made by the Kjeldahl method. The melting points recorded in parentheses are those listed by Dyson, Hunter and Morris.[5]

Summary

A number of substituted thioureas have been made by the action of α-naphthyl isothiocyanate upon primary and secondary aliphatic amines. These compounds are solids which may be used in identification of the amines.

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The Structure of the Acids Obtained by the Oxidation of Triisobutylene

BY JAMES B. CONANT AND GEORGE W. WHELAND

Butlerow[1] obtained an acid by the oxidation of triisobutylene to which he assigned the empirical formula $C_{11}H_{22}O_2$. He suggested that the acid was probably di-*tert*-butylmethylacetic acid. Spiegler[2] many years later reported the formation of the same acid by the oxidation of a pigment from black wool, but in view of the results of the present investigation, his identification seems very doubtful.

We have investigated Butlerow's acid using rather large amounts of material and have found that it is in reality a mixture of two acids. The material described by Butlerow and prepared according to his directions melts at 66–70°; the two component acids into which it can be separated melt at 88–89° and 129–129.5°, respectively. The two components were present in approximately equal amounts. A mixture of the two acids appears to be identical with Butlerow's material in all particulars. The separation may be effected either by a fractional extraction of an ethereal solution with sodium carbonate or by taking advantage of the difference in the mode of reaction of the two acid chlorides with aqueous ammonia. The acid chloride of the alpha acid (the lower melting) is converted into the amide while the beta acid chloride regenerates the free acid. The latter is easily separated from the amide of the alpha acid by virtue of its solubility in dilute alkali.

Both the alpha and beta acids have the empirical formula $C_{12}H_{24}O_2$ and not $C_{11}H_{22}O_2$ which Butlerow assigned to his material. The empirical formula was established by the analyses of the free acids, the methyl esters, and the *p*-chloroanilides. Because of the well-known difficulties of burning compounds with highly branched chains, the carbon analyses

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(1) Butlerow, *Ber.*, **12**, 1482 (1879); *J. Russ. Phys.-Chem. Soc.*, **11**, 203 (1879).

(2) Spiegler, *Beitr. Chem. Physiol. Pathol.*, **4**, 40–50 (1903); *Chem. Zentr.*, **2**, 128 (1903).

were sometimes as much as 0.6% low for the C_{12} formula but always too high for the C_{11} formula. It was undoubtedly this difficulty in the combustion which led Butlerow astray. Thus the carbon content calculated for $C_{11}H_{22}O_2$ is 71.0% and for $C_{12}H_{24}O_2$ is 72.0%. A series of analyses of the pure alpha and beta acids gave 71.4, 71.6, 72.2, and 71.8, 71.7. The chlorine content of the mixed chlorides was 16.0 as compared with 16.2 for the C_{12} formula and 17.3 for the C_{11} formula. Similarly, the halogen content of each of the *p*-chloroanilides agreed with the C_{12} formula and not the C_{11} formula. The analytical evidence is so complete that there can be no doubt about the composition of the two isomeric acids.

Both acids appear to be trisubstituted acetic acids since they are not brominated by the Hell–Volhard–Zelinsky procedure and are extremely slowly esterified by the usual methods. Using a 3% solution of hydrochloric acid in methyl alcohol and operating at 100°, it required eleven days for the alpha ester to be half esterified while in the same time no appreciable quantity of the beta ester was formed. In a parallel experiment dimethylethylacetic acid was converted almost completely into the ester in one day at 100°. Using Menschutkin's[3] standard procedure with equivalent quantities of isobutyl alcohol and acid at 155° for one hour, only about 1% of either the alpha or beta acid was esterified. Menschutkin reports that under these conditions secondary acids are 21.5–29.0% esterified and tertiary acids 0.4–8.3%.

The acid strengths of both acids have been measured by Halford[4] by an electrometric titration in a homogeneous medium. In 50% aqueous ethyl alcohol, the alpha acid is 1.1 *pK* units weaker than acetic acid, and the beta acid 1.7 units weaker; in 40% aqueous butyl carbitol the values were 1.6 and 2.0, respectively. This diminution in strength as compared with acetic acid is in accord with Halford's findings in respect to other substituted acetic acids. There can be no doubt from his results that both substances contain a carboxyl group.

