

of cyclopropyl ketone 7. The analytical sample was obtained by thick layer chromatography on silical gel using 1:1 ether-benzene as the solvent.

*Anal.* Calcd for  $C_{12}H_{18}O$ : C, 80.85; H, 10.18. Found: C, 80.62; H, 10.18.

**4-Methyl-1(9)-octalin-2-one (21).**—To a solution of 30 g of the pyrrolidine enamine of cyclohexanone in 200 ml of benzene was added 17.0 g of *trans*-3-penten-2-one.<sup>23</sup> The mixture was then heated at reflux for 24 hr.<sup>22</sup> A buffer solution made up of 25 ml of acetic acid, 25 ml of water, and 12.5 g of sodium acetate was added and the solution was heated at reflux for 4 hr. Isolation with benzene and distillation gave 13.8 g of octalone 21, bp 88–90° (0.6 mm). This material was obtained as a mixture of  $\alpha,\beta$  and  $\beta,\gamma$  double bond isomers. The pure conjugated isomer was obtained by cooling a hexane solution of the mixture in Dry Ice-acetone whereupon pure enone 21 crystallized and was obtained free of the  $\beta,\gamma$  isomer:  $\lambda_{max}^{flm}$  5.98 and 6.17  $\mu$ m;  $\delta_{TMS}^{C14}$  5.52 (vinyl H) and 1.06 ppm ( $CH_3$ , d,  $J = 6.0$  Hz).

*Anal.* Calcd for  $C_{11}H_{16}O$ : C, 80.44; H, 9.82. Found: C, 80.63; H, 9.84.

**4,9-Dimethyldecalin-3-one (22).**—To a cooled (0°), stirred suspension of cuprous iodide (4.90 g) in 100 ml of anhydrous ether was added 35 ml of 1.6 M methyllithium.<sup>2</sup> To this clear solution was added 1.03 g of enone 21 in 15 ml of ether. After

(22) G. Stork, A. Brizzolara, H. K. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

1 hr, the mixture was poured into a saturated ammonium chloride solution. Isolation with ether (an ammonium hydroxide wash was used to remove the suspended copper salts) and short path distillation afforded 1.04 g (90%) of ketone 22 as a colorless oil: bp 100° (bath temperature) at 0.2 mm;  $\lambda_{max}^{flm}$  5.85  $\mu$ m;  $\delta_{TMS}^{C14}$  1.12 ( $CH_3$ ) and 0.98 ppm ( $CH_3$ , d,  $J = 6.0$  Hz). The analytical sample was secured *via* a second distillation.

*Anal.* Calcd for  $C_{12}H_{20}O$ : C, 79.94; H, 11.18. Found: C, 80.15; H, 11.09.

**Registry No.**—3, 33021-03-3; 4, 32970-11-9; 5, 32970-12-0; 6, 32970-13-1; 7a, 32980-02-2; 7b, 32980-03-3; 11, 32980-04-4; 13, 32980-05-5; 14, 32980-06-6; 16, 32970-14-2; 16 2,4-DNP, 32970-15-3; 17, 32970-16-4; 18, 32970-17-5; 19, 32980-07-7; 21, 32980-08-8; 22, 32980-09-9; 23a diol derivative, 32980-10-2; 23b diol derivative, 32971-05-4; 24a, 32971-06-5; 24b, 32971-07-6; 25a, 32980-11-3; 25b, 33015-67-7; lithium dimethylcopper, 32970-18-6.

**Acknowledgments.**—We thank the National Institutes of Health for their support of this work through a research grant (5 RO1 CA11089) and a predoctoral fellowship.

## A Mercury Salt Pathway for the Degradation of Carboxylic Acids to Alkyl Halides Using Halogen and Mercuric Oxide<sup>1</sup>

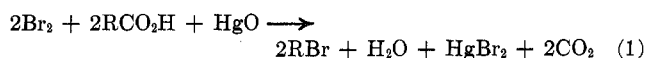
N. J. BUNCE

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*Received May 20, 1971*

The degradation of carboxylic acids to alkyl halides using the halogens and mercuric oxide involves the initial formation of the mercuric salt of the acid, followed by a normal Hunsdiecker reaction of the salt with halogen. The relative insensitivity of the technique to water by comparison with the Hunsdiecker reaction of a silver salt is a consequence of the solubility of the mercury salts in the reaction medium ( $CCl_4$ ). The synthetic applicability of the method is thus comparable with that of the Hunsdiecker reaction, with the additional limitation that those acids which fail to form mercury salts under the reaction conditions or which give insoluble salts cannot successfully be degraded.

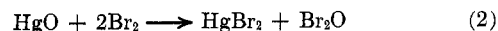
Some time ago, Cristol and Firth reported the degradation of carboxylic acids to alkyl bromides using bromine and mercuric oxide.<sup>2</sup> The technique had as an advantage over the analogous Hunsdiecker reaction of silver carboxylates the avoidance of having to prepare the pure dry silver salts, which is often difficult owing to their thermal instability. Furthermore, there was no need to maintain scrupulously anhydrous reaction conditions; indeed, water is one of the reaction products (eq 1)



Since this publication, scattered reports of the use of the reaction have appeared.<sup>3–6</sup> Davis and his co-workers showed<sup>7</sup> that  $CO_2$  was evolved on treatment of a wide variety of acids with bromine and mercury oxide, and noted that although a very limited number of other metal oxides could replace mercury oxide in the reaction,

the yields of  $CO_2$  using these other oxides were consistently poor.

Concerning the mechanism of the reaction, Cristol and Firth proposed<sup>2</sup> that the function of the mercuric oxide was to oxidize bromine to a positive halogen intermediate, which then reacted with the carboxylic acid to yield an acyl hypobromite. Jennings and Ziebarth<sup>8</sup> have formulated this sequence as eq 2 and 3.



The proposed acyl hypobromite then decomposes to alkyl bromide by the decarboxylation sequence (eq 4–6) established for the Hunsdiecker reaction.<sup>9–11</sup>



In this proposed sequence the intermediacy of the alkyl radical  $R\cdot$  has been established with some cer-

(1) Presented at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971, Abstract ORGN 020.

