cooled to 20°, and 2.0 g. of *p*-toluenesulfonyl chloride was added in one portion. The reaction was allowed to stand at room temperature overnight. An additional 7 ml. of dry pyridine was added, and a 1-ml. aliquot was removed for isolation of the hydroxy tosylate XV. Treatment of this aliquot with ice yielded solid which was collected and dried under high vacuum. Recrystallization from dry acetone yielded material, m.p. 97–98° dec., $[\alpha]_D$ −1.2° (*c* 0.4).

Anal. Calcd. for $C_{35}H_{56}SO_4$: C, 73.38; H, 9.85. Found: C, 73.43; H, 9.71.

4β-Methylcholesteryl *p*-Toluenesulfonate (XVI).—The pyridine solution of hydroxy tosylate XV was cooled to 0°, and 4 ml. of thionyl chloride was added dropwise with stirring. After 10 min. at 0°, 100 ml. of ether was added. The ether solution was cautiously treated with water. The ether was washed with a saturated solution of sodium bicarbonate followed by water. The ether solution was dried and concentrated to dryness *in vacuo* yielding a crystalline solid. Recrystallization from dry acetone yielded 1.4 g., m.p. 98–100° dec., $[\alpha]_D$ −77.8° (*c* 1).

Anal. Calcd. for $C_{35}H_{54}SO_3$: C, 75.73; H, 9.79. Found: C, 75.36; H, 9.53.

Hydrolysis of 4α-Methylcholesteryl *p*-Toluenesulfonate (IX).—A solution of 400 mg. of IX in 60 ml. of acetone and 10 ml. of water containing 400 mg. of potassium acetate was kept at reflux for 12 hr. Then most of the acetone was removed under reduced pressure. The remainder was extracted with ether; the ether solution was dried and concentrated to dryness *in vacuo* yielding 300 mg. of crystalline product. This material was chromatographed upon 5 g. of Merck neutral alumina. Elution with pentane yielded 60 mg. of oil which failed to crystallize. The ultraviolet spectrum of this oil was similar to that of XX. Further elution with benzene–ether (1:1) yielded 180 mg. of XVIII, m.p. 99–101°, $[\alpha]_D$ +18° (*c* 1). The analytical sample prepared by recrystallization from acetone had m.p. 101–102°.

Anal. Calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.07. Found: C, 83.90; H, 12.01.

Elution with chloroform afforded 60 mg. of crystalline material. Upon recrystallization from acetone, this material had m.p. 164–165°, $[\alpha]_D$ −16°, identical with a sample of 4α-methylcholesterol (X).

Hydrolysis of 4β-Methylcholesteryl *p*-Toluenesulfonate (XVI).—A solution of 2.0 g. of tosylate XVI was dissolved in 300 ml. of acetone and 50 ml. of water containing 2.1 g. of potassium acetate. This reaction mixture was kept at reflux overnight. The acetone was removed under vacuum, and the residue was thoroughly extracted with ether. The ether solution was dried and concentrated *in vacuo* to a gum, 1.4 g. Chromatography upon 60 g. of Merck alumina yielded 1.20 g. of 4-methyl-$\Delta^{3,5}$-cholestadiene (XX), identified by comparison with a known sample. Further elution with benzene–ether (1:1, 3:7) gave 110 mg. of crystalline material which upon recrystallization from acetone yielded 90 mg. of XIX, m.p. 113–114°, $[\alpha]_D$ −40° (*c* 0.4).

Anal. Calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.07. Found: C, 84.00; H, 12.30.

Further elution with chloroform gave 6 mg. of material identified as 4β-methylcholesterol (XVII) by comparison with a known sample prepared by the method of Julia.[13]

Chromium Trioxide–Pyridine Oxidation of IX.—To a chromium trioxide–pyridine complex, prepared by portionwise addition of 24 mg. of chromium trioxide to 0.25 ml. of pyridine, was added a solution of 24 mg. of IX in 0.25 ml. of pyridine. The reaction mixture was stored at room temperature overnight. Ice was added followed by water, and the final mixture was extracted with six portions of chloroform. The combined extracts were washed with dilute hydrochloric acid, a saturated solution of sodium bicarbonate, and finally with water. The organic layer was dried and concentrated to dryness under reduced pressure. The resulting gum, 27 mg., possessed infrared absorption (CCl_4) at 5.91 μ, and no ultraviolet absorption above 225 mμ. Chromatography upon neutral alumina (Merck) yielded 17 mg., m.p. 100–106°.

Anal. Calcd. for $C_{28}H_{48}O$: C, 84.35; H, 11.63. Found: C, 84.00; H, 11.82.

Chromium Trioxide–Pyridine Oxidation of XIX.—The required oxidizing complex was prepared by portionwise addition of 43 mg. of chromium trioxide to 0.50 ml. of pyridine. A solution of 43 mg. of XIX in 0.50 ml. of pyridine was added, and the reaction mixture was allowed to stand at room temperature overnight. Isolation of the product by the method used yielded a gum weighing 47 mg. This material possessed infrared absorption (CCl_4) at 5.83 and 5.93 μ (C=O in ratio of 2:5, respectively). Chromatography upon Merck basic alumina yielded 21 mg., m.p. 97–99°, λ_{max}^{EtOH} 257 mμ (ε 13,700).

Anal. Calcd. for $C_{28}H_{46}O$: C, 84.35; H, 11.63. Found: C, 84.10. H, 11.40.

Dehydration of XIX.—A 9-mg. sample of XVIII in benzene was charged to a Woelm acid-washed alumina column. After 0.5 hr., elution with pentane yielded 5 mg., m.p. 71–72°, undepressed upon admixture with an authentic sample of 4-methyl-$\Delta^{3,5}$-cholestadiene (XX).

Acknowledgment.—The authors wish to thank Prof. J. Rocek of this department for several illuminating discussions. Also, the invaluable assistance of Prof. P. von R. Schleyer of Princeton University is acknowledged for determining the n.m.r. spectra.