All attempts to obtain definite degradation products of these acids have so far failed. An amide could be obtained only from the alpha acid; this amide was very resistant to hydrolysis by alcoholic sodium hydroxide but was readily converted into the acid by the action of nitrous acid. When treated with potassium hydroxide and bromine, the amide underwent the Hofmann rearrangement but the product was apparently a disubstituted urea $(C_{11}H_{23}NH)_2CO$. All attempts to hydrolyze this compound with boiling methyl alcoholic potassium hydroxide failed. Oxidation of the alpha or beta acids with chromic acid yielded no solid products or materials which could be identified. The beta acid was slowly decomposed by concentrated sulfuric acid at room temperature, while the alpha acid was not attacked by this reagent. After twenty

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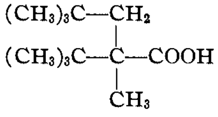
(3) Menschutkin, *Ber.*, **12**, 2168 (1879).

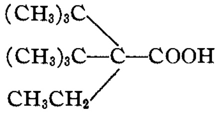
(4) Halford, THIS JOURNAL, **53**, 2944 (1931).

hours, the products from the beta acid were a non-acidic oil boiling above 200°, dimethylethylacetic acid (identified as the solid amide), and a small amount of an acidic compound boiling above 200°.

The evidence at hand is much too meager to permit of the assignment of structural formulas for the two acids, but the two following may be suggested very tentatively



Alpha acid



Beta acid

If the two *tert*-butyl groups of tri-isobutylene are still intact in the two acids, then these two formulas are the only ones which can be written for a tertiary acid $C_{12}H_{24}O_2$. The greater speed of esterification of the alpha acid would indicate that it is less highly substituted (on the alpha carbon atom) and is the basis for the assignment of the two formulas as indicated. It is clear that a rearrangement is involved in the formation of these acids by the oxidation of tri-isobutylene[5] and there is no assurance that the tertiary butyl groups have retained their structure. If these groups are changed in the process the number of possible formulas for even a tertiary acid is very large and there is no evidence at present available to distinguish between all the various possibilities.

Experimental Part

Tri-isobutylene.—This was a product obtained in the commercial preparation of unsaturated hydrocarbons by the dehydration of *tert*-butyl alcohol. For the purpose of comparison, a sample was prepared in accordance with Butlerow's[1] directions. When this sample was oxidized in the manner described below, the acid thus obtained proved to be identical with the mixed acid obtained from the commercial material. The identification was by mixed melting points not only with the mixed acids but also with the alpha and beta acids separately.

Preparation of Mixed Acids.—Five hundred grams of finely ground sodium dichromate was dissolved in 1000 cc. of water and 800 cc. of concentrated sulfuric acid, and to the solution was added in the course of four or five hours 100 g. of tri-isobutylene (with mechanical stirring). The temperature was kept between 30 and 40°. After standing overnight, the reaction mixtures from two runs were combined and steam distilled until a white solid began to collect in the condenser. The distillate was discarded, and the residue in the flask was poured while still hot into a large earthenware crock to cool. The product slowly came to the top in the form of an oil which later solidified to a dark green crust. This was treated with aqueous potassium hydroxide, the chromium hydroxide was filtered off and the product was then precipitated by acidifying the filtrate with hydrochloric acid. A considerable additional quantity of acid was obtained by extracting the chromium hydroxide and the filter papers with hot potassium hydroxide solution. The crude acid thus obtained was still not perfectly white, and melted at 55–60°, but was used without further purification in most of the subsequent work. The total yield of crude product from nineteen runs was 525 g.

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(5) McCubbin, THIS JOURNAL, **53**, 356 (1931); McCubbin and Adkins, *ibid.*, **52**, 2547 (1930).

The Mixed Acid Chlorides.—Fifty grams of the mixed acid was treated with 50 g. of thionyl chloride and allowed to stand overnight. The mixture was then distilled and the material boiling at 113–116° under 20 mm. pressure was collected as product. The yield was 45 g.; n_D^{23} 1.4489.

Anal. Calcd. for $C_{12}H_{23}OCl$: Cl, 16.23. Calcd. for $C_{11}H_{21}OCl$: Cl, 17.3. Found: Cl, 15.9, 16.0.

