TABLE II

CYCLIZATION OF OTHER *o*-BENZYLPHENONES (I)

R′	R	P_2O_5, g.[a]	Yield II, %
C_6H_5	C_6H_5[b]	2	48.5[c]
C_6H_5	C_6H_5	5	60[d]
H	p-C_6H_4Cl[e]	5	44[f]
H	p-C_6H_4CN[g]	4[h]	...[i]
H	p-$C_6H_4OCH_3$	5[j]	60[k]

[a] Except as noted, 500 mg. of ketone was used. [b] Bradsher and Smith, *J. Am. Chem. Soc.*, 65, 451 (1943). [c] M.p. 245–247° (lit.[b] 245–247°). [d] M.p. 240–243.5°. [e] Ref. 5. [f] M.p. 176.5–179° (lit.[5] 179–180°). In addition, 97 mg. of ketone, m.p. 72–73° (lit.[9] 73°) was recovered. [g] Ref. 9. [h] Reaction using 370 mg. of ketone. [i] Ketone (258 mg.) was recovered, m.p. 103.5–105° (lit.[9] 104.5–105°). [j] M.p. 69–70°, Ref. 10. [k] Yellow shiny needles, m.p. 165.5–166.5°. The analytical sample, crystallized from ethanol, melted at 168–168.5°. *Anal.* Calc'd for $C_{21}H_{16}O$: C, 88.73; H, 5.65. Found: C, 89.03; H, 6.05.

tion of hydrobromic and acetic acids.[9] The attempted cyclization of 2-benzyl-4′-methoxybenzophenone (I, R = *p*-$C_6H_4OCH_3$; R′ = H) with hydrobromic and acetic acids yielded only an impure brown oil.[10]

In a single preliminary experiment, it was shown that the dehydration of *o*-benzylbenzoic acid to anthrone could be brought about in 39% yield using the sulfur dioxide medium. While the sulfur dioxide–phosphorus pentoxide combination, when used in the cyclization of *o*-benzyl phenones, gives a yield almost consistently poorer than that obtained with the boiling hydrobromic-acetic acid mixture, the low temperature at which cyclodehydration occurs in the sulfur dioxide medium makes it of possible interest in cyclizations involving heat-sensitive compounds.

EXPERIMENTAL

General procedure. The entire apparatus, consisting of a 200 ml. 3-necked flask with a mechanical stirrer and dry ice condenser fitted with a calcium chloride tube, was dried by heating with a flame before use. About 50 ml. of liquid sulfur dioxide from a tank was run into the flask and the ketone (usually 500 mg.) was added. Stirring was begun and the phosphorus pentoxide added. The reaction mixture (usually yellow) was mechanically stirred for several hours, at the end of which about 20 ml. of carbon tetrachloride was added. The mixture was allowed to stand until the ice first formed had melted, and most of the sulfur dioxide had evaporated. The carbon tetrachloride and water layers were separated, and the water washed twice more with carbon tetrachloride. The carbon tetrachloride layer was washed three times with water, dried over calcium chloride, and then concentrated. Ethanol was added to the concentrate and the solution concentrated further to remove the carbon tetrachloride and to induce crystallization.

Effect of the cyclizing medium upon 9-phenylanthracene. The reaction vessel was charged with 50 ml. of liquid sulfur dioxide and 467 mg. of 9-phenylanthracene (theoretical yield from 500 mg. of ketone), and 2 g. of phosphorus pentoxide. The mixture was stirred for 2 hr. and worked up in the usual way. In two runs, the yield was 373 mg. (80%), m.p. 151–153.5° in the first and 384 mg. (82%), m.p. 151–154.5° in the second. Evaporation of the mother liquors yielded a dark reddish brown material (50 mg.; 26 mg.).

Cyclization of o-benzylbenzoic acid. One-half gram of *o*-benzylbenzoic acid[11] in 50 ml. of sulfur dioxide was stirred for 2 hr. with 5 g. of phosphorus pentoxide and the mixture worked up as in the standard procedure. Light yellow needles of 9-anthrone were obtained, m.p. 152–154° (lit.[12] 154°); yield, 176 mg. (39%).

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[10] F. A. Vingiello, Ph.D. thesis (1947).

[11] Barnett, Cook and Nixon, *J. Chem. Soc.*, 504 (1927).

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Symmetrical N,N,N′,N′-Tetraalkylpiperazinium Di-alkylsulfates

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Smith, Curry, and Eifert[1] have described the preparation of a series of symmetrical N,N′-dialkylpiperazines, in which the alkyl groups were *n*-octyl, *n*-decyl, *n*-dodecyl, *n*-tetradecyl, and *n*-hexadecyl. From them they prepared the corresponding dihydrobromides, N,N′-dialkyl-N,N′-dimethylpiperazinium di-methiodides and N,N′-dialkyl-N,-N′-diethyl-piperazinium di-ethiodides. They described one piperazinium di-alkylsulfate, N,N′-di-*n*-tetradecyl-N,N′-dimethyl-piperazinium di-methylsulfate.

