Khim.*, **5**, 481 (1936)

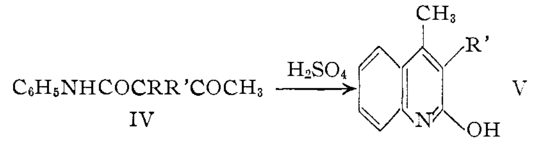
[6] After the manner of G. B. Crippa and E. Scevola, *Gazz. chim. ital.*, **67**, 327 (1937).

[7] A. L. Searles and H. G. Lindwall, THIS JOURNAL **68**, 988 (1946).

[8] A. L. Searles and R. J. Kelly, *ibid.*, **77**, 6075 (1955).

[9] D. J. Cook and W. C. Lawall, *ibid.*, **70**, 1918 (1948).

[10] B. M. Dubinin and G. V. Chelintsev, *Zhur. Obshchei Khim.*, **7**, 2365 (1937).



place with all examples of IV except α-methyl-α-acetylpropionalide (R = R′ = CH_3). When both alkyl groups were the same, one of them was lost; when both were primary and normal, the larger was lost; and when one was isopropyl or benzyl, it was lost preferentially to any of the others. Yields in these transformations varied from fair to quantitative. The time of reaction, while not always critical, did affect the amount and quality of V. If carried out for an insufficient period, isolation and purification of the product was made difficult; if allowed to proceed too long, decomposition and charring occurred. For most anilides one hour at 96° (steam-bath temperature) was sufficient. While this was not the ideal period for all compounds it was adhered to whenever possible so that comparisons of results would be facilitated. Mixed melting points with authentic samples[7,8,11] were employed to establish the identities of V.

TABLE II

CYCLIZATIONS OF α,α-DISUBSTITUTED ACETOACETANILIDES[a]

α-Groups present		α-Group lost	Reaction time, min.	Yield, %
Methyl	Methyl	Neither	60	64
Methyl	Ethyl	Ethyl	60[h]	43[h]
Methyl	Propyl	Propyl	120	69
Methyl	Butyl	Butyl	20[b]	98
Methyl	Benzyl	Benzyl	60[b,c]	100
Ethyl	Ethyl	Ethyl	60[d]	60
Ethyl	Propyl	Propyl	600[e]	56
Ethyl	Isopropyl	Isopropyl	60	66
Ethyl	Butyl	Butyl	70[d]	97
Ethyl	Benzyl	Benzyl	60[c]	99
Propyl	Propyl	Propyl	180	30
Propyl	Isopropyl	Isopropyl	75	60
Butyl	Isopropyl	Isopropyl	75	40
Benzyl	Benzyl	Benzyl	60[c]	6[f]
Benzyl	Benzyl	Benzyl	60[c]	13[g]

[a] Unless otherwise indicated all reactions involved concentrated sulfuric acid at 96°. [b] At 85°. [c] 74% sulfuric acid was used. [d] At 90°. [e] Plus 12 hours at 25°. [f] 86% of unreacted starting compound was recovered from the reaction mixture. [g] At reflux temperature; extensive charring occurred and no starting compound could be recovered. [h] Yields at 30°: 31% in 16 hr.; 41% in 23 hr.; 37% in 3 days.

Analysis of the product obtained from the reaction of sulfuric acid with α-methyl-α-acetylpropionanilide (IV, R = R′ = CH_3) showed that the elements of water rather than those of an alcohol had been lost. Its ultraviolet absorption spectrum and melting point differed markedly from those of its precursor and those of 3,4-dimethylcarbostyril (the compound which would have been produced had the reaction involved loss of a methyl group). Its chemical properties were likewise different: it gave a brilliant scarlet color with sulfuric acid, reacted rapidly with aqueous permanganate, and evolved no HBr upon decolorizing a solution of bromine in chloroform. The labile unsaturation implied by the latter reactions was confirmed quantitatively by hydrogenation under conditions which would have had no effect on V, and suggested the structure VIa for this cyclization product. (The relevant ultraviolet absorption spectra are shown in Fig. 1.)