Separation of the Mixed Acid into its Components. (a) Through Acid Chloride.—The crude mixed acid was transformed into the acid chloride by the action of thionyl chloride, and then treated with concd. aqueous ammonia. After a few hours the solution was acidified and then extracted with ether. The acid matter was extracted with dilute sodium hydroxide, the amide remaining in the ether layer. The beta acid was recovered by acidifying the water layer. Obtained in this way, it was contaminated with traces of the alpha acid which could be removed by crystallization from alcohol and water. The ether layer contained the amide of the alpha acid. The best method of purification was to dissolve the crude material in concentrated sulfuric acid and let stand for about a week. This treatment destroyed some gummy impurity, and furnished a satisfactory product. The amide was hydrolyzed to the free acid by dissolving in about ten parts of concentrated sulfuric acid and adding slowly to the thoroughly cooled solution two parts of sodium nitrite dissolved in as little water as possible.

(b) By Fractional Extraction.—One hundred grams (0.5 mole) of crude mixed acid was dissolved in about 500 cc. of ether and extracted with small portions of dilute sodium bicarbonate. This removed some oily acids present in the crude material, but left the alpha and beta acids in the ether solution. The ether was then extracted with 600 cc. of 5% sodium carbonate solution (0.26 mole) in several portions. The combined aqueous extracts were acidified cautiously and extracted with ether. In this way the original mixed acid was divided into two approximately equal fractions, which were then themselves divided in the same manner. In the second set of extractions only half as much sodium carbonate was used as in the first. The two internal fractions thus obtained were united with the next portion of the acid to be separated, and the two external fractions were evaporated to dryness. The residue from the most easily extracted fraction weighed about 25 g. and was crude alpha acid, while that from the least easily extracted fraction weighed the same and was crude beta acid. (See Table.)

Disubstituted Urea from the Alpha Amide.—5.5 Grams of the amide of the alpha acid was added to a solution of 6 g. of bromine in 30 cc. of 30% potassium hydroxide. The mixture was heated gently for a few hours and then allowed to stand overnight. The reaction mixture was extracted with ether and the ether extracted with dilute hydrochloric acid. From the aqueous extracts no basic material could be obtained, but when the ether layer was evaporated to dryness a solid product was obtained, which after crystallization from alcohol melted at 164–165°. The yield of purified product was 3.3 g.

Anal. Calcd. for $C_{23}H_{48}N_2O$: C, 74.9; H, 13.1; N, 7.6; mol. wt., 368. Found: C, 74.3, 74.8; H, 12.2, 12.4; N, 7.8, 8.0; mol. wt. (freezing benzene), 359, 384.

All attempts to hydrolyze the urea failed. The material was recovered unchanged after boiling with alcoholic potassium hydroxide for eight hours.

Rates of Esterification

(a) With Isobutyl Alcohol.—0.2500 Gram of the acid was sealed off with 0.0925 g. (the equivalent quantity) of isobutyl alcohol. The mixture was then heated for one hour at 155°, at the end of which time the capsule was broken. The contents were then dissolved in alcohol, and the unreacted acid titrated with standard sodium hydroxide.

Alpha acid: 0.2500 g., 0.2483 unreacted, 0.7% reacted. Beta acid, 0.2500 g., 0.2476 unreacted, 1% reacted.

Acids	M. p., °C.	Formula	Equiv. wt. Calcd.	Equiv. wt. Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Acid chlorides B. p., °C.	Acid chlorides Press., mm.
Alpha	88–89	$C_{11}H_{22}O_2$	186	200	71.0	71.4	11.8	11.7		
		$C_{12}H_{24}O_2$	200	201	72.0	71.6	12.1	12.1	120–123	40
						72.2		11.8		
Beta	129	$C_{11}H_{22}O_2$	186	206	71.0	71.8	11.8	11.9	128–133	
		$C_{12}H_{24}O_2$	200	202	72.0	71.7	12.1	12.0		50
				203		72.0		12.1		
				199						

The esters of the acids were prepared from the acid chlorides in the usual manner.