(2) S. J. Cristol and W. C. Firth, *J. Org. Chem.*, **26**, 280 (1961).

(3) F. W. Baker, H. D. Holtz, and L. M. Stock, *ibid.*, **28**, 514 (1963).

(4) J. S. Meek and D. T. Osuga, *Org. Syn.*, **43**, 9 (1963).

(5) J. W. Wilt and J. A. Lundquist, *J. Org. Chem.*, **29**, 921 (1964).

(6) D. I. Davies and P. Mason, *J. Chem. Soc. C*, 288 (1971).

(7) J. A. Davis, J. Herynk, S. Carroll, J. Bunds, and D. Johnson, *J. Org. Chem.*, **30**, 415 (1965).

(8) P. W. Jennings and T. D. Ziebarth, *ibid.*, **34**, 3216 (1969).

(9) C. V. Wilson, *Org. React.*, **9**, 332 (1957).

(10) R. G. Johnson and R. K. Ingham, *Chem. Rev.*, **56**, 219 (1956).

(11) D. D. Tanner and N. J. Bunce in "The Chemistry of the Carbonyl Halides," S. Patai, Ed., Wiley-Interscience, New York, N. Y., to be published.

tainty. Cristol and his coworkers<sup>2,12,13</sup> showed that the ratio of exo and endo bromides from the degradation of an exo and endo pair of norbornane-2-carboxylic acids was the same whichever isomeric acid was used. Furthermore, the ratio was the same as that observed in the degradation of the silver salts of the same acids by the Hunsdiecker reaction,<sup>14</sup> in which the involvement of R· is well established.<sup>9-11</sup> It has also been shown<sup>3</sup> that in the degradation of bicyclo[2.2.2]octane-1-carboxylic acid in carbon tetrachloride, the expected bromide was accompanied by the typical free radical by-product 1-chlorobicyclo[2.2.2]octane.

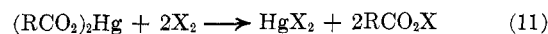
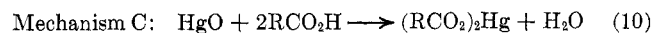
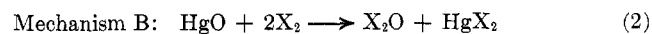
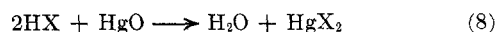
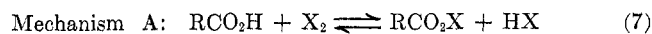
The purpose of the present study was to attempt to secure more evidence for the mechanism of the reaction for the steps in between the starting carboxylic acid and the formation of the penultimate product, the radical R·. Additional interest in the question was raised by observations<sup>2,3,6,13</sup> that iodine may replace bromine in the mercuric oxide-halogen reaction. If the sequence of eq 2-6 were being followed, this would demand the intermediacy of iodine monoxide, which has hitherto never been prepared. It was hoped that a study of the mechanism of the mercury oxide-halogen degradation might shed some light on the possible existence of the unknown iodine monoxide.

### Results and Discussion

The first objective was to obtain evidence for intermediacy of the acyl hypohalite. This was achieved by trapping the hypohalite intermediate with an olefin; the interaction of acetic acid, mercury oxide, and iodine in the presence of cyclohexene afforded an excellent yield of 2-iodocyclohexyl acetate, the cyclohexene adduct of acetyl hypiodite.<sup>15</sup> The reported isolation of iodolactones from two 2-norbornene-endo-5-carboxylic acids using mercury oxide and iodine<sup>17</sup> may likewise be viewed as intramolecular entrapment of an intermediate acyl hypiodite.

**Possible Routes to the Acyl Hypohalite.**—Having placed the intermediacy of the acyl hypohalite on a reasonably secure foundation is good evidence in support of the partial reaction sequence 4-6 for the production of the alkyl halide, since this same intermediate is known to participate in the Hunsdiecker reaction.<sup>9-11</sup> However, this does not *a priori* prove the correctness of the complete reaction sequence 2-6. It was the purpose of this research to consider alternative possible reaction mechanisms, since, in any reaction in which three reactants are involved, it is likely that two of

them combine before reaction with the third. Reasonable routes to the acyl hypohalite for the three possible combinations are shown in mechanisms A, B, and C.



There seems to be little evidence in support of mechanism A, in which the mercuric oxide serves simply to remove the HX formed in equilibrium 7. Equilibria of this type are known to be very unfavorable, positive halogen compounds of all kinds being rapidly destroyed by the halogen acids.<sup>18-20</sup> It would thus seem unlikely that so weak a base as mercuric oxide would be an efficient scavenger for mere traces of the halogen acid, and there would also seem to be no reason why other metal oxides could not replace mercuric oxide in this capacity; yet no other is as effective.<sup>7</sup> There is additional evidence pointing to the unfavorability of equilibria of type 7: acyl hypohalites are known to be particularly reactive in electrophilic aromatic substitution, more so than the elemental halogens;<sup>21-24</sup> yet solutions of chlorine and of bromine in acetic acid both halogenate exclusively by way of the elemental halogen.<sup>25,26</sup> This indicates that the concentration of the acetyl hypohalite in such solutions must be vanishingly small, and, on the basis of the above arguments, mechanism A was rejected from further consideration.

To help choose between mechanisms B and C, a series of experiments was carried out on the degradation of valeric, isobutyric, pivalic, and phenylacetic acids. The products of the degradation of the acids with mercury oxide and both bromine and iodine were studied, and the results were compared with the analogous degradations of the silver and the mercuric salts with the same halogens. The results of the study are summarized in Table I.