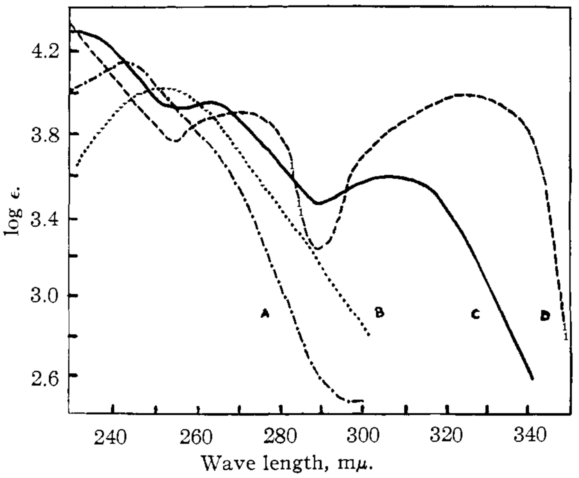
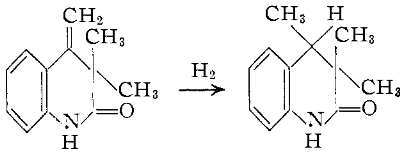
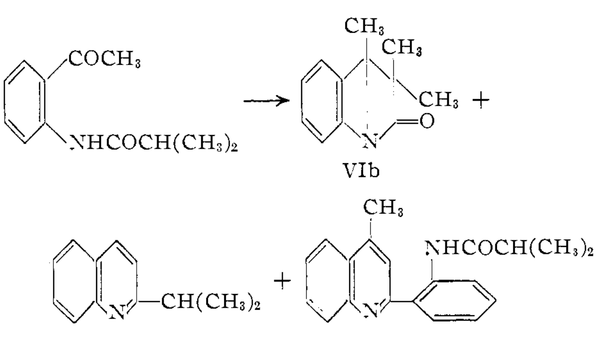


Fig. 1.—Ultraviolet absorption spectra in ethanol: A, α-acetyl-α-methylpropionanilide (IV, R = R′ = CH_3); B, 3,3,4-trimethyl-1,2,3,4-tetrahydro-2-quinolone (VII); C, 2-hydroxy-3,4-dimethylquinoline (V, R′ = CH_3); D, 3,3-dimethyl-4-methylene-1,2,3,4-tetrahydro-2-quinolone (VIa).



VIa VII

This structure is further indicated by the fact that the compound has apparently been prepared previously. Camps[12] reported that when 2-(isobutyrylamido)-acetophenone was allowed to react with aqueous base there were formed three products, one of which he formulated as VIb. Its melting point (143–144°) corresponds to that we have observed for VIa (144–146°), as do empirical formula and analyses. On these bases, then, and by analogy with the reaction of 2-(propionylamido)-acetophenone with aqueous base to yield 3,4-dimethylcarbostyril (V, R = CH_3),[13] we believe the



---

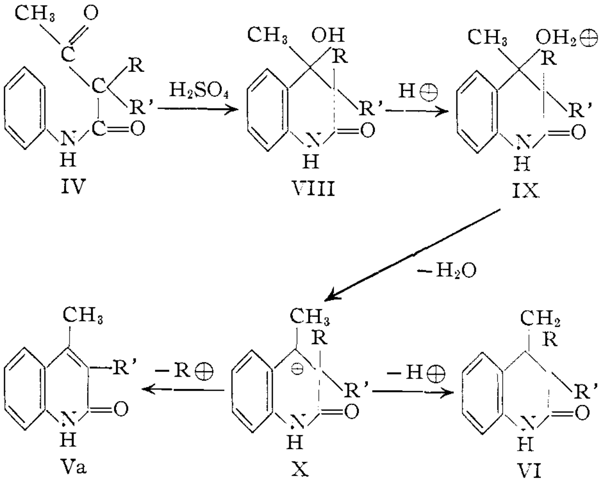
[11] Mixtures of V exhibit sufficient m.p. depressions to render this a reliable method.

[12] R. Camps, *Arch. pharm.*, **239**, 591 (1901).

[13] R. Camps, *ibid.*, **237**, 659 (1899).