Electrophilic Substitution of the Benzenethiols. II. Acylbenzene- and Acyltoluenethiols[1,2]

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Received May 3, 1963

Acylarylthiols are prepared from arylthiol precursors. The new procedure comprises protection of the sulfur atom with a carboxymethyl group, acylation of the aromatic ring, and, finally, removal of the protective group.

An earlier paper[4] described a new method of obtaining monohaloarylthiols from arylthiols. A summary of the steps involved is provided by equation 1.

This scheme suggested an attractive means of obtaining acylarylthiols, compounds previously preparable only by tedious, classical methods, or by the use of a more complex approach.[5] A survey of the literature revealed no examples of the Friedel–Crafts acylation of arylmercaptoacetic acids, though Dann and Kokorudz[6] report formation of *p*-acetylphenylmercaptoacetic acid in very low yield by the action of hydrogen fluoride on phenylmercaptoacetic acid. In view of the ease with

$$C_6H_5SH \longrightarrow C_6H_5SCH_2CO_2H \xrightarrow[-H^+]{X^+} XC_6H_4SCH_2CO_2H \xrightarrow[H_2O_2]{H^+} XC_6H_4SH \quad (1)$$

(1) This work is the subject of Canadian, United States, and other patent applications.

(2) Presented at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962.

(3) Arapahoe Chemicals, Inc., Boulder, Colo.

(4) D. Walker and J. Leib, *J. Org. Chem.*, **27**, 4455 (1962).

(5) D. S. Tarbell and A. H. Herz, *J. Am. Chem. Soc.*, **75**, 4657 (1953).

(6) O. Dann and M. Kokorudz, *Chem. Ber.*, **86**, 1449 (1953).

TABLE I

ACETYLATION OF ARYLMERCAPTOACETIC ACIDS

Starting material	Solvent	Product	Yield, %	M.p., °C.	Analyses[a] Found C	H	S
$C_6H_5SCH_2CO_2H$	$C_6H_5NO_2$	4-$CH_3COC_6H_4SCH_2CO_2H$[b]	62	156–158	...	...	...
	CS_2–$C_6H_5NO_2$		96				
2-$CH_3C_6H_4SCH_2CO_2H$	$C_6H_5NO_2$	4-CH_3CO-2-$CH_3C_6H_3SCH_2CO_2H$	57	118–119	58.69	4.98	14.35
	CS_2–$C_6H_5NO_2$		90				
3-$CH_3C_6H_4SCH_2CO_2H$	$C_6H_5NO_2$	2-CH_3CO-3(5)-$CH_3C_6H_3SCH_2CO_2H$[c]	2	161–162[d]	58.69	5.42	14.52
		4-CH_3CO-3-$CH_3C_6H_3SCH_2CO_2H$	77				
	CS_2–$C_6H_5NO_2$	4-CH_3CO-3-$CH_3C_6H_3SCH_2CO_2H$	94	121–122	58.75	5.58	14.41
4-$CH_3C_6H_4SCH_2CO_2H$	$C_6H_5NO_2$	5-Methylbenzo[*b*]thiophen-3-ol	25	98–100	...	...	...
	CS_2–$C_6H_5NO_2$	2-CH_3CO-4-$CH_3C_6H_3SCH_2CO_2H$	70	161–162	58.59	5.27	14.54

[a] Calcd. for $C_{11}H_{12}O_3S$: C, 58.93; H, 5.4; S, 14.28. [b] Methyl ester, b.p. 175° (1 mm.), m.p. 42–43° (petroleum ether, b.p. 30–60°). *Anal.* Calcd. for $C_{11}H_{12}O_3S$: C, 58.93; H, 5.4; S, 14.28. Found: C, 58.47; H, 5.21; S, 13.82. [c] Gives a yellow color on warming with mineral acids.

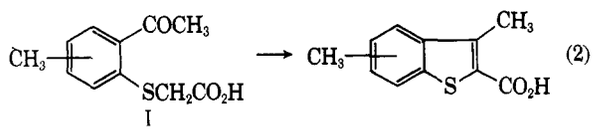
which arylmercaptoacetic acids are known to cyclize to thioindigoid dye intermediates,[6,7] acylation of these acids under Friedel–Crafts catalysis might be expected to lead, at least in part, to the formation of benzo[*b*]-thiophen-3-ols. However, absence of any confirmatory data led us to study the acylation of arylmercaptoacetic acids in the hope of obtaining acylarylmercaptoacetic acids. We expected that these latter acids would be cleaved to acylarylthiols by the action of hydrogen peroxide in the presence of mineral acids (equation 1).

This paper describes the acetylation and benzoylation of phenylmercaptoacetic acid and of all three tolylmercaptoacetic acids, as well as the preparation of acylarylthiols, and their disulfides, from the acylarylmercaptoacetic acids thus obtained.

Results and Discussion

Acylarylmercaptoacetic Acids. A. Acetylations in Nitrobenzene.—Phenylmercaptoacetic acid and *o*-tolyl- and *m*-tolylmercaptoacetic acids were acetylated in nitrobenzene to give good yields of *p*-acetylarylmercaptoacetic acids (see Table I).

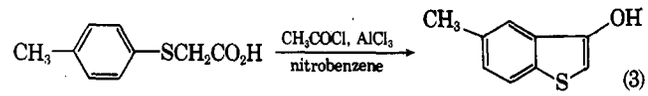
In the case of the acetylation of *m*-tolylmercaptoacetic acid a very small amount of 2-acetyl-3(or 5)-methylphenylmercaptoacetic acid (I) was also obtained. The *ortho* orientation of the acetyl group with respect to the sulfur atom was established by cyclization to a benzo[*b*]thiophene (equation 2).



