[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

Mercaptocarboxylic Acids as Reagents for the Identification of Carbonyl Compounds

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RECEIVED JULY 8, 1952

Mercaptoacetic acid, α-mercaptopropionic acid, β-mercaptopropionic acid, α,β-dimercaptopropionic acid and α-mercaptolauric acid have been investigated as reagents for the identification of carbonyl compounds. A number of new derivatives have been prepared, characterized, and identified by analysis. Mercaptoacetic acid and β-mercaptopropionic acid were found to be the most generally useful reagents in this group. Standard conditions have been developed for the preparation, purification and titration of derivatives.

The preparation of carbonyl derivatives whose molecular weights may be determined by simple chemical methods has been the subject of much study.[2] Those derivatives which met the usual standards for purposes of identification required time-consuming procedures for the determination of molecular weight, while the few derivatives whose molecular weights could be determined by titration were unsatisfactory from other points of view. In the present study mercaptoacetic acid, β-mercaptopropionic acid, α,β-dimercaptopropionic acid and α-mercaptolauric acid have been investigated as reagents for the identification of carbonyl compounds. In each case the derivative formed is a mercaptal or mercaptol having free carboxyl groups which may be titrated with standard base (Tables I and II).

The water-insolubility of α-mercaptolauric acid rendered it unsatisfactory for the procedures reported below, and α,β-dimercaptopropionic acid involved difficulties in the preparation and purification of derivatives. While α-mercaptopropionic acid yielded the highest melting derivatives they did not melt sharply, possibly because of the simultaneous formation of racemic and *meso*-reaction products. Mercaptoacetic acid was the most satisfactory reagent for most simple aldehydes and ketones excepting low molecular weight aldehydes, whose derivatives are inconveniently soluble in water. β-Mercaptopropionic acid was most satisfactory for low molecular weight aldehydes and also for many higher molecular weight carbonyl compounds which do not dissolve readily in mercaptoacetic acid.

With regard to the scope and limitations of the reaction, Posner[3] made an extended investigation of the factors which inhibit mercaptol formation, and his conclusions have been verified in the present study. Nitro, hydroxyl, carboxyl, amino, carbonyl and halide groups in positions alpha, and sometimes beta to the carbonyl group tend to inhibit the reaction, as do the same groups when present on an aromatic nucleus, especially when ortho to the carbonyl-bearing carbon atom. Olefinic and acetylenic groups not only inhibit mercaptol formation but may also lead to equivocal results as mercaptans add to unsaturated linkages. Nitriles,[4] alkyl halides and diazonium salts[5] may also be expected to react with mercaptocarboxylic acids.

Certain limitations of mercaptol formation are useful in the separation of carbonyl compounds. For example, it was found possible to separate cyclohexanone from isophorone by reaction with mercaptoacetic acid, as the former readily yielded a solid mercaptol while the latter formed an oil. When the derivative is refluxed with aqueous mineral acid the carbonyl compound and mercaptan are regenerated.[6]

The derivatives reported below are generally stable and in most cases are easily prepared and purified in excellent yield. Their melting points fall in a convenient range and are often distinctively different for isomers or neighbors in a homologous series.

Acknowledgment.—The authors are indebted to Drs. Doris L. Clegg, W. C. Woodland and E. V. Piel for the analyses reported in the Experimental Part.

Experimental Part

The following procedure was generally followed: 0.05–0.1 ml. of a liquid carbonyl compound (or 0.1 g. of a solid) was added to 0.2 ml. of mercaptocarboxylic acid. Hydrogen chloride was passed through the mixture for about 2 minutes, or until heavy precipitation occurred. After 15 minutes the crystalline derivative was separated and recrystallized from water or dilute acetic acid, or occasionally from ether or chloroform. Formaldehyde and glyoxal were found to react with mercaptocarboxylic acids in dilute aqueous solution. A 70% aqueous solution of mercaptoacetic acid was used for most of the reactions reported here. It reacted spontaneously with aldehydes and required hydrogen chloride as catalyst only with ketones. However, hydrogen chloride hastened the reaction and resulted in better yields in all cases.