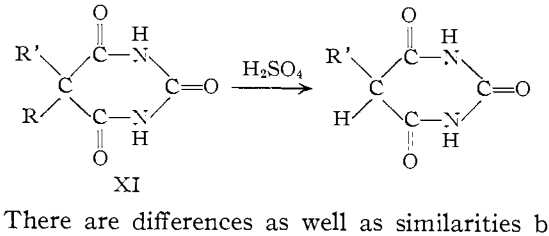
structure VIa may definitely be assigned both to the product of our reaction and Camps.

The mechanism of the transformations we have observed may be visualized as



The initial intermediate VIII formed is readily protonated by the sulfuric acid to yield IX; upon dehydration there is produced from this X, which may either lose the more stable derivable carbonium ion (R⊕) to give Va (the lactam form of V) or a proton to give VI. Both processes lead to an increase in resonance energy, the former to a higher degree, since VI not only lacks the continuous bicyclic conjugation of V, but would be less favored to form because of its exocyclic double bond.[14] If this mechanism is correct it would be expected, as has indeed been observed, that the groups which gave rise to the most stable carbonium ions would be those most easily ejected from the system. Conversely, the least stable carbonium ions would be removed with the greatest difficulty or not at all, which has also been observed. The clean-cut nature of these differentiations encourages the belief that this reaction may prove a convenient means of determining carbonium ion stabilities, especially where such stabilities are closely comparable in magnitude.

While this research was in progress there was published a report of an apparently similar dealkylation reaction of lesser scope.[15] Certain 5,5-dialkylbarbituric acids (XI, R′ = primary alkyl, R = secondary alkyl or benzyl) suffered loss of an alkyl group on long standing with concentrated sulfuric acid at room temperature. A carbonium ion mechanism was shown to be involved here also.



There are differences as well as similarities between the dealkylations suffered by IV and XI. The reaction of the latter is considerably slower; for example, α-acetyl-α-methylbutyranilide (IV, R = C_2H_5, R′ = CH_3) required only a day for completion of reaction at room temperature, as compared to the usual fortnight's period under the same conditions reported by Maynert and Washburn for XI. Although benzyl and secondary alkyl groups were more easily removed from each system than primary alkyl groups, the latter cannot be removed at all from XI, whereas any but methyl may be removed from IV. The existence of a ring system capable of aromatization is apparently necessary for dealkylation with both IV and XI. The only products that could be isolated from dealkylations of IV were those where cyclization had occurred. It does not seem probable that ring-closure is dependent upon prior dealkylation, since acyclic derivatives of malonic acid related to XI do not dealkylate under comparable conditions.[15] Furthermore, α-methyl-α-acetylpropionanilide (IV, R = R′ = CH_3) could be cyclized without dealkylation.

The yields of carbostyrils from the dealkylative cyclizations of IV varied from 6 to 100%. In no instance was it possible to isolate from the reaction any other product. The fate of the remainder of the β-ketoanilide therefore could not be determined. It was felt that under the conditions employed any other products initially formed would probably be decomposed. In the hope of preserving the identity of these products several examples of IV were subjected to treatment with sulfuric acid of varying aqueous concentrations.

When sulfuric acid of between 60 and 90% was used the reactions proceeded as described for the concentrated acid. (Advantage was taken of this fact by using the 74% sulfuric acid that is known to repress sulfonation of free phenyl groups[8] whenever IV contained an α-benzyl group.) Lower acid concentrations were also tested. For example, upon refluxing with 30% sulfuric acid for four days, α-acetyl-α-benzylpropionanilide (IV, R = CH_3, R′ = $CH_2C_6H_5$) gave 19% of 3-methyl-4-phenylbutanone, 8.7% of the expected carbostyril and 67% of unchanged starting compound; under the same conditions both α-acetyl-α-ethylbutyranilide (IV, R = R′ = C_2H_5) and α-acetyl-α-methylvaleranilide (IV, R = CH_3, R′ = $CH_2CH_2CH_3$) were recovered quantitatively from the reaction mixture unchanged.

Experimental[16]

The following procedures typify the variations applied in the course of preparing, isolating and purifying the compounds cited in this paper.