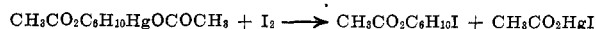
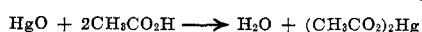
The case in support of mechanism B is the observation by Jennings and Ziebarth that bromine monoxide degrades valeric acid to 1-bromobutane, albeit in a yield inferior to that obtained in the mercury oxide-bromine reaction.<sup>3</sup> In mechanism B the original proposal has been amended by replacing eq 3 by eq 9; this takes account of the fact that more than 0.5 mol of alkyl bromide may be formed per mole of bromine. Several factors suggest that this mechanism is not being followed, however. First, since bromine monoxide is thermally very unstable, it might be expected that the reaction would be more successful at room temperature than at reflux, but such is not the case.

(12) S. J. Cristol, J. R. Douglass, W. C. Firth, and R. E. Krall, *J. Org. Chem.*, **27**, 2711 (1962).

(13) S. J. Cristol, L. K. Gaston, and T. Tiedeman, *ibid.*, **29**, 1279 (1964).

(14) Since the exo/endo ratio of bromides is also markedly dependent on the chain transfer reagent<sup>13</sup> this observation also constitutes indirect evidence for the participation of the acyl hypobromite as an intermediate.

(15) It could be argued that the formation of 2-iodocyclohexyl acetate does not demand the intermediacy of acetyl hypiodite in this reaction, since the mercuration of cyclohexene is an alternative possibility.<sup>16</sup>



Even if this were the case, the substance of the proposal presented below for the degradation mechanism would not be altered, because this sequence of reactions also involves the mercuric carboxylate as a necessary intermediate.

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(17) A. J. Solo and B. Singh, *J. Org. Chem.*, **32**, 567 (1967).

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(21) P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution, Nitration and Halogenation," Butterworths, London, 1959, Chapters 8-10.

(22) Y. Hatanaka, R. M. Keefer, and L. J. Andrews, *J. Amer. Chem. Soc.*, **87**, 4280 (1965).

(23) Y. Ogata and K. Nakajima, *Tetrahedron*, **20**, 43, 2751 (1964).

(24) N. J. Bunce and L. O. Urban, *Can. J. Chem.*, **49**, 821 (1971).

(25) P. W. Robertson, *J. Chem. Soc.*, 1267 (1954).

(26) P. B. D. de la Mare and M. Hassan, *J. Chem. Soc.*, 1519 (1958).

TABLE I  
COMPARISON OF SEVERAL METHODS OF DEGRADATION OF  
CARBOXYLIC ACIDS TO ALKYL HALIDES

Method <sup>a</sup>	—X = Br, reflux—		—X = Br, 25 <sup>b</sup> —		—X = I, reflux—	
	RBr, %	RCO <sub>2</sub> R, %	RBr, %	RCO <sub>2</sub> R, %	RI, %	RCO <sub>2</sub> R, %
Valeric Acid <sup>c</sup>						
HgO/X <sub>2</sub>	63	None	21	None	36	35
Hg <sup>2+</sup> salt/X <sub>2</sub>	81	None	61	None	64	21
Ag <sup>+</sup> salt/X <sub>2</sub> <sup>d</sup>	85	None	73	None	67	33
X <sub>2</sub> O <sup>e</sup>	14	None				
Isobutyric Acid <sup>c</sup>						
HgO/X <sub>2</sub>	47	None	20	None	1 <sup>e</sup>	15
Hg <sup>2+</sup> salt/X <sub>2</sub>	63	None	56	None	<1 <sup>e</sup>	30
Ag <sup>+</sup> salt/X <sub>2</sub> <sup>d</sup>	75	4	77	<1	<1 <sup>e</sup>	80
Pivalic Acid <sup>c</sup>						
HgO/X <sub>2</sub>	<1 <sup>c</sup>	33 <sup>f</sup>				
Hg <sup>2+</sup> salt/X <sub>2</sub>	<1 <sup>c</sup>	18 <sup>f</sup>				
Ag <sup>+</sup> salt/X <sub>2</sub> <sup>d</sup>	<1 <sup>c</sup>	25 <sup>f</sup>				
X <sub>2</sub> O	13 <sup>c</sup>	None <sup>f</sup>				
Phenylacetic Acid <sup>f</sup>						
HgO/X <sub>2</sub>	None	28	<1	4	None	26
Basic Hg <sup>2+</sup> salt/X <sub>2</sub>	4	7	2	2		
Normal Hg <sup>2+</sup> salt/X <sub>2</sub>	34	18	40	None	16	63
Ag <sup>+</sup> salt/X <sub>2</sub> <sup>d</sup>	58	21	26	2	6	73
X <sub>2</sub> O <sup>e</sup>	7	None				

<sup>a</sup> Duplicate reactions on a 2–4 mmol scale in 10 ml of CCl<sub>4</sub> as solvent unless noted otherwise. <sup>b</sup> 25° implies room temperature; this was 25 ± 3°. <sup>c</sup> Products analyzed by vpc. <sup>d</sup> All data on silver salts from ref 27. <sup>e</sup> Solvent was Freon 113. <sup>f</sup> Analyzed by nmr.

Second, analysis of the by-products of the reaction shows that in addition to alkyl halides, the symmetrical esters RCO<sub>2</sub>R are frequently formed. We have previously shown, in silver salt–halogen systems, that esters arise by a route involving the metal salt,<sup>27</sup> and it is hard to envision a pathway to these esters that involves bromine monoxide rather than the metal salt.

The strongest evidence against mechanism B is the observation that, whereas pivalic and phenylacetic acids give no more than traces of alkyl bromide on degradation with bromine and mercury oxide, the bromine monoxide reaction by contrast does afford detectable amounts of these bromides. There would seem to be no reason why all the acids studied should not react similarly if Br<sub>2</sub>O were an intermediate. Particularly compelling is the case of pivalic acid; this acid is virtually impossible to degrade to bromide by a metal salt reaction, because the product is destroyed as it is formed in a rapid reaction with further metal salt.<sup>27</sup> This acid yields only ester on degradation with mercury oxide and bromine; yet, with preformed Br<sub>2</sub>O, *tert*-butyl bromide (but not *tert*-butyl pivalate) is produced. The only previous report of a successful degradation of pivalic acid was also using a salt-free route, halogen exchange between pivalic acid and *tert*-butyl hypoiodite,<sup>28</sup> a process analogous to exchange with Br<sub>2</sub>O. Thus the mercury oxide–bromine reaction, which gives ester but no *tert*-butyl bromide, behaves like a metal salt reaction rather than a positive halogen exchange process.

