Mercury(II) Acetate-assisted Oxidative Hydrolysis of Thiosemicarbazones of Benzaldehyde, Acetophenone and Benzophenone by Potassium Bromate

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Thiosemicarbazones of benzaldehydes, acetophenones and benzophenones are oxidatively hydrolysed by potassium bromate, {Br^V}, in the presence of mercury(II) acetate, as Hg^{II} forms a complex with sulphur atoms, increasing the lability of the N–H bond. The rates of these reactions are less susceptible to the electronic influence of the substituents at the phenyl ring compared with other oxidants, showing that *N*-bromate ester formation is the rate-determining step of this reaction. Such *N*-bromate ester formation seems to occur more readily with Hg^{II}-sulphur complexes.

Although the reaction of thallium triacetate with semicarbazones of acetophenone and substituted acetophenones yielded the carbonyl compound in ~65–90% yield after long reflux times together with an acylated by-product,[1] with (substituted) benzaldehyde semicarbazones the respective aldehydes were regenerated by the same oxidant in ~90% yield at ambient temperature.[2] Among the non-metal oxidants, potassium bromate seems to be a better choice for a simple regeneration of carbonyl compounds from semicarbazones.[3] The present work describes another method of oxidative hydrolysis of thiosemicarbazones of benzaldehydes, acetophenones and benzophenones under mild conditions by using potassium bromate (Br^V), yielding the respective carbonyl compound in ~80% yield at ambient temperature. Under identical conditions, Br^V reactions with thiosemicarbazones proceed faster (20- to 30-times) than those with the corresponding semicarbazones, facilitating the regeneration of carbonyl compounds.

Results and Discussions

Table 1 summarises the kinetic data of the potassium bromate oxidation of benzaldehyde, acetophenone and benzophenone thiosemicarbazones in 50% aq. acetic acid with 0.20 mol dm^{-3} $HClO_4$ at 31 ± 0.2 °C, in the presence of 0.010 mol dm^{-3} $Hg(OAc)_2$. The added $Hg(OAc)_2$ removes Br^- (one of the products of the reaction) as a complex, so that the Br^V reaction, unhindered by the presence of Br_2, can be studied.[4] The reaction exhibits total second-order kinetics—first order with respect to both thiosemicarbazone and Br^V. Hence the rate law for the reaction is given by eqn. (1). The rate of Br^V oxidation of a thiosemicarbazone is unaffected by increasing concentration of $HClO_4$ at constant ionic strength. Perhaps protonation of the substrate does not occur in the slow step, and the non-protonated form may be the reactive species.

$$\frac{-d[Br^V]}{dt} = k_2[Br^V][\text{thiosemicarbazone}] \qquad (1)$$

In the Br^V oxidation of benzaldehyde/acetophenone semicarbazone, for an increase in concentration of $Hg(OAc)_2$ from 5.0×10^{-3} to 40×10^{-3} mol dm^{-3}, the increase in rate is only *ca.* 40%, while in the Br^V oxidation of benzaldehyde/acetophenone thiosemicarbazone for a change in concentration of $Hg(OAc)_2$ from 0.010 to 0.015 mol dm^{-3} there is an abnormal increase in rate to the extent of 15- to 27-times (Table 1). A similar rate enhancement, due to added $Hg(OAc)_2$ at a concentration 0.030 mol dm^{-3}, has been observed even at 1.0 mol dm^{-3} $HClO_4$. It has been reported that an N–Hg^{II} complex is formed when $Hg(OAc)_2$ is refluxed with semicarbazones at 50–60 °C for 2 h.[5] Under the reaction conditions, the percentage of such an N–Hg^{II} complex formed may be low and that may not be the reason for the observed abnormal increase in rate. With thiosemicarbazones, the Hg^{II} salt forms a complex both at the sulphur atom and at the imino nitrogen,[6] the former possibly being more strongly bound than the latter. In 0.20 mol dm^{-3} $HClO_4$ a yellow precipitate is formed when 0.030 mol dm^{-3} $Hg(OAc)_2$ is used and the yellow precipitate accounts for all the Hg^{II}. This precipitate may possibly be an =S–Hg^{II} complex of the thiosemicarbazone. Such an =S–Hg^{II} complex does not precipitate at 1.0 mol dm^{-3} $HClO_4$ with 0.030 mol dm^{-3} $Hg(OAc)_2$, as the solubility of such an =S–Hg^{II} complex may be increased in 1.0 mol dm^{-3} $HClO_4$. Such a sulphur-bound Hg^{II} complex seems to facilitate *N*-bromate ester formation and hence increases the rate of the reaction.

The formation of such an Hg^{II}-bound thiosemicarbazone complex is evidenced spectrophotometrically, when the Hg^{II} solution is mixed with the thiosemicarbazone. A highly absorbing species is observed spectrophotometrically (such a species is not observed in an Hg^{II}–semicarbazone solution).