α-Acetyl-α-methylpropionanilide.—α-Acetylpropionanilide (19.1 g., 0.100 mole) was dissolved in a solution of sodium (4.60 g., 0.200 mole) in commercial absolute ethanol (250 ml.). Methyl iodide (28.4 g., 0.200 mole) was then introduced, and the resulting solution refluxed for 4.5 hours. Thrice, at two-hour intervals, portions (7.1 g., 0.050 mole) of methyl iodide were added, and the reaction mixture was allowed to stand overnight at room temperature after the last addition. It was then concentrated to a volume of 75 ml. and filtered, the residue being rejected. Water was added to the filtrate until solidification occurred. The mixture was filtered, and the precipitate pressed free of mother liquor and washed with two 50-ml. portions of 30% aqueous ethanol. The mother liquor yielded no further precipitate

---

(14) H. C. Brown, J. H. Brewster and H. Schechter, THIS JOURNAL, **76**, 467 (1954).

(15) E. W. Maynert and E. Washburn, *ibid.*, **75**, 700 (1953).

(16) Melting points are uncorrected.

upon being diluted with water to 800 ml. After vacuum drying over potassium hydroxide the product weighed 17.5 g. (85.4% of theory); recrystallization from aqueous ethanol gave transparent needles melting at 87.5–88.0°.

α-Acetyl-α-methylvaleranilide.—α-Acetylpropionanilide (95.5 g., 0.500 mole) was dissolved in a solution of sodium (11.5 g., 0.50 mole) in commercial absolute ethanol (500 ml.). *n*-Propyl bromide (61.5 g., 0.500 mole) was added, and the resulting mixture refluxed until neutral to litmus. Water was added until separation of an insoluble pale yellow liquid was complete. The latter was then separated from the aqueous phase and dissolved in 400 ml. of ether. This ethereal solution was washed thrice with equal volumes of water and dried over calcium chloride. The ether was removed by slow evaporation, and the residual liquid refrigerated. After several days it became semi-solid. Crystallization from diethylene glycol and then from low boiling petroleum ether gave white platelets melting at 55.5–57.5°. After vacuum drying the product weighed 63.1 g. (54.1% of theory).

α-Acetyl-α-isopropylcaproanilide.—α-Acetylcaproanilide (23.0 g., 0.099 mole) was dissolved in a solution of sodium (3.5 g., 0.15 mole) in commercial absolute ethanol (100 ml.). Isopropyl bromide (40.0 g., 0.325 mole) was added and the resulting mixture refluxed until neutral to litmus. Water (200 ml.) was added and the solution was steam distilled until the residue was free of alkyl halide. After cooling the residue was extracted with 200 ml. of ether. This ethereal extract was washed with water, dried over alumina, filtered and concentrated by evaporation. After distillation at 200–204° (2 mm.) the product was obtained as a viscous, yellow liquid weighing 21.7 g. (84.3% of theory). The 2,4-dinitrophenylhydrazone, prepared in the usual way, melted at 219–222°.

The Action of Sulfuric Acid on α-Acetyl-α-methylcaproanilide.—α-Acetyl-α-methylcaproanilide (25.0 g.) was dissolved in 96.6% sulfuric acid (125 ml.). The solution was heated at 85° for 20 minutes. (Initially the solution was light red but after ten minutes heating it had acquired a very dark red coloration.) It was poured into a mixture of 1250 ml. of water and crushed ice. The resultant mixture was allowed to stand until the ice had melted, whereupon the pale yellow solid which had precipitated was filtered off and washed with several portions of water. Recrystallization from aqueous ethanol gave three crops of white needles, total weight 17.1 g. (98% of theory). Their melting point (269–270°) was not depressed upon admixture with an authentic sample of 2-hydroxy-3,4-dimethylquinoline.

The Action of Sulfuric Acid on α-Acetyl-α-ethylcaproanilide.—α-Acetyl-α-ethylcaproanilide (25.0 g.) was dissolved in 96.6% sulfuric acid (100 ml.). The solution was heated at 90° for 70 minutes. (By the end of this period the solution had acquired a dark red coloration.) It was poured into a liter of water and crushed ice. The mixture so obtained was allowed to stand until the ice had melted, whereupon the acid solution was decanted from the yellow semi-solid precipitate which had formed. The precipitate was suspended in a saturated solution of potassium carbonate (200 ml.) and covered with a layer of ether (50 ml.). This mixture was agitated until neutralization of the residual acid was complete. The ether was removed by evaporation and the solid filtered from the aqueous solution. This solid was then crystallized twice from a benzene–methanol mixture. Fine needles were obtained whose melting point (228–229°) was not depressed upon admixture with an authentic sample of 2-hydroxy-3-ethyl-4-methylquinoline. The total weight of product was 17.3 g. (97% of theory).