I (2)

The position of the methyl group in the benzene ring was not established although the compound I isolated by us appeared to possess properties similar to those previously described[8] for 2-acetyl-3-methylphenylmercaptoacetic acid.

Friedel–Crafts acetylation of *p*-tolylmercaptoacetic acid could not be carried out in nitrobenzene, possibly owing to steric hindrance of the bulky nitrobenzene–aluminum chloride–acetyl chloride complex; instead, cyclization to 5-methylbenzo[*b*]thiophen-3-ol (II) appeared to be the predominant reaction (equation 3).



II (3)

The structure of 5-methylbenzo[*b*]thiophen-3-ol (II) was established by converting this material to 5-methylbenzo[*b*]thiophene-2,3-dione.[9]

B. Acetylations and Benzoylations in Carbon Disulfide–Nitrobenzene.—In the preferred method of acylating arylmercaptoacetic acids carbon disulfide containing a small amount of nitrobenzene was employed as the reaction medium. The final reaction mixture was decomposed in the usual way and the desired acylarylmercaptoacetic acid simply filtered. Very high yields of substantially pure product were thus obtained.

Phenylmercaptoacetic acid and all three tolylmercaptoacetic acids were acetylated by this method (see Table I). The acetyl group entered the position *para* to the sulfur atom except in the case of *p*-tolylmercaptoacetic acid where substitution occurred *ortho* to the sulfur atom. In the latter case the *ortho* orientation of the acetyl group was established by cyclizing 2-acetyl-4-methylphenylmercaptoacetic acid to 3,5-dimethylbenzo[*b*]thiophene-2-carboxylic acid.

Under the conditions used for preparing 2,4-dinitrophenylhydrazones of 2-acetyl-4-methylphenylmercaptoacetic acid and 4-acetyl-2-methylphenylmercaptoacetic acid esterification of the carboxylic acid group also took place.

Benzoylation of phenylmercaptoacetic acid and *o*-tolyl- and *m*-tolylmercaptoacetic acids proceeded in the same facile manner as did acetylation (see Table II). On the other hand *p*-tolylmercaptoacetic acid could not be benzoylated by any of the methods described. This failure may again be largely due to steric hindrance (compare the acetylation of *p*-tolylmercaptoacetic acid in nitrobenzene).

Acylarylthiols and Their Disulfides.—The acylarylmercaptoacetic acids were readily converted to acylarylthiols by the oxidative acid-catalyzed cleavage reaction described in the preceding paper.[4] However, since the acylarylthiols were only slightly volatile in steam, and could not be removed as formed, the thiol produced in the scission competed with unchanged

(7) K. Holzle, *Experientia*, **3**, 149 (1947).

(8) F. Krollpfeifer, K. L. Schneider, and A. Wissner, *Ann.*, **566**, 139 (1950).

(9) The method used was the same as that employed by P. Friedlander, A. Bezdrik, and P. Koeniger, *Ber.*, **41**, 235 (1908), for converting benzo[*b*]-thiophen-3-ol to benzo[*b*]thiophene-2,3-dione.

TABLE II

BENZOYLATION OF ARYLMERCAPTOACETIC ACIDS

Starting material	Product	Yield, %	M.p., °C.	Analyses—Calculated—C	H	S	Found—C	H	S
$C_6H_5SCH_2CO_2H$	4-$C_6H_5COC_6H_4SCH_2CO_2H$	90	134–135	66.16	4.44	11.73	66.09	4.46	11.71
2-$CH_3C_6H_4SCH_2CO_2H$	4-C_6H_5CO-2-$CH_3C_6H_3SCH_2CO_2H$	86	124–125	67.11	4.93	11.2	67.73	5.07	10.88
3-$CH_3C_6H_4SCH_2CO_2H$	4-C_6H_5CO-3-$CH_3C_6H_3SCH_2CO_2H$	50	102–103	67.11	4.93	11.2	67.40	5.26	11.05

TABLE III

CLEAVAGE OF ACYLARYLMERCAPTOACETIC ACIDS (1.25 *M* H_2O_2)

Acylarylmercaptoacetic acid	Products	Yield,[c] %	M.p. or b.p., (mm.) °C.	Analyses—Calculated—C	H	S	Found—C	H	S
	Unchanged acid	28	156–158						
4-$CH_3COC_6H_4SCH_2CO_2H$	4-$CH_3COC_6H_4SH$	26	135–136 (7)						
	$(4\text{-}CH_3COC_6H_4S\text{-})_2$	27	97–98						
	Unchanged acid	19							
4-CH_3CO-2-$CH_3C_6H_3SCH_2CO_2H$	4-CH_3CO-2-$CH_3C_6H_3SH$	17	146–147 (6)[a]	65.02	6.06	19.29	65.20	6.11	18.94
	$(4\text{-}CH_3CO\text{-}2\text{-}CH_3C_6H_3S\text{-})_2$	53	112.5–113.5	65.42	5.49	19.40	65.83	5.68	19.05
	Unchanged acid	27							
4-CH_3CO-3-$CH_3C_6H_3SCH_2CO_2H$	4-CH_3CO-3-$CH_3C_6H_3SH$	18	139–140 (7)	65.02	6.06	19.29	64.76	6.21	19.60
	$(4\text{-}CH_3CO\text{-}3\text{-}CH_3C_6H_3S\text{-})_2$	40	60–61	65.42	5.49	19.40	65.29	5.32	19.50
	Unchanged acid	33							
4-$C_6H_5COC_6H_4SCH_2CO_2H$	4-$C_6H_5COC_6H_4SH$[b]	27	71–72	72.86	4.71	14.96	72.72	4.48	14.50
	$(4\text{-}C_6H_5COC_6H_4S)_2$	35	126–127	73.21	4.25	15.03	73.12	4.21	14.80

[a] M.p. 30–31°. [b] *p*-Nitrobenzoyl ester, m.p. 157–158°. Calcd. for $C_{20}H_{13}O_4NS$: C, 66.10; H, 3.61; N, 3.86; S, 8.82. Found: C, 65.97; H, 3.63; N, 3.66; S, 8.65. [c] Based on starting acid.