Substituent Effect.—The rate of Br^V oxidation of the thiosemicarbazones of benzaldehyde, acetophenone and benzophenone is less sensitive to the substituent in the phenyl ring compared with other oxidants (Table 2). Even the introduction of a strongly electron-withdrawing group such as *p*-NO_2 and an electron-donating group such as *p*-Me has little effect on the rate of reaction (Table 2). As the reactivity of the thiosemicarbazone of benzaldehyde is comparable to that of acetophenone/benzophenone thiosemicarbazone with no α-C–H bond, possibly the α-C–H bond of benzaldehyde thiosemicarbazone is not involved in the slow step of the reaction. The formation of the respective aldehyde/ketone as the product in considerable yield is also in favour of such a reaction sequence.

Under the same reaction conditions, the thiosemicarbazone seems to undergo oxidation faster than does the corresponding semicarbazone (Table 2), since the (postulated) Hg^{II} complex with the sulphur of the thiosemicarbazone seems to enhance the activity of the N–H bond, facilitating its reaction with bromate.

Mechanism.—As the rates of Br^V oxidation of thiosemicarbazones of benzaldehydes, acetophenones and benzophenones are insensitive to substituent effects and yield the respective aldehydes and ketones, a reaction sequence involving

Table 1 Kinetic data for Br^V oxidation of thiosemicarbazones[a]

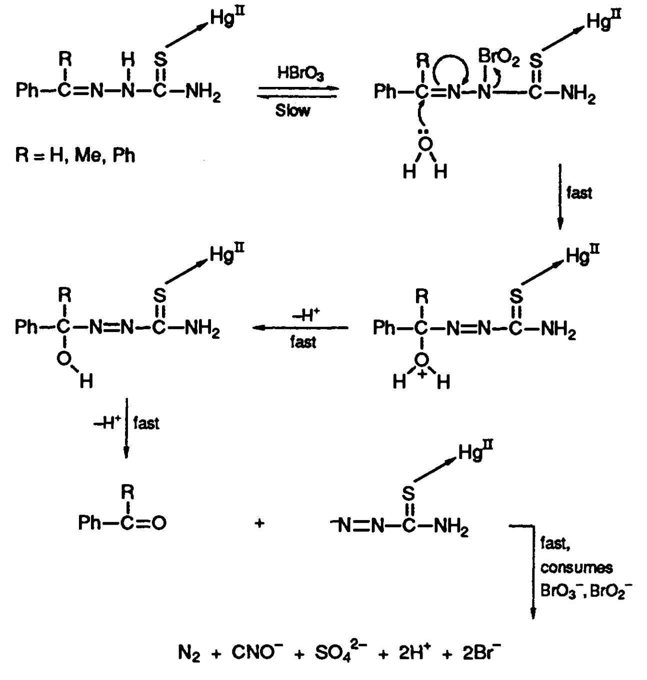
R^1	R^2	$10^3[R_2C_6H_4\text{-}\overset{R^1}{C}{=}N\text{-}\overset{H}{N}\text{-}\overset{S}{\overset{\|}{C}}\text{-}NH_2]$/ mol dm^{-3}	$10^4[Br^V]$/mol dm^{-3}	$10^3\,k_1/s^{-1}$[b]	k_2/dm^3 mol^{-1} s^{-1}
H	H	5.0	5.0	0.95	0.190
		5.0	10.0	1.09	0.22
		10.0	5.0	1.93	0.193
		20.0	20.0	3.8	0.19
		5.0	5.0	1.14	0.23[c]
		5.0	5.0	1.06	0.21[d]
		5.0	5.0	1.02	0.20[e]
		5.0	5.0	1.034	0.21[f]
		5.0	5.0	1.046	0.21[g]
		5.0	5.0	1.050	0.21[h]
		5.0	5.0	15.0	3.0[i]
		5.0	5.0	19.0	3.8[j]
Me	H	5.0	5.0	1.40	0.28
		5.0	10.0	1.40	0.28
		10.0	5.0	2.7	0.27
		5.0	5.0	1.50	0.30[c]
		5.0	5.0	1.60	0.32[d]
		5.0	5.0	44	8.8[i]
Ph	H	5.0	5.0	1.60	0.32
		5.0	10.0	1.60	0.32
		10.0	5.0	3.2	0.32

[a] Reactions were carried out at 31 ± 0.2 °C in 50% aq. acetic acid and 0.20 mol dm^{-3} $HClO_4$ in the presence of 0.010 mol dm^{-3} $Hg(OAc)_2$ unless otherwise mentioned. [b] $-d\ln[Br^V]/dt = k_1$ (s^{-1}). [c] In 0.10 mol dm^{-3} $HClO_4$ at an ionic strength of 0.20 mol dm^{-3}. [d] In 0.050 mol dm^{-3} $HClO_4$ at constant ionic strength of 0.20 mol dm^{-3}. [e] In 0.1 mol dm^{-3} $HClO_4$ at an ionic strength of 1.0 mol dm^{-3}. [f] In 0.40 mol dm^{-3} $HClO_4$ at an ionic strength of 1.0 mol dm^{-3}. [g] In 0.80 mol dm^{-3} $HClO_4$ at an ionic strength of 1.0 mol dm^{-3}. [h] In 1,0 mol dm^{-3} $HClO_4$ at an ionic strength of 1.0 mol dm^{-3}. [i] In 0.015 mol dm^{-3} $Hg(OAc)_2$. [j] In 0.020 mol dm^{-3} $Hg(OAc)_2$.