The Action of Sulfuric Acid on α-Acetyl-α-benzylpropionanilide.—α-Acetyl-α-benzylpropionanilide (7.00 g.) was dissolved in 74% sulfuric acid (300 ml.) and the solution heated for an hour at 85°. (By the end of this period it had acquired a deep yellow-green color.) The reaction mixture was poured into 1550 ml. of crushed ice and water with vigorous stirring. A finely divided white solid precipitated. This was filtered from the solution after the ice had melted and washed successively with water, saturated aqueous sodium carbonate and finally again with water. After vacuum drying over calcium chloride it weighed 4.30 g. (100% of theory). Crystallization from aqueous methanol gave fine needles whose melting point (268–270°) was not depressed upon admixture with an authentic sample of 2-hydroxy-3,4-dimethylquinoline.

The Action of Sulfuric Acid on α-Acetyl-α-benzyl-β-phenylpropionanilide.—α-Acetyl-α-benzyl-β-phenylpropionanilide (1.00 g.) was added to 50 ml. of 74% sulfuric acid and the mixture heated at 96° for one hour. There were two liquid phases present throughout this period. The aqueous layer was separated while still hot and poured into 100 ml. of cold water. The mixture thus formed was filtered and the solid residue washed with water. After crystallization from ethanol the product was in the form of small, transparent needles melting at 238–240° and weighing 0.043 g. (6% of theory). There was no depression in melting point upon admixture with an authentic sample of 2-hydroxy-3-benzyl-4-methylquinoline. The organic layer, which solidified on cooling, was crystallized from ethanol giving 0.86 g. (86% recovery) of unreacted starting compound melting at 117°.

When this reaction was repeated at reflux temperature extensive charring took place; however, a yield of 13% of 2-hydroxy-3-benzyl-4-methylquinoline was obtained. No starting compound could be isolated under these conditions.

The Action of Sulfuric Acid on α-Acetyl-α-benzylpropionanilide.—α-Acetyl-α-benzylpropionanilide (9.00 g.) was refluxed for 4 days with 30% sulfuric acid. The resulting mixture was steam distilled until the condensing liquid was clear. The distillate was extracted several times with ethyl ether, and the combined extracts dried above calcium chloride. After removal of the ether, the residual liquid distilled at 135–137° (15 mm.) and weighed 0.981 g. The 2,4-dinitrophenylhydrazone, prepared in the usual manner, was in the form of light orange needles melting at 78.5–80.5°. The boiling point previously reported for 3-benzyl-2-butanone is 127–130° (12 mm.)[17] and the melting point of its 2,4-dinitrophenylhydrazone 81°.[18] The yield of ketone was 19% of theory.

After the steam distillation, considerable insoluble solid remained in the reaction flask. This was filtered while the mixture was still hot, and the residue thus obtained crystallized from aqueous ethanol. A total of 6.00 g. of white needles identified (mixed m.p.) as starting compound was isolated in three crops; this represents a 67% recovery.

Upon refrigeration of the first filtrate in the preceding paragraph a white solid precipitated. This was filtered from the solution and crystallized from aqueous ethanol. The long white needles thus obtained weighed 0.478 g. (8.7% of theory); their melting point (269–271°) was not depressed upon admixture with an authentic sample of 2-hydroxy-3,4-dimethylquinoline.

3,3-Dimethyl-4-methylene-1,2,3,4-tetrahydro-2-quinolone (VIa).—α-Acetyl-α-methylpropionanilide (45.0 g.) was dissolved in 92.7% sulfuric acid (120 ml.). The bright red solution so obtained was heated at 96° for one hour. (At the end of this period the intensity of its color was undiminished.) It was poured into a liter of crushed ice and water. A flocculent precipitate formed and was filtered from the solution as soon as the ice had melted. The precipitate was dissolved in ethyl ether, and the ethereal solution washed with several portions of cold water. The ethereal layer was then allowed to evaporate at room temperature. A residue of pale yellow crystals remained. This was placed in a Soxhlet cup and extracted continuously with petroleum ether (250 ml.). By this process 26.2 g. (64% of theory) of very pale yellow powder was extracted. Crystallization from methanol produced fine, transparent needles melting at 144–146° which gave a brilliant scarlet color with concentrated sulfuric acid. The residue in the extraction cup was a vitreous red semi-solid which could not be made to crystallize and which was therefore not further investigated.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 77.0; H, 6.95; N, 7.49. Found: C, 76.6; H, 6.87; N, 7.43.