These arguments lead to the conclusion that mechanism C probably represents the reaction pathway.

(27) N. J. Bunce and N. G. Murray, *Tetrahedron*, **27**, 5323 (1971).

(28) D. H. R. Barton, H. P. Faro, E. P. Serebryakov, and N. F. Woolsey, *J. Chem. Soc.*, 2438 (1965).

There is a strong similarity in product distribution between the mercury oxide–halogen technique and the normal Hunsdiecker reaction using either the mercuric or the silver salts of the acids (the difference between the silver and mercuric salts of phenylacetic acid is taken up below). In favor of this pathway is the ease of reaction at reflux at which temperature bromine monoxide must be very quickly decomposed, and the lack of necessity of postulating the presumably even more unstable iodine monoxide as an intermediate. In control experiments it was found that, whereas mercury oxide and bromine react in solution only very slowly, incompletely, and at low temperature to afford bromine monoxide, the reaction between the oxide and, say, valeric acid to give the mercuric salt is rapid, especially at reflux, and essentially quantitative. It was observed that both the red and the yellow forms of mercury oxide were almost equally effective in promoting salt formation, as also they were in the degradation reaction.<sup>7</sup>

**Effects of Water.**—A curious feature of the mercuric oxide–halogen degradation is its relative insensitivity to moisture. Cristol and Firth were unable to explain this useful insensitivity, but argued on other grounds against a mercury salt pathway, and raised the possibility that a positive halogen intermediate might be involved.<sup>2</sup> Since the arguments above seem to favor the mercury salt route, the two views must be reconciled. The answer appears to lie in the fact that, unlike their silver counterparts, aliphatic mercury carboxylates are freely soluble in hot carbon tetrachloride, the usual reaction medium. Thus the mercury salt and the halogen may interact homogeneously, and in a different phase from the CCl<sub>4</sub>-insoluble water. For the CCl<sub>4</sub>-insoluble silver salts, both the salt and any water present are found at the solvent interface, where reaction with the halogen must occur. In this case the acyl hypohalite is very susceptible to attack by water as it is being formed. The arguments are illustrated for the valeric acid system in Table II.

TABLE II  
INFLUENCE OF WATER ON THE DEGRADATION OF  
VALERIC ACID AND ITS SALTS TO 1-BROMOBUTANE

	RBr from HgO/Br <sub>2</sub> , %	RBr from Hg <sup>2+</sup> salt/Br <sub>2</sub> , %	RBr from Ag <sup>+</sup> salt/Br <sub>2</sub> , %
CCl <sub>4</sub> at Reflux			
Dry	63	81	85
Wet <sup>a</sup>	61	60	17
CCl <sub>4</sub> at 25°			
Dry	21	61	73
Wet <sup>a</sup>	18	17	4
CH <sub>3</sub> CN at Reflux			
Dry	14	42	39
Wet <sup>a</sup>	11	8	2

<sup>a</sup> Added water was in the amount of 0.1 ml (6 mmol) in 10 ml of dry solvent. The reactions were all on a scale of approximately 2 mmol of valerate, and were carried out in duplicate.

From Table II the notable features are (i) the similarity of behavior of the mercury salt and the silver salt in dry solvents; (ii) the similarity between the mercury salt and the mercury oxide system in wet

solvents; and (iii) the insensitivity of the mercury oxide system to added water. These may be explained as follows. In carbon tetrachloride at reflux neither mercury system is strongly influenced by water because the salt is soluble. At room temperature the acyl hypohalite presumably decomposes more slowly<sup>24,29</sup> and so in a wet solvent there is more chance for hydrolysis to occur. Thus the mercury oxide technique, in which water is a by-product, is at a disadvantage at room temperature even in the absence of added water. In acetonitrile, however, all three methods are strongly adversely affected by water because the acyl hypobromite and the water are present in a single phase; once again the mercury oxide method is less successful because of the water formed as a by-product.

**Successful Degradation by HgO-Br<sub>2</sub> Correlated with Salt Formation.**—If mechanism C indeed represents the reaction pathway, there must exist a parallel between those acids which give mercury salts (preferably soluble ones) under the reaction conditions and those that degrade successfully to alkyl halides. This question has been examined for a number of carboxylic acids of different structure with the results summarized in Table III.

TABLE III  
CORRELATION OF BROMIDE FORMATION FROM RCO<sub>2</sub>H-HgO-Br<sub>2</sub> WITH THE PRODUCT OF THE ACTION OF MERCURY OXIDE ON THE ACID

Acid	RBr, %	Hg <sup>2+</sup> Salt	
		Type <sup>a</sup>	Solubility <sup>b</sup>
Valeric	69 <sup>c</sup>	Normal	Soluble
Heptanoic	38 <sup>d</sup>	Normal	Soluble
Nonanoic	70 <sup>d</sup>	Normal	Soluble
Isodecanoic	42 <sup>d</sup>	Normal	Soluble
Isobutyric	47 <sup>c</sup>	Normal	Soluble
2-Ethylhexanoic	53 <sup>d</sup>	Normal	Soluble
Pivalic	<1 <sup>c</sup>	Normal	Soluble
Phenylacetic	<1 <sup>c</sup>	Basic	Insoluble
Benzilic	79 <sup>d,f</sup>	Normal	Soluble
		Basic	Insoluble
Benzoic	14 <sup>c</sup>	Basic	Insoluble
<i>p</i> -Toluic	11 <sup>d</sup>	?	Insoluble
<i>p</i> -Nitrobenzoic	42 <sup>d</sup>	?	Insoluble
<i>o</i> -Nitrobenzoic	58 <sup>d</sup>	Normal <sup>g</sup>	Insoluble
<i>p</i> -Chlorobenzoic	<1 <sup>c</sup>	?	Insoluble
3,5-Dinitrobenzoic	None	No reaction	

<sup>a</sup> Normal (RCO<sub>2</sub>)<sub>2</sub>Hg; basic (RCO<sub>2</sub>)<sub>2</sub>Hg·HgO. <sup>b</sup> In CCl<sub>4</sub>. <sup>c</sup> Estimated by vpc. <sup>d</sup> Isolated material. <sup>e</sup> Estimated by nmr. <sup>f</sup> Product was benzophenone. <sup>g</sup> Probably normal; see Experimental Section.