Extending our studies in the fields of morpholinium and thiamorpholinium alkyl sulfates[2] the above series of symmetrical N,N′-dialkylpiperazines has been lengthened to include N,N′-di-*n*-octadecylpiperazine and two series of N,N′-dialkyl-N,N′-dimethyl-piperazinium di-methylsulfates and N,N′-dialkyl-N,N′-diethyl-piperazinium di-ethylsulfates have been prepared.

EXPERIMENTAL

N,N′-Dialkylpiperazines were prepared by refluxing 0.05 mole of anhydrous piperazine (Bios Laboratories, Inc.) with 0.12 mole of alkyl bromide in 30–40 ml. of absolute alcohol for 18–24 hr. After cooling, the resultant salt was filtered and redissolved in alcohol. The solution was made alkaline with dilute sodium hydroxide and the resultant precipitate of the free amine was filtered, washed with water, refiltered, and, after air drying, was recrystallized from ethyl acetate. The dialkylpiperazines are white waxy solids, insoluble in water and only slightly soluble in cold alcohol and ethyl acetate. The yields obtained varied from 55% to 85%. The melting points were in substantial agreement with those given by Smith, Curry, and Eifert.[1] N,N′-di-*n*-octadecylpiperazine melts at 97–98°C., uncorr.

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[1] D. R. Smith, J. W. Curry and R. L. Eifert, *J. Am. Chem. Soc.*, 72, 2969 (1950).

[2] W. F. Hart, M. E. McGreal and J. B. Niederl, *J. Am. Chem. Soc.*, 66, 1610 (1944); 68, 714 (1946); 70, 618 (1948); 71, 3569 (1949); *J. Org. Chem.*, 14, 579 (1949).

TABLE I

SYMMETRICAL N,N,N',N'-TETRAALKYLPIPERAZINIUM DI-ALKYLSULFATES

$[(R)(R')N(CH_2CH_2)_2N(R)(R')]^{++}2R'SO_4^-$

R	R'	Formula	M.P., °C.[a]	C Calc'd	C Found	H Calc'd	H Found	N Calc'd	N Found
n-Decyl	Methyl	$C_{28}H_{62}N_2O_8S_2$	179–180	54.31	54.10	10.09	9.68	4.52	4.85
n-Decyl	Ethyl	$C_{32}H_{70}N_2O_8S_2$	165–166	56.93	57.11	10.45	10.49	4.15	4.10
n-Dodecyl	Methyl	$C_{32}H_{70}N_2O_8S_2$	275 dec.	56.93	57.16	10.45	10.39	4.15	4.08
n-Dodecyl	Ethyl	$C_{36}H_{78}N_2O_8S_2$	250 dec.	59.13	58.92	10.75	10.90	3.84	3.87
n-Tetradecyl[b]	Methyl	$C_{36}H_{78}N_2O_8S_2$	265 dec.	59.13	58.14	10.75	10.40	3.84	3.76
n-Tetradecyl	Ethyl	$C_{40}H_{86}N_2O_8S_2$	236 dec.	61.02	61.75	11.01	11.23	3.55	3.44
n-Hexadecyl	Methyl	$C_{40}H_{86}N_2O_8S_2$	260 dec.	61.02	61.02	11.01	11.10	3.55	3.52
n-Hexadecyl	Ethyl	$C_{44}H_{94}N_2O_8S_2$	250 dec.	62.66	63.20	11.23	11.19	3.32	3.29
n-Octadecyl	Methyl	$C_{44}H_{94}N_2O_8S_2$	258 dec.	62.66	63.16	11.23	10.91	3.32	3.20
n-Octadecyl	Ethyl	$C_{48}H_{102}N_2O_8S_2$	242 dec.	64.09	64.81	11.43	11.56	3.11	3.05

[a] Melting points are uncorrected. [b] Reference 1.

Anal. Calc'd for $C_{40}H_{82}N_2$: C, 81.20; H, 13.98; N, 4.73. Found: C, 80.89; H, 14.02; N, 4.77.

N,N,N',N'-Tetralkylpiperazinium di-alkylsulfates were prepared by dissolving 0.02 mole of the dialkylpiperazine in a sufficient volume of boiling ethyl acetate, adding 0.042 mole of the redistilled dialkyl sulfate and refluxing for 3 hr. The reaction mixture was chilled filtered, and the product recrystallized from ethyl acetate. In the case of N,N'-di-*n*-octadecylpiperazine, ethyl isovalerate was used as the reaction solvent. The yields obtained varied from 35 to 45%.