3,3,4-Trimethyl-1,2,3,4-tetrahydro-2-quinolone.—A mixture of 3,3-dimethyl-4-methylene-1,2,3,4-tetrahydro-2-quinolone (0.200 g., 0.00107 mole), absolute ethanol (50 ml.) and platinum (formed by reduction of 0.050 g. of platinum oxide) was vigorously stirred in an atmosphere of hydrogen at atmospheric pressure and 33°. Hydrogen (27.9 ml., 0.0011 mole) was absorbed within ten minutes, whereupon uptake ceased. The solution was filtered and the filtrate allowed to evaporate at room temperature. A

---

[17] M. T. Bogert and D. Davidson, THIS JOURNAL, **54**, 334 (1932).

[18] L. H. Briggs, G. C. De Ath and S. R. Ellis, *J. Chem. Soc.*, 61 (1942).

white solid (0.194 g., 96% of theory) melting at 165–166° remained. This compound does not give a colored solution when dissolved in concentrated sulfuric acid.

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.2; H, 7.94; N, 7.41. Found: C, 76.0; H, 7.75; N, 7.07.

NEW YORK 53, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Cyclic Diacyl Peroxides. I. Monomeric Phthaloyl Peroxide[1]

BY FREDERICK D. GREENE

RECEIVED OCTOBER 17, 1955

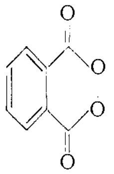
The synthesis and physical properties of monomeric phthaloyl peroxide are reported. From the decomposition of the peroxide in benzene at 80° were isolated carbon dioxide, *o*-phenylbenzoic acid, "polymeric" acid, phthalic acid, benzoic acid, biphenyl and 3,4-benzcoumarin. The mechanism of decomposition in benzene is discussed in terms of induced decomposition *via* a radical chain reaction. The decomposition is accelerated by trichloroacetic acid, leading to phthalic anhydride. The relative rates of decomposition in carbon tetrachloride, benzene and styrene are $1:140:10^5$. The decomposition in styrene does not produce polystyrene. The possibility of ring strain, electronic in origin rather than steric, is suggested to account for the unusual reactivity of the peroxide.

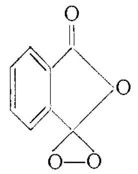
Although a large number of compounds are known which contain the oxygen–oxygen grouping, only a few incorporate this unit in a ring. Of these, the best characterized are the ozonides and the *endo*-peroxides.[2] A few cyclic alkyl peroxides are known: cyclic peroxides from the oxygenation of bicyclohexenyl and 1-phenylcyclohexene,[3] 3,3,5,5-tetramethyl-1,2-dioxacyclopentane and the homologous six-membered ring compound.[4] Cyclic diacyl peroxides were reported in 1894[5] but the compounds to which a cyclic structure was originally assigned were actually polymeric.[6,7] Monomeric cyclic diacyl peroxides have been reported recently by Kleinfeller and Rastadter[8] and by Russell.[9] We have been interested in the study of compounds of this class from two standpoints: the intrinsic interest associated with a new type of structure and interest in the diradicals, which might be produced by the decomposition of such systems. This report will deal with the unusual behavior of phthaloyl peroxide.

Results

Synthesis.—Reaction of phthaloyl chloride with an ethereal solution of hydrogen peroxide and sodium carbonate affords phthaloyl peroxide in good yield. Material containing 99.5% of the theoretical active oxygen content (by iodometric titration) may be obtained by recrystallization. The compound has the following physical properties: m.p. 126–127°, exploding violently at 130°; density, 1.56 g. cm.$^{-3}$; soluble in chloroform, methylene chloride and moderately soluble in hot benzene, carbon tetrachloride and cyclohexane; very sensitive to shock.[10] Cryoscopic determinations of the molecular weight in benzene solution gave values of 167, 170, 173, an average of 3–4% above the calculated value of 164. The presence of a small amount of dimeric (or higher) material may be responsible for this discrepancy.