TABLE IV

CLEAVAGE OF ACYLARYLMERCAPTOACETIC ACIDS (2.0–2.5 *M* H_2O_2)

Acylarylmercaptoacetic acid	Moles of H_2O_2 per mole of mercapto acid	Disulfide	M.p., °C.	Yield, %
4-$CH_3COC_6H_4SCH_2CO_2H$	2.0	$(4\text{-}CH_3COC_6H_4S)_2$	96–97[a]	84
4-CH_3CO-2-$CH_3C_6H_3SCH_2CO_2H$	2.0	$(4\text{-}CH_3CO\text{-}2\text{-}CH_3C_6H_3S)_2$	112.5–113.5[a]	80
4-CH_3CO-3-$CH_3C_6H_3SCH_2CO_2H$	2.0	$(4\text{-}CH_3CO\text{-}3\text{-}CH_3C_6H_3S)_2$	60–61[a]	82
4-$C_6H_5COC_6H_4SCH_2CO_2H$	2.0	$(4\text{-}C_6H_5COC_6H_4S)_2$	126–127[a]	86
4-C_6H_5CO-2-$CH_3C_6H_3SCH_2CO_2H$	2.5[c]	$(4\text{-}C_6H_5CO\text{-}2\text{-}CH_3C_6H_3S)_2$	Viscous oil[b]	21
4-C_6H_5CO-3-$CH_3C_6H_3SCH_2CO_2H$	2.2	$(4\text{-}C_6H_5CO\text{-}3\text{-}CH_3C_6H_3S)_2$	Viscous oil[b]	84

[a] These materials were identical with those prepared as described in Table III. [b] These materials could not be isolated as solids. No elemental analyses were obtained. [c] This experiment gave 56% acidic product (not identified), 21% disulfide, and 23% thiol, b.p. 172–175 (1 mm.), m.p. 81–82 (petroleum ether, b.p. 88–98°). *Anal.* Calcd. for $C_{14}H_{12}OS$: C, 73.65; H, 5.3; S, 14.04. Found: C, 73.44; H, 5.31; S, 14.08.

sulfide for the oxidizing agent. Thus, the products of the interaction of one mole of acylarylmercaptoacetic acid and one and a quarter moles of hydrogen peroxide were unchanged acid and acylarylthiol mixed with the corresponding disulfide. Yields of thiol and disulfide, based on conversion of acylarylmercaptoacetic acid, were consistently better than 70% (see Table III). By using two moles of hydrogen peroxide per mole of acylarylmercaptoacetic acid disulfides were produced directly usually in over 80% yield (see Table IV). In some cases the crude disulfides were oily; however, trituration with aqueous sodium hydroxide frequently converted oily to granular products. The oiliness was probably due, in major part, to the presence of thiols.

Most of the hydrogen peroxide cleavage reactions were carried out at 100°. In one cleavage reaction carried out at 60°, using two and a half moles of hydrogen peroxide, substantial amounts of acylarylsulfonylacetic acid accompanied a low yield of di(acylaryl) disulfide.

Reduction of di(acylaryl) disulfides to the corresponding thiols generally did not prove satisfactory[10] (see Table V). Reduction of di(4-benzoyl-3-methylphenyl) disulfide with zinc and acetic acid led to the formation of 4-benzyl-3-methylbenzenethiol in fair yield. Considerable resin formation was apparent in almost all of the reductions carried out, perhaps because of formation of styrene derivatives and/or condensation of thiol and keto groups.

Another approach to the preparation of acylarylthiols was to oxidize the acylarylmercaptoacetic acids to acylarylsulfinylacetic acids and hydrolyze the latter in boiling dilute mineral acid. Moderate yields of acylarylthiols were obtained in this way though some di-

(10) Since the work described in this paper was completed a new method of preparing arylthiols from disulfides has been published: J. R. Campbell, *J. Org. Chem.*, **27**, 2207 (1962). This method may offer a promising approach to the preparation of acylarylthiols from di(acylaryl) disulfides.

TABLE V

REDUCTION OF DI(ACYLARYL) DISULFIDES

Disulfide	Thiol	Yield, %	M.p. or b.p. (mm.), °C.
$(4\text{-}CH_3COC_6H_4S\text{-})_2$	$4\text{-}CH_3COC_6H_4SH$[a]	29	133–136 (7)
$(4\text{-}CH_3CO\text{-}2\text{-}CH_3C_6H_3S\text{-})_2$	$4\text{-}CH_3CO\text{-}2\text{-}CH_3C_6H_3SH$[a]	15	150–154 (7)[b]
$(4\text{-}C_6H_5CO\text{-}3\text{-}CH_3C_6H_3S\text{-})_2$	$4\text{-}C_6H_5CH_2\text{-}3\text{-}CH_3C_6H_3SH$[c]	42	128 (0.2)

[a] These materials were identical with those prepared as described in Table III. [b] M.p. 30–31° (petroleum ether, b.p. 30–60°). [c] *Anal.* Calcd. for $C_{14}H_{14}S$: C, 78.45; H, 6.58; S, 14.96. Found: C, 78.42; H, 6.81; S, 15.40. S-Benzoyl derivative, m.p. 65–66° (aqueous methanol). *Anal.* Calcd. for $C_{21}H_{18}OS$: C, 79.21; H, 5.7; S, 10.06. Found: C, 79.48; H, 5.76; S. 10.04.