The dialkyl sulfates are white waxy solids, insoluble in ether and are only slightly soluble in cold alcohol and ethyl acetate. They are only slightly soluble in hot mineral oil.

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The Conjugative Effect of the Dimethylsulfonio Group in an Aliphatic System

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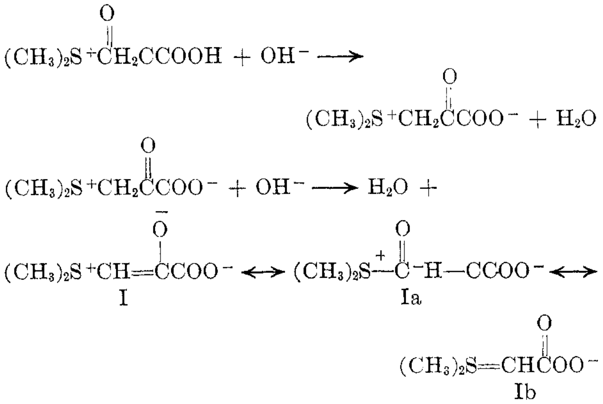
In connection with the preparation of sulfonium compounds as possible lipotropic agents,[1] we observed that dimethylsulfoniopyruvic acid bromide behaves as a diprotic acid. Indeed, the two endpoints are readily determined with methyl orange and phenolphthalein, respectively. The corresponding methyl and ethyl esters behave as monoprotic acids, pK_a, 5.5. The potentiometric titration curves for acid and ester are shown in Fig. 1. It seemed unlikely that the unusually high acidity is due solely to the inductive effect of the electron-withdrawing dimethylsulfonio group, but rather to the resonance stabilization of the conjugate base (I) in which the dimethylsulfonio group is conjugated with the keto group by expanding its sulfur valence shell to ten



$$(CH_3)_2S^+CH_2\overset{O}{\overset{\|}{C}}COOH + OH^- \longrightarrow (CH_3)_2S^+CH_2\overset{O}{\overset{\|}{C}}COO^- + H_2O$$

$$(CH_3)_2S^+CH_2\overset{O}{\overset{\|}{C}}COO^- + OH^- \longrightarrow H_2O + \underset{\text{I}}{(CH_3)_2S^+CH{=}\overset{\bar{O}}{\overset{|}{C}}COO^-} \longleftrightarrow \underset{\text{Ia}}{(CH_3)_2S\overset{+}{-}\overset{O}{\overset{\|}{C}}{}^{-}H-COO^-} \longleftrightarrow \underset{\text{Ib}}{(CH_3)_2S{=}CH\overset{O}{\overset{\|}{C}}OO^-}$$

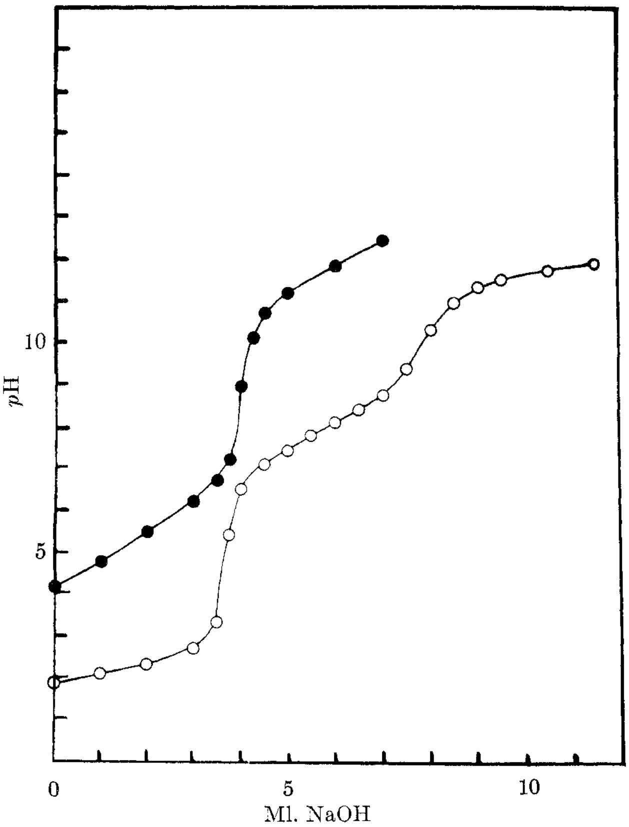


Fig. 1.—TITRATION CURVES FOR DIMETHYLSULFONIO DERIVATIVES OF PYRUVIC ACID. DOTS, ESTER; CIRCLES, ACID.

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[1] N. F. Blau, J. W. Johnson, and C. G. Stuckwisch, *J. Am. Chem. Soc.*, **76**, 5106 (1954).