Neutral equivalents were determined by standard methods.[7] Table III illustrates the precision obtainable in the determination of neutralization equivalents. Potentiometric titrations showed that the mercaptals are moderately strong dibasic acids and that the dimercaptals are moderately strong tetrabasic acids which can be satisfactorily titrated to a phenolphthalein end-point. Derivatives with an ortho phenolic group could also be titrated with phenolphthalein, but those containing a para phenolic group required methyl red, and even then did not titrate to sharp end-points.

(1) Abstracted from the thesis submitted by Myron J. Lover in partial fulfillment of the requirements for the degree of Doctor of Philosophy at New York University.

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(5) F. E. Condo, E. T. Hinkel, A. Fassero and R. L. Shriner THIS JOURNAL, **59**, 230 (1937).

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(7) J. B. Niederl and V. Niederl, "Micromethods of Quantitative Organic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1942 pp. 66-68.

TABLE I

DERIVATIVES OF ALDEHYDES

Aldehyde	Reagent[a]	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Acetaldehyde	C	79–80	$C_8H_{14}O_4S_2$	40.32	40.59	5.92	5.82
n-Butyraldehyde	A	59–63	$C_8H_{14}O_4S_2$	40.32	40.28	5.92	5.92
Benzaldehyde	D	78–78.5	$C_{10}H_{10}O_2S_2$	46.50	46.78	3.90	4.20
Glyoxal	A	189	$C_{10}H_{14}O_8S_4$	30.73	30.81	3.61	3.59
n-Butyraldehyde	B	58–59	$C_{10}H_{18}O_4S_2$	39.20	39.46	5.92	5.99
n-Heptaldehyde	A	57	$C_{11}H_{20}O_4S_2$	47.11	47.63	7.18	7.31
Cinnamaldehyde	D	98–100	$C_{12}H_{12}O_2S_2$	50.87	50.96	3.91	3.91
Piperonal	A	134–135.5	$C_{12}H_{12}O_6S_2$	45.56	45.60	3.83	3.83
p-Methoxybenzaldehyde	A	121.5–122.5	$C_{12}H_{14}O_5S_2$	47.66	47.72	4.67	4.61
Vanillin	A	134–135	$C_{12}H_{14}O_6S_2$	45.27	45.27	4.43	4.23
2,3-Dimethoxybenzaldehyde	A	134–135	$C_{13}H_{16}O_6S_2$	46.97	47.47	4.85	4.98
3,4-Dimethoxybenzaldehyde	A	121–122	$C_{13}H_{16}O_6S_2$	46.97	46.82	4.85	4.50
n-Heptaldehyde	B	65–67	$C_{13}H_{24}O_4S_2$	50.62	50.69	7.84	7.87
Piperonal	C	129–130	$C_{14}H_{16}O_6S_2$	48.82	48.96	4.68	4.76
p-Methoxybenzaldehyde	B	110–110.5	$C_{14}H_{18}O_5S_2$	50.89	50.98	5.49	5.25
p-Methoxybenzaldehyde	C	139.5–141	$C_{14}H_{18}O_5S_2$	50.89	51.18	5.49	45.7
Glyoxal	B	162	$C_{14}H_{22}O_8S_4$	36.77	37.00	4.97	5.17
2,3-Dimethoxybenzaldehyde	B	99–100	$C_{15}H_{20}O_6S_2$	49.98	49.90	5.59	5.50

[a] A, mercaptoacetic acid; B, β-mercaptopropionic acid; C, α-mercaptopropionic acid; D, α,β-dimercaptopropionic acid.