TABLE VI

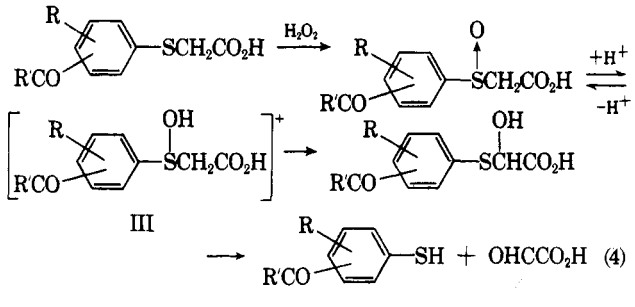
ACYLARYLSULFINYLACETIC ACIDS

Acylarylsulfinylacetic acid	Yield, %	M.p., °C.	Analyses—Calculated C	H	S	Found C	H	S
$4\text{-}CH_3COC_6H_4SOCH_2CO_2H$	47	136–137	53.09	4.45	14.13	53.58	4.68	13.89
$4\text{-}CH_3CO\text{-}2\text{-}CH_3C_6H_3SOCH_2CO_2H$	100[a]	Syrup	...	...	...	...	...	...
$2\text{-}CH_3CO\text{-}4\text{-}CH_3C_6H_3SOCH_2CO_2H$	90	181–182 dec.	54.98	5.03	13.34	55.32	5.12	12.91
$4\text{-}C_6H_5CO\text{-}3\text{-}CH_3C_6H_3SOCH_2CO_2H$	100[a]	Syrup	...	...	...	...	...	...

[a] Crude yield.

sulfide was frequently found among the reaction products (see Table VI).

It was noticed from qualitative observations, that the acid-catalyzed hydrolytic cleavage of acylarylsulfinylacetic acids occurred at a slower rate than was the case with the haloarylsulfinylacetic acids.[4] While this may be due in part to the lower solubility of the acylarylsulfinylacetic acids alternative reasoning is possible. The sulfinyl group in acylarylsulfinylacetic acids would, on account of the deactivating acyl group, be expected to be less "basic" than the same group in the halo- or alkylarylsulfinylacetic acids. The less "basic" arylsulfinylacetic acid would not be expected to form easily the conjugate acid III necessary for the rearrangement (equation 4).[11]



(4)

In regard to the necessity of formation of a conjugate acid it is interesting to note that hydrogen peroxide oxidation of *p*-nitrophenylmercaptoacetic acid to *p*-nitrobenzenethiol and di(*p*-nitrophenyl) disulfide also proceeded with some difficulty. In this case, even at 100°, the oxidizing agent quite successfully competed with proton at the *p*-nitrophenylsulfinylacetic acid stage with the result that *p*-nitrophenylsulfonylacetic acid was also formed. The importance of the formation of conjugate acids to the rearrangement of arylsulfinyl acetic acids (ref. 4 and equation 4) is further emphasized by the inability of arylsulfonylacetic acids to form conjugate acids and hence rearrangement products.

(11) A referee has suggested that protonation of the carbonyl group may also be a factor in the difference between the halo- and acyl-substituted compounds.

Summary

The scheme outlined in equation 1 has been successfully applied to the preparation of acylarylthiols from arylthiol precursors. Yields of acylarylthiols obtainable directly according to equation 1 are only moderate; the process lends itself very well, however, to the direct preparation of high yields of di(acylaryl) disulfides. Although the present study of the new process has been limited to the acylation of benzenethiol and the three toluenethiols there seems no reason why it could not be extended to heterocyclic and condensed homocyclic aromatic ring systems. The new process is limited in its generality inasmuch as the position taken up by the entering acyl group depends on the substituents already in the ring.

Experimental[12]

Acetylations. A. In Nitrobenzene.—Aluminum chloride (3.3–4.0 moles) was added slowly to nitrobenzene (11 moles). Two-thirds of this solution was treated, at 0–5°, with acetyl chloride (1.1 moles); the remaining one-third was treated, at 0–5°, with the arylmercaptoacetic acid (1 mole). The acetyl chloride–aluminum chloride mixture was then added, over 1.5 hr., to the arylmercaptoacetic acid–aluminum chloride mixture. Throughout the addition the temperature was maintained at 8–10° with an ice–water bath. After completion of the addition the mixture was stirred at 7–10° for 1 hr. and then allowed to warm to room temperature during an additional 4 hr. The deeply colored nitrobenzene solution was decomposed by pouring it into a large excess of ice and hydrochloric acid; removal of the nitrobenzene by steam distillation left a crude acylarylmercaptoacetic acid.

The crude acetylation products from phenyl-, *o*-tolyl-, and *m*-tolylmercaptoacetic acids were solids at room temperature and were not steam volatile. These solids were partially purified by solution in aqueous sodium bicarbonate followed by filtration and acidification. Pure samples were obtained by crystallization first from water or aqueous methanol, and then from carbon tetrachloride containing a little methanol.

Only in the case of the acetylation of *m*-tolylmercaptoacetic acid were two acidic products isolated. Acidification of the sodium bicarbonate solution at 35° precipitated 4-acetyl-3-methylphenylmercaptoacetic acid, which was immediately filtered. A small amount of the second acid deposited when the filtrate was cooled. Further work (see subsequent reaction) showed that the second acid was 2-acetyl-3(or 5)-methylphenylmercaptoacetic acid.

(12) Temperatures are uncorrected. Microanalyses were by Drs. G. Weiler and F. B. Strauss, Oxford, England.

The product from the attempted acetylation of *p*-tolylmercaptoacetic acid was steam volatile. It was partially separated from the nitrobenzene during the steam distillation of the latter. Further work showed that this steam volatile solid was 5-methylbenzo[*b*]thiophen-3-ol (see subsequent reaction).