From Table III may be noted the strong correlation between the acids that form soluble salts and those that degrade successfully. In general the most successful reactions were observed where the carboxyl group of the acid was bonded to aliphatic carbon. The only exceptions in this category were pivalic acid, discussed above, and phenylacetic acid, which forms a very insoluble basic salt. All the other acids in this group form normal salts, whose compositions were confirmed by elemental analysis. In the case of phenylacetic acid the normal salt was prepared by an

alternative route, and was found to behave like the silver salt (Table I). However, the mercury oxide-halogen technique paralleled the behavior of the basic salt, which is formed under these conditions.

In the aromatic series the decarboxylation reaction was less generally successful, and correspondingly, insoluble mercury salts were usually formed. Indeed, because of the limited solubility of acids, salts, and mercury oxide in the reaction medium, it was difficult to isolate pure products from these acid-base reactions, and only one system, benzoic acid, was examined in detail. It was found that mercury oxide and benzoic acid give a basic salt upon refluxing in carbon tetrachloride. This material, (PhCO<sub>2</sub>)<sub>2</sub>Hg·HgO, is formed over a wide range of initial benzoic acid-mercury oxide ratios when benzoic acid is in excess, and has a definite composition and melting point. Treatment of this basic salt with acetone, however, leads to extraction of the normal salt (PhCO<sub>2</sub>)<sub>2</sub>Hg which may be recovered by filtration and removal of the acetone. This experience in the benzoic acid system made it impractical to attempt to separate the insoluble oxide-acid-mercury salt mixtures in the other aromatic series by extraction with solvents, for fear that the composition of these mixtures might be changed as a result. For most of the substituted benzoates it was ascertained simply that mercury-containing organic material had been formed. Interrelations between the mercury(II) benzoates are given in the Experimental Section.

**Conclusions and Synthetic Considerations.**—Comparison of the product distributions from the degradation of several acids by four methods (HgO-RCO<sub>2</sub>H-Br<sub>2</sub>; RCO<sub>2</sub>Ag-Br<sub>2</sub>; (RCO<sub>2</sub>)<sub>2</sub>Hg-Br<sub>2</sub>; RCO<sub>2</sub>H-Br<sub>2</sub>O) and correlation of the success of the first of these with formation of mercuric salts under the same conditions indicate that the reaction pathway involves the formation of a mercury salt of the acid. This is then converted to alkyl halide and/or ester by the route established for the Hunsdiecker and Simonini reactions. From this mechanism the following predictions may be made as to successful synthetic conditions for other systems. (1) The acid should form a mercury salt under the reaction conditions, and this should be soluble in the reaction medium. (2) A water-immiscible solvent should be used. (3) An elevated temperature favors a higher yield of halide. (4) Limitations on the applicability of the Hunsdiecker reaction of the silver or mercury salts apply also to the mercuric oxide technique. Thus tertiary (other than bridgehead)<sup>8</sup> acids do not degrade to halide, and the use of iodine as halogen frequently leads to ester RCO<sub>2</sub>R as the major reaction product.

Although requirement 1 for soluble salt formation excludes many, especially aromatic acids from successful use of the technique, for most aliphatic acids the simplicity of the method and avoidance of separately preparing the metal salt makes it an attractive alternative to the Hunsdiecker reaction. A further point is the ease of recovery of mercuric oxide from the spent mercury residues,<sup>30</sup> which could be an important cost factor in large scale use of the method. It should be noted, however, that the yields of halides are usually smaller than using the silver salt method (compare

(29) W. Bockemüller and F. W. Hoffmann, *Justus Liebigs Ann. Chem.*, **519**, 165 (1935).

(30) G. H. Cady, *Inorg. Syn.*, **5**, 156 (1957).

Table III with published<sup>10</sup> data for the Hunsdiecker reaction).<sup>30a</sup>

### Experimental Section

Solvents were reagent grade materials and were dried using activated molecular sieves. Red and yellow mercuric oxide were obtained from British Drug Houses Ltd.; the organic acids were purchased from the same source or from Aldrich Chemicals Inc. Metal salts were prepared as described below, and were dried at 65° for several days prior to use. Microanalyses were performed by Mr. H. S. McKinnon of this department.

Estimation of products formed was carried out by nmr or vpc after adding a weighed quantity of a suitable standard substance to the reaction mixture. Reactions were carried out in duplicate for these purposes, and three independent analyses were carried out for each reaction mixture. The instruments used were a Varian Associates A-60A nmr, and a Varian Aerograph Model A90-P3 vapor phase chromatograph. Infrared spectra were measured on a Beckman IR-5A instrument.

**Trapping of Acetyl Hypiodite with Cyclohexene.**—To a mixture of red mercuric oxide (2.0 g, 9 mmol) and cyclohexene (2.0 ml, 16 mmol) in glacial acetic acid (20 ml) was added iodine (2.0 g, 8 mmol). The mixture was stirred at room temperature for 0.5 hr, at which time the color of iodine was discharged. A control reaction in which the mercuric oxide was omitted was unreactive. After removal of mercuric iodide by filtration, the reaction mixture was poured into water (150 ml) and extracted with chloroform (four 25-ml portions). The organic phase was washed with sodium bicarbonate and with water and dried. The solvent was evaporated to leave a pale yellow oily residue (2.0 g) of 2-iodocyclohexyl acetate:  $\nu_{\max}$  1735  $\text{cm}^{-1}$  (ester); nmr ( $\text{CCl}_4$ )  $\tau$  4.9–5.5 (1 H, complex multiplet,  $>\text{CHOAc}$ ), 5.7–6.2 (1 H, complex multiplet,  $>\text{CHI}$ ), 8.0 (3 H, singlet,  $\text{CH}_3\text{CO-}$ ), 7.5–9.0 (8 H, complex multiplet, four  $>\text{CH}_2$  groups). A positive test for iodine was obtained.