Methyl ester of acids	B. p. °C.	Press., mm.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Mol. wt.[a] Calcd.	Mol. wt.[a] Found	n^{25}_D	d^{25}_4
Alpha ester	117–120	40	$C_{12}H_{24}O_2$	72.0	72.8	12.1	12.0	200	204		
			$C_{13}H_{26}O_2$	72.8	71.1	12.2	12.5	214	206	1.4265	0.8582
					73.3		12.4				
Beta ester	115–120	35	$C_{12}H_{24}O_2$	72.0	72.0	12.1	11.6	200	205		
			$C_{13}H_{26}O_2$	72.8	72.3	12.2	13.0	214	211	1.4437	0.8925

[a] By freezing point in benzene.

The chloroanilides were made by the action of chloroaniline on the acid chlorides. The alpha amide was made by the action of ammonia on the acid chloride.

	p-Chloroanilides of acids M. p., °C.	*p*-Chloroanilides of acids Formula	Chlorine, % Calcd.	Chlorine, % Found	Alpha amide M. p., °C.	Alpha amide Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Mol. wt. Calcd.	Mol. wt. Found
Alpha	187–187.5	$C_{17}H_{26}ONCl$	12.0	11.4	140–141	$C_{11}H_{23}ON$	71.3	71.9	12.5	12.5	7.6	6.7	185	241
		$C_{18}H_{28}ONCl$	11.5	11.2		$C_{12}H_{25}ON$	72.3	72.5	12.7	12.7	7.0		199	293
		$C_{17}H_{26}ONCl$	12.0											313
Beta	166.5-167	$C_{18}H_{28}ONCl$	11.5	11.6										

(b) **With Methyl Alcohol.**—The acid (0.0025 mole) was dissolved in 10 g. of absolute methyl alcohol containing 3% hydrochloric acid by weight. The solution was then heated at 100° in a sealed tube for a length of time depending upon the acid concerned. When the tube was finally broken open, the reaction mixture was evaporated down to remove the hydrochloric acid. The residue was then taken up in alcohol and titrated with standard sodium hydroxide. Such a rough procedure could be expected to give only approximate results, but the reactivities of the three acids varied so widely that no very great accuracy was required. The results obtained established conclusively the *relative* rates of esterification, and that was all that was desired.

Dimethylethylacetic acid: 1 day, 97.2% reacted. Alpha acid, 11 days, 50.5% reacted. Beta acid, 11 days, 0% reacted.

Attempts to Brominate the Mixed Acids.—Two grams of mixed acids and 0.25 g. of red phosphorus (carefully dried over phosphorus pentoxide) was treated with 3 cc. of anhydrous bromine drop by drop, the mixture being kept at 0°. After standing overnight at room temperature, 0.75 cc. of dry bromine was added, allowed to stand for forty-eight hours, and then heated on the steam-bath for four hours (an excess of bromine was still present). The mixture was decomposed with 50 cc. of absolute alcohol with which it was boiled for four hours. The esters were isolated in the usual manner and purified by washing with cold dilute sodium hydroxide. The boiling point of the mixed esters was 100–120° at 30 mm.; yield 1.8 g. Decomposition by sodium fusion of a sample and testing with silver nitrate showed a bromine content of less than 0.4%.

Summary

The acidic material obtained by Butlerow by oxidizing tri-isobutylene has been re-investigated. It has been found to be a mixture of approximately equal amounts of two acids, $C_{12}H_{24}O_2$. Both acids appear to be tertiary acids with highly branched groups.

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Preparation and Properties of *n*-Alkyl Ethers of β-*n*-Alkylcholine Salts

BY RANDOLPH T. MAJOR AND JOSEPH K. CLINE

After an extensive study of muscarine King reported in 1922 that muscarine chloride must have a molecular weight of about 210, that it was unchanged when it was boiled with deci-normal acid or alkali and that accordingly it must not be an ester or other compound which could be readily changed by acids or alkalies.[1]

Simonart found that the action of the esters of β-methylcholine on animals was in many respects very much like that of muscarine.[2] Unlike muscarine, however, these esters are readily hydrolyzed by hot alkalies.

Accordingly, several ethers of β-methylcholine as well as of other β-alkylcholines have been synthesized upon the suggestion of Doctor A.

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[1] King, *J. Chem. Soc.*, **121**, 1747 (1922).

[2] Simonart, *J. Pharmacol.*, **46**, 157 (1932).