B. In Carbon Disulfide–Nitrobenzene.—Acetyl chloride (1.1 moles) was added gradually to a suspension of aluminum chloride (3.3–4.1 moles) in carbon disulfide (16.5 moles) at 0–5° under ice-bath cooling. Arylmercaptoacetic acid (1 mole) was then sprinkled in gradually while the temperature was held below 10°. Small quantities of nitrobenzene were added periodically to ease stirring. The amount of nitrobenzene used varied from 0.5 to 2.5 moles. After all the acid had been added the suspension was stirred until evolution of hydrogen chloride had ceased. The mixture was decomposed by pouring it into a large excess of ice and hydrochloric acid. Carbon disulfide was removed by distillation and the acetylarylmercaptoacetic acid was filtered, washed with petroleum ether (b.p. 88–98°), and dried. The product thus obtained was essentially pure. Analytical specimens were obtained by crystallization from water or a mixture of carbon tetrachloride and methanol.

The structure of 2-acetyl-4-methylphenylmercaptoacetic acid was established by converting it to 3,5-dimethylbenzo[*b*]thiophene-2-carboxylic acid (which see). Table I summarizes results of the acetylation experiments.

Partial Proof of Structure of 2-Acetyl-3(or 5)-methylphenylmercaptoacetic Acid.—The acidic by-product from the preparation of 4-acetyl-3-methylphenylmercaptoacetic acid was shown to contain an acetyl group in an *ortho* position to the sulfur atom by the following experiment.

The acid (0.01 mole), m.p. 161–162° dec., was boiled in 20% hydrochloric acid (20 ml.) for 5 hr. The solid product was filtered and crystallized twice from aqueous acetic acid. The yield of pure 3,4(or 3,6)-dimethylbenzo[*b*]thiophene-2-carboxylic acid, m.p. 261–262° dec., was 90%.

Anal. Calcd. for $C_{11}H_{10}O_2S$: C, 64.05; H, 4.89; S, 15.54. Found: C, 63.71; H, 5.07; S, 15.65.

Proof of Structure of 5-Methylbenzo[*b*]thiophen-3-ol.—Steam distillation of the decomposed reaction mixture from the attempted acetylation of *p*-tolylmercaptoacetic acid in nitrobenzene gave a steam volatile solid, m.p. 96–98°. A single crystallization from petroleum ether (b.p. 88–98°) gave colorless needles, m.p. 98–100°. The literature[6] reports a melting point of 101–102° for 5-methylbenzo[*b*]thiophen-3-ol.

The compound, m.p. 98–100°, was converted to 5-methylbenzo[*b*]thiophene-2,3-dione by a known method.[9] 5-Methylbenzo[*b*]thiophene-2,3-dione was obtained as red prismatic needles, m.p. 146–147° (aqueous methanol) (lit.[13] m.p. 144–145°).

Anal. Calcd. for $C_9H_6O_2S$: S, 17.99. Found: S, 17.76.

Proof of Structure of 2-Acetyl-4-methylphenylmercaptoacetic Acid.—The acid (2 g.) was heated in 30% aqueous sodium hydroxide (20 ml.) for 5 hr. Dilution of the suspension with water followed by acidification gave a quantitative yield of 3,5-dimethylbenzo[*b*]thiophene-2-carboxylic acid, m.p. 262–264° dec. Recrystallization from acetic acid gave an analytically pure sample, m.p. 263–264° dec. (lit.[8] m.p. 262°).

Anal. Calcd. for $C_{11}H_{10}O_2S$: C, 64.05; H, 4.89; S, 15.54. Found: C, 63.91; H, 5.13; S, 15.65.

Preparation of 2,4-Dinitrophenylhydrazones.—Derivatives of 2-acetyl-4-methylphenylmercaptoacetic acid and 4-acetyl-2-methylphenylmercaptoacetic acid were prepared in the following way. A suspension of 2,4-dinitrophenylhydrazine (0.25 g.) in boiling ethanol (20 ml.) was treated with concentrated hydrochloric acid (2 ml.) and the mixture heated until a clear solution resulted. The acetyl compound (0.25 g.) was added to this solution. The mixture was boiled for 10 min., allowed to stand for 30 min., cooled, and filtered. The crystals thus obtained were purified by recrystallization from ethanol. Analysis showed that the carboxy group had been esterified during this process. 2,4-Dinitrophenylhydrazone of ethyl 2-acetyl-4-methylphenylmercaptoacetate had m.p. 142°.

Anal. Calcd. for $C_{19}H_{20}N_4O_6S$: C, 52.77; H, 4.66; N, 12.96; S, 7.41. Found: C, 52.41; H, 4.22; N, 13.24; S, 7.39.

2,4-Dinitrophenylhydrazone of ethyl 4-acetyl-2-methylphenylmercaptoacetate had m.p. 122–123°.

Anal. Calcd. for $C_{19}H_{20}N_4O_6S$: N, 12.96; S, 7.41. Found: N, 12.89; S, 7.25.

Benzoylations.—Aluminum chloride (4 moles) was suspended in carbon disulfide (80 moles), and benzoyl chloride (1.1 moles) was added over 15 min. The temperature was held below 15° with an ice–water bath. Arylmercaptoacetic acid (1 mole) was sprinkled in over 20 min. while the temperature was held at about 15°. Nitrobenzene (about 2 moles in all) was added periodically to ease stirring. After the arylmercaptoacetic acid had been added, the mixture was held at 15° for 1.5 hr., and then allowed to warm to room temperature in 4 hr. The reaction mixture was decomposed in the usual way, carbon disulfide was removed by distillation, and the benzoylmercaptoacetic acid was collected by filtration. The crude product was partially purified by dissolving it in aqueous sodium bicarbonate, filtering, and acidifying. Further purification was effected by crystallization from carbon tetrachloride containing a very small amount of petroleum ether (b.p. 88–98°). Table II summarizes results of the benzoylation experiments.