**Comparative Degradation of Acids by Different Reagents (Table I).**—The following procedures are representative.

**A. Valeric Acid with Iodine and Mercuric Oxide.**—A mixture of red mercuric oxide (2.0 g, 9 mmol), valeric acid (0.418 g, 4.10 mmol), and carbon tetrachloride (12 ml) was heated to reflux, and iodine (0.732 g, 2.89 mmol) was added. Heating continued for 0.5 hr by which time the color of iodine was discharged. 1-Bromobutane (1.03 mmol) was added to the reaction mixture for analysis by vpc (10% SE-30 on acid-washed Chromosorb W, 90°). 1-Iodobutane (1.46 mmol) and *n*-butyl valerate (0.72 mmol) were formed.

**B. Mercury Phenylacetate with Bromine at 25°.**—To a mixture of mercuric phenylacetate (0.694 g, 1.47 mmol) and carbon tetrachloride (10 ml) was added 1.0 ml of a 2.38 *M* solution of bromine in carbon tetrachloride. The mixture was stirred for 2.5 hr, and then 1.0 ml of a 1.19 *M* solution of benzyl chloride in carbon tetrachloride was added. The mixture was evaporated down and the residue was analyzed by nmr. Comparison of the areas of the resonances due to  $\text{PhCH}_2\text{Cl}$  ( $\tau$  5.6) with  $\text{PhCH}_2\text{Br}$  ( $\tau$  5.7) and  $\text{PhCH}_2\text{CO}_2\text{CH}_2\text{Ph}$  ( $\tau$  5.0 and 6.5) indicated that these compounds were formed to the extent of 0.98 and <0.01 mmol, respectively.

**C. Pivalic Acid with Bromine Monoxide.**—To a well-stirred mixture of bromine (5 ml) in dry Freon 113 (100 ml) cooled to 5° was added mercuric oxide (25 g) in 5-g portions at 10-min intervals. After a total reaction time of 1 hr, analysis of aliquots of the mixture<sup>30</sup> showed it to be 0.90 *M* in  $\text{Br}_2$  and 0.11 *M* in  $\text{Br}_2\text{O}$ . A 15-ml aliquot of the  $\text{Br}_2\text{-Br}_2\text{O}$  solution was added to a mixture of pivalic acid (0.111 g, 1.09 mmol) and dry Freon 113 at reflux, and heat was supplied for 10 min. After the addition of 0.138 g (1.0 mmol) of 1-bromobutane, vpc analysis (SE-30, 55°) indicated that 0.14 mmol of *tert*-butyl bromide had been

produced. Removal of the excess bromine and the solvent gave a residue (0.098 g) which on analysis by nmr was found to consist of pivalic acid [ $\tau$  -1.8,  $\text{CO}_2\text{H}$ , and 8.8,  $(\text{CH}_3)_3\text{C}$ ] and to be lacking in *tert*-butyl pivalate ( $\tau$  8.6 and 8.9).

**Influence of Water on the Degradation of Valerate Derivatives (Table II).**—The following procedure is typical. To a mixture of mercuric valerate (0.669 g, 1.66 mmol) in dry acetonitrile to which had been added 1% v/v water (10 ml) was added bromine (2.85 mmol). After heating to reflux for 0.5 hr, isoamyl bromide (1.79 mmol) was added to the cooled solution as a vpc standard. Vpc analysis (SE-30, 90°) indicated that 0.23 mmol of 1-bromobutane had been formed.

**Small-Scale Degradations of Carboxylic Acids (Table III).**—The following procedures are typical.

**A. Heptanoic Acid.**—A mixture of heptanoic acid (5.0 g, 38 mmol), mercuric oxide (11.0 g, 51 mmol), and  $\text{CCl}_4$  (70 ml) was heated to reflux, and a solution of bromine (6.0 g, 37 mmol) in  $\text{CCl}_4$  (10 ml) was added. After 15 min at reflux the mixture was filtered and the filtrate was washed with dilute sodium hydroxide and water, and dried. Removal of the solvent afforded 4.6 g of crude product, an oil, which was distilled to give 1-bromohexane (2.2 g, 38%), bp 154–157° (lit.<sup>31</sup> 156°).

**B. *o*-Nitrobenzoic Acid.**—A mixture of *o*-nitrobenzoic acid (1.0 g, 6 mmol), yellow mercury oxide (2.0 g, 9 mmol), and  $\text{CCl}_4$  (20 ml) was heated to reflux, and bromine (1.0 g, 6.2 mmol) was added. After 3 hr at reflux, the cooled solution was filtered, washed, and evaporated as above to give a residue (0.70 g, 58%) of crude *o*-nitrobromobenzene which solidified on standing, mp 33–36°. Recrystallization from ethanol gave the pure product, mp 39–41° (lit.<sup>31</sup> 43°), whose ir spectrum was consistent with the assigned structure.

**Preparation of Mercury Salts.**—Interaction of the carboxylic acids and mercuric oxide was studied at reflux in  $\text{CCl}_4$ . The products of the reactions were in many cases known compounds, but were subjected to elemental analysis to confirm their constitutions.

**Mercuric Valerate.**—A mixture of yellow mercuric oxide (15 g, 69 mmol) and valeric acid (14 g, 138 mmol) was heated to reflux in  $\text{CCl}_4$  (200 ml) for 2 hr, with the water formed in the reaction being removed by azeotropic distillation with  $\text{CCl}_4$ . The hot solution was filtered [when mercuric oxide (1.9 g) was recovered] and allowed to cool, when mercuric valerate (23.6 g, 85%), mp 93–95°, was obtained. *Anal.* Calcd for  $\text{C}_{10}\text{H}_{18}\text{O}_4\text{Hg}$ : C, 29.81; H, 4.47. Found: C, 29.81; H, 4.54.