Structure.—The two structures that warrant consideration are I and II. Although both structures are without close analogy in the literature, a distinction may be made


I


II

on the basis of spectroscopic evidence. The ultraviolet absorption spectra of phthaloyl peroxide (A), phthalic anhydride (B), ψ-phthaloyl chloride (3,3-dichlorophthalide, C) and phthalide (D) are shown in Fig. 1. The great similarity between the spectra of phthaloyl peroxide and phthalic anhydride is strong evidence for structure I. The infrared absorption spectrum of monomeric phthaloyl peroxide in carbon tetrachloride exhibits a single moderately sharp peak at 1768 cm.$^{-1}$ with a slight shoulder at 1750 cm.$^{-1}$ and two very weak bands at 1719 and 1702 cm.$^{-1}$ (Davison reports the spectral bands for polymeric phthaloyl peroxide at 1805 and 1783 cm.$^{-1}$ in Nujol).[11] Acyclic diacyl peroxides normally possess two well-defined maxima in the carbonyl region, separated by 20 cm.$^{-1}$ (*e.g.*, benzoyl peroxide: 1792 and 1772 cm.$^{-1}$).[12] Although the lactone band of phthalides and 3-substituted phthalides shows strong absorption in the infrared[12] at 1750–1770 cm.$^{-1}$, structure I might be expected to show absorption in this region (at lower wave numbers than the acyclic diacyl peroxides) because of the conjugation of the carbonyl groups through the benzene ring. The presence of a small amount of II is not excluded by the spectral data but structure I is favored as the major, if not sole, component.

Decomposition in Benzene.—A degassed sample of phthaloyl peroxide in benzene was decomposed at 80° and the products were isolated by initial division into a neutral and acid fraction by extraction with 5% aqueous sodium bicarbonate solution. The following products were obtained: biphenyl (less than 1%), 3,4-benzcoumarin (0.5%), benzoic acid (5%), phthalic acid (7%), *o*-phenylbenzoic acid (50%) and "polymeric" acid (*ca.* 25%). Carbon dioxide, 78% (based on one mole of carbon dioxide per mole of peroxide) was determined separately by absorption on Ascarite. From a product analysis carried out by chromatography on silica gel, the product composition was similar except that phthalic anhydride (2%) replaced half of the phthalic acid. The first five products listed above were identified by comparison of the infrared spectra and melting points with authentic samples. A sample of 3,4-benzcoumarin was

---

(1) Presented before the Organic Division of the 128th meeting of the American Chemical Society in Minneapolis, Minnesota, September, 1955.

(2) W. Bergmann and M. J. McLean, *Chem. Revs.*, **28**, 367 (1941).

(3) H. Hock and M. Siebert, *Chem. Ber.*, **87**, 554 (1954). See also A. Mustafa and A. M. Islam, *J. Chem. Soc.*, S81 (1949); J. L. Bolland and H. Hughes, *ibid.*, 492 (1949); G. Wittig and W. Gaub, *Chem. Ber.*, **80**, 367 (1947).

(4) R. Criegee and G. Paulig, *ibid.*, **88**, 712 (1955).

(5) H. v. Pechmann and L. Vanino, *ibid.*, **27**, 1510 (1894).

(6) A. Baeyer and V. Villiger, *ibid.*, **34**, 762 (1901).

(7) H. A. Shah, F. Leonard and A. V. Tobolsky, *J. Polymer Sci.*, **7**, 537 (1951).

(8) H. Kleinfeller and K. Rastadter, *Angew. Chem.*, **65**, 543 (1953).

(9) K. E. Russell, THIS JOURNAL, **77**, 4814 (1955).

(10) Preliminary tests have shown that the peroxide is exploded by the impact from a 2 kg. weight dropped from a height of 2 cm. We are indebted to Dr. Handrick of Arthur D. Little, Inc., for this information.

(11) W. H. T. Davison, *J. Chem. Soc.*, 2456 (1951).

(12) J. F. Grove and H. A. Willis, *ibid.*, 882 (1951).