Acylarylthiols and Disulfides from Acylarylmercaptoacetic Acids. A. 1.25 Moles of Hydrogen Peroxide at 100°.—Acylarylmercaptoacetic acid (0.1 mole) was refluxed in water (200 ml.) containing sulfuric acid (11 g.). Hydrogen peroxide (0.1 mole as a 30% aqueous solution) was added dropwise to the refluxing mixture over a period of about 15 min. After addition of the hydrogen peroxide was completed the mixture was refluxed for 20 min. and a further 0.025 mole of hydrogen peroxide added over 10 min. The suspension was refluxed an additional 2 hr. and cooled. The oily product was extracted with ether and the ether layer extracted first with aqueous sodium bicarbonate and then with sodium hydroxide. Acidification of the sodium hydroxide extract gave acylarylthiol. Evaporation of the ether layer generally gave an oily disulfide which became granular on trituration with aqueous sodium hydroxide. Aqueous methanol was used to crystallize the disulfides. Petroleum ether (b.p. 63–69°) was used to crystallize the solid thiols. Table III summarizes the results obtained.

B. 2.0–2.5 Moles of Hydrogen Peroxide at 100°.—Acylarylmercaptoacetic acid (0.1 mole) was refluxed in water (200 ml.) containing sulfuric acid (4 g.). Hydrogen peroxide (0.1 mole as a 30% aqueous solution) was added dropwise to the refluxing mixture over a period of about 20 min. Some 20 min. after addition of the first 0.1 mole of hydrogen peroxide, another 0.05 mole was added over 10 min. About 15 min. later an additional 0.05 mole of hydrogen peroxide was added and the mixture refluxed an additional 90 min. In those cases where the product was oily, trituration with aqueous sodium hydroxide frequently gave a manageable solid product. Aqueous methanol proved a useful solvent for crystallization. Table IV summarizes the results obtained.

C. 2.5 Moles of Hydrogen Peroxide at 60°.—A suspension of finely powdered 4-acetyl-3-methylphenylmercaptoacetic acid (0.15 mole) in 10% hydrochloric acid (150 ml.) was heated to 60°. Hydrogen peroxide (0.15 mole as a 30% aqueous solution) was added dropwise over 15 min. After stirring for 30 min. an additional 0.15 mole of hydrogen peroxide was added over 10 min. One hour later a further 0.075 mole of hydrogen peroxide was added and the mixture stirred an additional 2 hr. The temperature was maintained at 60° throughout the reaction. After cooling to 10° the solid product was filtered and extracted with aqueous sodium bicarbonate. The sodium bicarbonate solution on acidification gave 4-acetyl-3-methylphenylsulfonylacetic acid (14%), m.p. 146–148°. A single crystallization from water yielded needles, m.p. 150–151°.

Anal. Calcd. for $C_{11}H_{12}O_5S$: C, 51.54; H, 4.72; S, 12.51; equiv. wt., 256.3. Found: C, 51.91; H, 4.54; S, 12.04; equiv. wt., 255.5.

The solid insoluble in aqueous sodium bicarbonate was oily in appearance. Treatment with aqueous sodium hydroxide gave a granular product, m.p. 57–59°. Crystallization from aqueous methanol yielded di(4-acetyl-3-methylphenyl) disulfide (26%) as plates, m.p. 60–61°. The sodium hydroxide on acidification gave a small amount of an unidentified resinous product.

Acylarylsulfonylacetic acids are undoubtedly formed in most oxidation reactions which use excess hydrogen peroxide. In addition to the cited preparation of 4-acetyl-3-methylphenylsulfonylacetic acid, we isolated 4-acetylphenylsulfonylacetic acid, m.p. ~170° dec., and 4-acetylphenylmethyl sulfone from the aqueous liquors from the acid-catalyzed oxidation cleavage of 4-acetylphenylmercaptoacetic acid. The crude acid, m.p. ~170° dec., was converted to 4-acetylphenylmethyl sulfone by heating at 160–180° for 3 hr. A specimen of this sulfone, when crystallized from water, melted at 127–128°.

(13) C. E. Dalgliesh and F. G. Mann, *J. Chem. Soc.*, 893 (1945).

TABLE VII

ACID-CATALYZED CLEAVAGE OF ACYLARYLSULFINYLACETIC ACIDS

Acylarylsulfinylacetic acid	Thiol	Yield, %	B.p. (mm.), °C.
4-CH_3CO-2-$CH_3C_6H_3SOCH_2CO_2H$	4-CH_3CO-2-$CH_3C_6H_3SH$	43	143–144 (5)
2-CH_3CO-4-$CH_3C_6H_3SOCH_2CO_2H$	2-CH_3CO-4-$CH_3C_6H_3SH$[a]	45	139–140 (5.5)
4-C_6H_5CO-3-$CH_3C_6H_3SOCH_2CO_2H$	4-C_6H_5CO-3-$CH_3C_6H_3SH$[b]	39	152 (2)

[a] M.p. 32–33°. *Anal.* Calcd. for $C_9H_{10}OS$: C, 65.02; H, 6.06; S, 19.29. Found: C, 65.20; H, 6.19; S, 19.01. Disulfide, m.p. 178° (aqueous methanol). *Anal.* Calcd. for $C_{18}H_{18}O_2S_2$: C, 65.42; H. 5.49; S, 19.40. Found: C, 65.84; H, 5.47; S, 19.01. [b] *Anal.* Calcd. for $C_{14}H_{12}OS$: C, 73.65; H, 5.3; S, 14.04. Found: C, 74.15; H, 5.69; S, 13.24. S-Benzoyl derivative, m.p. 97.5–98.5 (methanol). *Anal.* Calcd. for $C_{21}H_{16}O_2S$: C, 76.18; H, 4.85; S, 9.64. Found: C, 76.72; H, 4.95; S, 9.68.

Anal. Calcd. for $C_9H_{10}O_3S$: C, 54.53; H, 5.08; S, 16.17. Found: C, 54.32; H, 4.91; S, 15.95.