Similar procedures were used to prepare the following mercuric carboxylates.

**Mercuric isobutyrate**, mp 103–105°. *Anal.* Calcd for  $\text{C}_5\text{H}_8\text{O}_4\text{Hg}$ : C, 25.60; H, 3.73. Found: C, 25.67; H, 3.89.

**Mercuric pivalate**, mp 234–236°. *Anal.* Calcd for  $\text{C}_{10}\text{H}_{18}\text{O}_4\text{Hg}$ : C, 29.81; H, 4.47. Found: C, 29.75; H, 4.65.

**Mercuric heptanoate**, mp 106–108°. *Anal.* Calcd for  $\text{C}_{14}\text{H}_{26}\text{O}_4\text{Hg}$ : C, 36.6; H, 5.66. Found: C, 36.69; H, 5.75.

**Mercuric 2-ethylhexanoate**, mp 66–71°. *Anal.* Calcd for  $\text{C}_{16}\text{H}_{30}\text{O}_4\text{Hg}$ : C, 39.45; H, 6.16. Found: C, 39.77; H, 6.43.

**Mercuric nonanoate**, mp 106–108°. *Anal.* Calcd for  $\text{C}_{18}\text{H}_{34}\text{O}_4\text{Hg}$ : C, 41.95; H, 6.60. Found: C, 42.57; H, 6.69.

**Mercuric isodecanoate (oil) and mercuric benzilate**, mp 66–70° dec, could not be freed completely from the parent acid, and were not obtained analytically pure. In the case of the reaction of benzilic acid with mercuric oxide, the insoluble basic salt was also obtained, mp 188–195° dec. *Anal.* Calcd for  $\text{C}_{28}\text{H}_{52}\text{O}_7\text{Hg}_2$ : C, 38.5; H, 2.53. Found: C, 38.87; H, 2.49.

A similar preparative procedure applied to other acids gave basic salts as follows. These compounds were generally very insoluble, and gave rather less satisfactory elemental analyses.

**Basic mercury phenylacetate**,  $(\text{PhCH}_2\text{CO}_2)_2\text{Hg} \cdot \text{HgO}$ , mp 200–205°. *Anal.* Calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_5\text{Hg}_2$ : C, 27.9; H, 2.03. Found: C, 29.72, 30.01; H, 1.82, 1.85. The normal salt,  $(\text{PhCH}_2\text{CO}_2)_2\text{Hg}$ , mp 115–118°, was prepared alternatively by the action of a solution of mercuric nitrate in nitric acid on an aqueous solution of sodium phenylacetate which had been made neutral to litmus using dilute nitric acid. *Anal.* Calcd for  $\text{C}_{16}\text{H}_{14}\text{O}_4\text{Hg}$ : C, 40.7; H, 2.97. Found: C, 40.81; H, 2.88.

**Basic mercuric benzoate**  $(\text{PhCO}_2)_2\text{Hg} \cdot \text{HgO}$ , mp 171–172°. *Anal.* Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_5\text{Hg}_2$ : C, 25.5; H, 1.52. Found:

(30a) NOTE ADDED IN PROOF.—The results quoted in the tables were all obtained using equimolar amounts of  $\text{Br}_2$  and  $\text{RCO}_2\text{H}$ . Improved yields of alkyl bromides may be obtained by increasing the mole ratio of  $\text{Br}_2$  to 1.1 or 1.2; this probably offsets hydrolysis of  $\text{RCO}_2\text{Br}$  by the by-product water. For larger scale preparations the technique of J. Cason and D. M. Walba [*J. Org. Chem.*, **37**, 669 (1972)] in which the water formed is removed continuously by azeotropic distillation with solvent, would probably be most advantageous. These authors have come to similar conclusions regarding the probable mechanism of the  $\text{RCO}_2\text{H-HgO-Br}_2$  reaction. The present author thanks Professor Cason for making available his results prior to publication.

(31) "Handbook of Chemistry and Physics," 49th ed, Chemical Rubber Co., Cleveland, Ohio, 1968.

C, 26.16; H, 1.54. (Another sample, Found: C, 24.24; H, 1.50.) Extraction of this material with acetone followed by filtration to remove mercuric oxide and evaporation of the solvent afforded the normal salt,  $(\text{PhCO}_2)_2\text{Hg}$ , mp 118–122°. *Anal.* Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_4\text{Hg}$ : C, 38.0; H, 2.26. Found: C, 39.07; H, 2.50. Another sample had mp 120–129°. Found: C, 38.38; H, 2.39. When aqueous acetone was used as the extraction agent, the product was mainly mercuric benzoate monohydrate, mp 140–149°. *Anal.* Calcd for  $\text{C}_{14}\text{H}_{12}\text{O}_5\text{Hg}$ : C, 36.4; H, 2.60. Found: C, 36.26; H, 2.21.

**Mercuric benzoate monohydrate** was formed by interaction of aqueous mercuric nitrate and sodium benzoate solutions, mp 161–163° (lit.<sup>11</sup> 165°). *Anal.* Calcd for  $\text{C}_{14}\text{H}_{12}\text{O}_5\text{Hg}$ : C, 36.4; H, 2.60. Found: C, 36.52; H, 2.21. An attempt to obtain the anhydrous salt by azeotropic distillation of the water with  $\text{CCl}_4$  was unsuccessful.

**Hydrolysis of Hydrated Mercuric Benzoate.**—Suspension of hydrated mercuric benzoate (3.0 g) in boiling water (100 ml) for 1 hr gave an off-white solid (2.1 g, mp >360°) which analyzed for a basic mercuric salt  $(\text{PhCO}_2)_2\text{Hg} \cdot 2\text{HgO}$ . *Anal.* Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_6\text{Hg}_3$ : C, 19.2; H, 1.14. Found: C, 18.87; H, 1.07.