TABLE II

DERIVATIVES OF KETONES

Ketone	Reagent[a]	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Butanone	A	106–107.5	$C_8H_{14}O_4S_2$	40.32	40.17	5.92	6.12
Acetone	C	166–171	$C_9H_{16}O_4S_2$	42.84	42.87	6.39	6.24
Cyclohexanone	A	131.5–132	$C_{10}H_{16}O_4S_2$	45.43	45.76	6.10	6.18
4-Methyl-2-pentanone	A	84–85	$C_{10}H_{18}O_4S_2$	45.09	44.96	6.81	7.00
Butanone	C	126.5–127	$C_{10}H_{18}O_4S_2$	45.09	44.98	6.81	7.04
2-Heptanone	A	74–75	$C_{11}H_{20}O_4S_2$	47.12	47.28	7.19	6.96
p-Hydroxyacetophenone	A	122 dec.	$C_{12}H_{14}O_5S_2$	47.66	47.54	4.67	4.44
Cyclohexanone	C	124–126	$C_{12}H_{20}O_4S_2$	49.29	40.56	6.89	7.06
4-Methyl-2-pentanone	B	101–101.5	$C_{12}H_{22}O_4S_2$	48.95	49.14	7.53	7.56
2-Heptanone	B	87.5–89	$C_{13}H_{24}O_4S_2$	50.62	50.77	7.84	7.93
2-Heptanone	C	121–123	$C_{13}H_{24}O_4S_2$	50.62	50.78	7.84	7.79
n-Butyrophenone	A	155–156	$C_{14}H_{18}O_4S_2$	53.48	53.36	5.77	5.60
n-Butyrophenone	B	103–104	$C_{16}H_{22}O_4S_2$	56.11	56.40	6.47	6.57
2,4-Pentanedione	B	121 dec.	$C_{17}H_{28}O_8S_4$	41.78	42.13	5.77	5.95
7-Tridecanone	A	84–85	$C_{17}H_{32}O_4S_2$	56.01	56.43	8.85	8.83
p-Phenylacetophenone	A	170–172 dec.	$C_{18}H_{18}O_4S_2$	59.65	60.17	5.01	5.08
2,5-Hexanedione	B	175 dec.	$C_{18}H_{30}O_8S_4$	43.01	43.28	6.02	6.14
2,5-Hexanedione	C	186–190 dec.	$C_{18}H_{30}O_8S_4$	43.01	43.47	6.02	5.27
7-Tridecanone	C	113–114	$C_{19}H_{36}O_4S_2$	59.37	59.31	8.97	9.55

[a] See footnote *a*, Table I.

A series of approximately 30 previously reported[8] mercaptals derived from mercaptoacetic acid and from α- and β-mercaptopropionic acids was prepared by the procedure outlined above, which was found in all cases to yield the expected derivative. Tables I and II record only new members prepared in this study.

Compounds which failed to yield derivatives with the reagent indicated in each case were *p*-nitrobenzaldehyde-B, benzalacetophenonedibromide-A and benzil-A. Derivatives difficult to purify or otherwise unsatisfactory were obtained in the following: acrolein-A, arabinose-B, citral-A and -B, *d*-citronellal-A and -B, crotonaldehyde-A and -B, 2,4-dihydroxybenzaldehyde-A and -B, *p*-dimethylaminobenzaldehyde-A, fural-A, *o*-hydroxybenzaldehyde-B, *m*-hydroxybenzaldehyde-A and -B, acetylacetone-A, benzalacetophenone-A, benzoylformic acid-A, *o*-benzoylbenzoic acid-A, diacetyl-A, *o*-hydroxyacetophenone-A and B, *p*-hydroxyacetophenone-B, isophorone-A, mesityl oxide-A and *p*-phenylacetophenone-B (see footnote *a*, Table I).

TABLE III

NEUTRALIZATION EQUIVALENTS[a]

Compound	Calcd.	Found I	Found II
a	157.2	157.2	158.0
b	165.2	165.0	165.8
c	154.2	154.6	155.0
d	126.1	125.5	126.1
e	173.2	173.9	172.8

[a] Determined by students at Hunter College under the direction of Dr. Doris L. Clegg. These may be regarded as typical results, as the compounds were chosen at random by Dr. Clegg.

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