This material gave no depression of melting point with an authentic sample prepared from 4-acetylphenylmethyl sulfide[14] by hydrogen peroxide oxidation.[15]

Thiols from Di(acylaryl) Disulfides.—The disulfide (0.05 mole) was refluxed in acetic acid (1 mole) and water (2 moles) and the mixture treated, over a period of 40 min., with zinc dust (0.3 to 0.4 mole). After refluxing for an additional 3 hr. the mixture was poured into water. Excess zinc was removed by adding a little concentrated hydrochloric acid. The oil was taken up in ether and crude thiol extracted from this with aqueous sodium hydroxide. Acidification of the sodium hydroxide solution gave crude thiol which was redissolved in ether; the ether was washed with water and dried. The ether was distilled and the thiol purified by vacuum distillation.

The reduction of di(4-benzoyl-3-methylphenyl) disulfide using zinc and acetic acid gave 4-benzyl-3-methylbenzenethiol as the major product. Table V summarizes the results obtained.

Acylarylthiols from Acylarylsulfinylacetic Acids. A. Preparation of Acylarylsulfinylacetic Acids.—Acylarylmercaptoacetic acid (0.1 mole) was suspended in 75% acetic acid (250 ml.) and the mixture stirred and heated to about 60°. Hydrogen peroxide (0.1 mole as a 30% aqueous solution) was added over 50 min. at this temperature. The mixture was kept at 60° for 5 hr. and allowed to stand overnight. Half of the solvent mixture was removed under vacuum at 50–60° (rotary evaporator). Cooling of the acetic acid solution sometimes led to crystallization of the acylarylsulfinylacetic acid. In a few cases the acylarylsulfinyl acetic acid was obtained as a sirup by complete evaporation of the aqueous acetic acid. Table VI summarizes the results obtained.

(14) G. B. Bachman and C. L. Carlson, *J. Am. Chem. Soc.*, **73**, 2857 (1951).

(15) U. S. Patent 2,802,033 (1957) to E. I. du Pont de Nemours and Co.

B. Cleavage of Acylarylsulfinylacetic Acids.—Acylarylsulfinylacetic acid (0.05 mole) was refluxed in 6% sulfuric acid (200 ml.) for 5 to 6 hr. The oily suspension was extracted with ether and the ether extracted first with aqueous sodium bicarbonate and then with aqueous sodium hydroxide. Acidification of the sodium bicarbonate extracts usually gave some acidic material (2-acetyl-4-methylphenylsulfinylacetic acid gave some high melting acid, probably 3,5-dimethylbenzo[*b*]thiophene-2-carboxylic acid or its sulfoxide). Acidification of the sodium hydroxide extracts gave the crude thiols which were purified by distillation. The neutral ether layer on evaporation usually yielded a small quantity of the disulfide (the neutral product from 2-acetyl-4-methylphenylsulfinylacetic acid was complex). Table VII summarizes the results obtained.

Hydrogen Peroxide Oxidation of 4-Nitrophenylmercaptoacetic Acid.—4-Nitrophenylmercaptoacetic acid (0.05 mole) was finely ground and suspended in water (55 ml.) containing 80% phosphoric acid (3 ml.). The suspension was boiled and hydrogen peroxide (0.055 mole as a 30% aqueous solution) added over about 30 min. Steam was passed in during the peroxide addition and for 1 hr. after that. The solid in the reaction flask turned first to a yellow oil and finally to a solid. About 0.5 g. of product steam distilled; this proved to be a mixture of about equal weights of 4-nitrobenzenethiol, m.p. 76–77°, and di(4-nitrophenyl) disulfide, m.p. 179–180°. The contents of the reaction flask were filtered and the solid extracted with aqueous sodium bicarbonate. Acidification of this extract gave 3 9 g. of acidic material, m.p. 155–160°. Several crystallizations of the latter from methanol afforded 4-nitrophenylsulfonylacetic acid, m.p. 168° dec.

Anal. Calcd. for $C_8H_7NO_6S$: N, 5.71; S, 13.06. Found: N, 5.76; S, 13.40.

The solid insoluble in aqueous sodium bicarbonate was di(4-nitrophenyl) disulfide, m.p. 175–177°. Crystallization from acetic acid gave a pure product, m.p. 180–181°

The Reaction between Acenaphthenequinone and Phenyllithium

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Received March 4, 1963

The reaction between acenaphthenequinone and phenyllithium gave the expected *trans*-1,2-diphenyl-1,2-acenaphthenediol in low yields as well as four other solid products. Two of these were known compounds. The structures of one of the other products (II) and of several new compounds related to it have been established. II is the result of the unusual 1,4-addition of phenyllithium to an aryl ketone.

The reaction between acenaphthenequinone and phenylmagnesium bromide gave *trans*-1,2-diphenyl-1,2-acenaphthenediol in 81% yield.[1] In the reactions of other quinones with organometallic reagents,[2] better yields of 1,2-addition products were obtained by the use of phenyllithium rather than phenylmagnesium bromide. The present study shows that acenaphthenequinone behaved more like phenanthrenequinone[3] and gave the *trans*-1,2-diphenyl-1,2-acenaphthenediol in poor yields, 10–28%, as well as several other solid products and a dark oil from which no more solid could be isolated either by crystallization or by chromatography. Naphthalic anhydride (1–6%) was isolated from five of the twenty-five reactions which were carried out. Fourteen of the reactions gave the lactone of 1-(diphenylhydroxymethyl)-8-naphthoic acid (I, 7–22%). These compounds were identified by comparison with known samples.[4] Four of the reactions gave small amounts of a lactone melting at 176°, which has not

(1) P. D. Bartlett and R. F. Brown, *J. Am. Chem. Soc.*, **62**, 2927 (1940).

(2) H. M. Crawford, *ibid.*, **61**, 3310 (1939); **70**, 1081 (1948); H. M. Crawford and M. McDonald, *ibid.*, **71**, 2681 (1949).

(3) H. M. Crawford, M. Lumpkin, and M. McDonald, *ibid.*, **74**, 4087 (1952).

(4) G. Wittig, M. Leo, and W. Wiemer, *Ber.*, **64**, 2405 (1931).