**Hydrolysis of Basic Mercuric Benzoate.**—Suspension of  $(\text{PhCO}_2)_2\text{Hg} \cdot \text{HgO}$  (1.0 g) in boiling water caused hydrolysis to occur. The orange product (0.7 g) analyzed for  $(\text{PhCO}_2)_2\text{Hg} \cdot 3\text{HgO}$  (*Anal.* Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_7\text{Hg}_4$ : C, 15.34; H, 0.91. Found: C, 14.60; H, 0.89.) but was apparently a mixture of starting material and mercuric oxide, mp 170–172°, undepressed by admixture with starting material. On cooling the filtered reaction mixture a small quantity (0.08 g) of hydrated mercuric benzoate was obtained, mp 161–165°. (Found: C, 36.18; H, 2.27.)

**Basic (?) Mercuric *o*-Nitrobenzoate.**—Interaction of *o*-nitrobenzoic acid and mercuric oxide in either  $\text{CCl}_4$  or  $\text{CHCl}_3$  gave, in addition to unreacted *o*-nitrobenzoic acid in solution and mercury oxide at the bottom of the flask, a yellow powder in suspension. The solution was decanted and the yellow powder was removed by filtration, mp 195–197° dec. Analysis indicated the composition  $3(\text{ArCO}_2)_2\text{Hg} \cdot \text{HgO}$ , but it is unclear whether the substance is a compound of this composition or is the normal salt, contaminated with mercuric oxide. (*Anal.* Calcd for  $\text{C}_{42}\text{H}_{24}\text{N}_6\text{O}_{25}\text{Hg}_4$ : C, 27.8; H, 1.32; N, 4.62. Found: C, 28.24; H, 1.26; N, 4.61.)

**Registry No.**—Mercuric oxide, 21908-53-2; 2-iodocyclohexyl acetate, 32865-61-5; mercuric valerate, 26719-05-1; mercuric isobutyrate, 19348-33-5; mercuric pivalate, 32276-77-0; mercuric heptanoate, 26719-06-2; mercuric 2-ethylhexanoate, 13170-76-8; mercuric nonanoate, 28043-55-2; mercuric benzilate, 32865-67-1; mercuric benzilate basic salt, 32839-01-3;  $(\text{PhCH}_2\text{CO}_2)_2\text{Hg} \cdot \text{HgO}$ , 32839-02-4;  $(\text{PhCH}_2\text{CO}_2)_2\text{Hg}$ , 14085-69-9;  $(\text{PhCO}_2)_2\text{Hg} \cdot \text{HgO}$ , 32839-03-5;  $(\text{PhCO}_2)_2\text{Hg}$ , 583-15-3; mercuric benzoate monohydrate, 32839-04-6;  $(\text{PhCO}_2)_2\text{Hg} \cdot 2\text{HgO}$ , 32839-05-7;  $3(\text{ArCO}_2)_2\text{Hg} \cdot \text{HgO}$  (Ar = *o*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>), 32839-06-8.

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## Notes

### Reaction Pathway in the Modified Hunsdiecker Reaction

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During the period since Cristol and Firth<sup>1</sup> published a simplified modification of the Hunsdiecker reaction for synthesis of bromides from carboxylic acid silver salts, the modified procedure, which utilizes a free carboxylic acid and mercuric oxide, has been used to advantage in several published investigations. The specific conditions employed in the published procedures have been rather diverse, as have the yields. In the initial report,<sup>1</sup> among the reactions carried out in boiling carbon tetrachloride solution was synthesis of heptadecyl bromide in 90% yield (crude) from stearic acid. In contrast, the "Organic Syntheses" procedure,<sup>2</sup> appearing subsequently, reported about 50% yield of cyclopropyl bromide, with tetrachloroethane as solvent at a temperature of 30–35°. In a procedure similar to that originally reported,<sup>1</sup> except that the acid and bromine were added concurrently to a boiling slurry of mercuric oxide in carbon tetrachloride, about 50%

yield was again realized for a small-ring bromide;<sup>3</sup> however, this same procedure applied to the half-ester of an open-chain dicarboxylic acid has given 90% yield of bromo ester.<sup>4</sup>

Since the literature provides little evidence concerning the mechanism of the modified Hunsdiecker reaction, or the best way in which to carry out the synthesis, we have investigated its application to myristic acid. Our considerable and varied experience<sup>5</sup> with the classical Hunsdiecker reaction suggested that most of the difficulties are likely to be encountered with a moderately high molecular weight aliphatic structure. To this end, there was examined a procedure for tridecyl bromide which was based on the original successful method,<sup>1</sup> with some modification in recognition of the "Organic Syntheses" procedure.<sup>2</sup> Subsequent investigations revealed that the most important modification was operation at 25–30° rather than in boiling carbon tetrachloride. In 15 runs by different people,<sup>6</sup> the highest yield was about 5% (cf. Table I, run 4).

(3) K. B. Wiberg and G. M. Lampmann, *J. Amer. Chem. Soc.*, **88**, 4432 (1966).

(4) John I. Crowley, Ph.D. Dissertation, University of California, Berkeley, 1971.

(5) See, *inter alia*, J. Cason and R. L. Way, *J. Org. Chem.*, **14**, 31 (1949); J. Cason and R. H. Mills, *J. Amer. Chem. Soc.*, **73**, 1354 (1951); J. Cason, M. J. Kalm, and R. H. Mills, *J. Org. Chem.*, **18**, 1670 (1953); J. Cason and M. J. Kalm *ibid.*, **19**, 1836 (1954).

(6) For several specific procedures, multiple runs were carried out by students in the advanced organic laboratory course at Berkeley. Of particular value was the work of Richard P. Fisher, Howard B. Gamper, Maria del Carmen Kutas, Ronald M. Rodehorst, and Thomas M. Yarnell.

(1) S. J. Cristol and W. C. Firth, Jr., *J. Org. Chem.*, **26**, 280 (1961).

(2) J. S. Meek and D. T. Osuga, *Org. Syn.*, **43**, 9 (1963).