Table 2 Substituent effect on the rate of Br^V oxidation of thiosemicarbazones[a,b]

$R^2C_6H_4\text{-}\overset{R^1}{C}{=}N\text{-}\overset{H}{N}\text{-}\overset{S}{\overset{\|}{C}}\text{-}NH_2$		k_2/dm^3 mol^{-1} s^{-1}	k_2/dm^3 mol^{-1} s^{-1}[c]
R^1	R^2		
H	H	0.19	(0.0062)
H	*p*-Me	0.22	(0.0068)
H	*p*-Cl	0.24	(0.0055)
H	*o*-NO_2	0.36	(0.0048)
Me	H	0.28	(0.0098)
Me	*p*-Cl	0.27	(0.0089)
Me	*p*-Me	0.27	(0.0101)
Me	*m*-NO_2	0.42	
Ph	H	0.32	(0.0048)
Ph	*p*-Me	0.31	
Ph	*p*-NO_2	0.44	
Ph	*m*-NO_2	0.42	

[a] Reactions were carried out in 50% aq. acetic acid in 0.20 mol dm^{-3} $HClO_4$ and 0.010 mol dm^{-3} $Hg(OAc)_2$ with initial concentration of reactants, $[Br^V] = 5.0 \times 10^{-4}$ mol dm^{-3} and [substrate] = 5.0×10^{-3} mol dm^{-3}. [b] The specific rate for the Br^V oxidation of the thiosemicarbazide is 1.12 dm^3 mol^{-1} s^{-1} under identical conditions. [c] The specific rates for the Br^V oxidation of the respective semicarbazones under identical conditions are given in parentheses.



Scheme 1

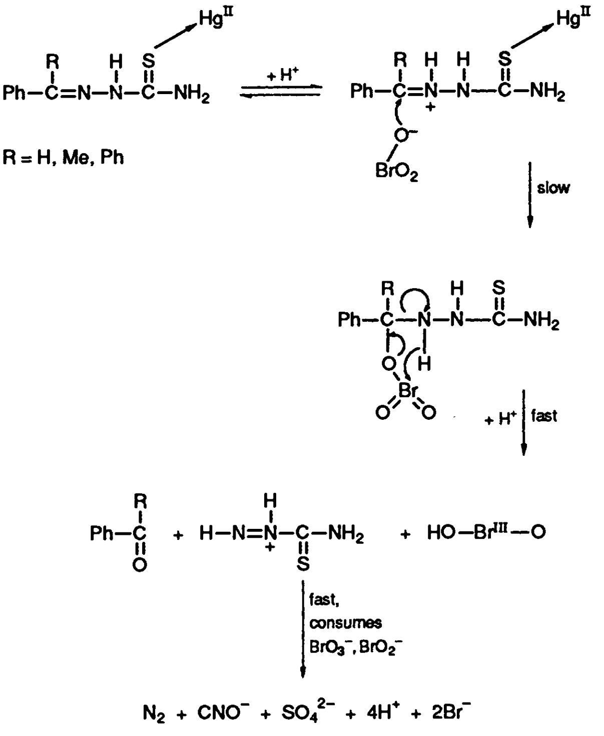
N-bromate ester formation in a slow step has been considered in Scheme 1. The rate of formation of such an *N*-bromate ester is generally unaffected by ring substituents.[7] As mercury(II) acetate forms a stable complex with sulphur, it may increase the acid strength of the N–H bond, facilitating *N*-bromate ester formation and hence enhancing the rate of the reaction. The specific rates for the Br^V oxidation of thiosemicarbazones of benzaldehyde, acetophenone and benzophenone are comparable, and this rules out the participation of an α-C–H bond of benzaldehyde in the rate-determining step.

Alternatively, it is possible that BrO_3^- can add on to the C=N bond of thiosemicarbazone, followed by electron transfer to Br^V in a subsequent step as given in Scheme 2. This may result in the ultimate formation of the respective carbonyl compound. In such a case, electron-withdrawing groups such as *m*-NO_2 should favour the nucleophilic attack by BrO_3^- while electron-releasing groups such as *p*-Me should retard the rate (which is not observed). Also, *ortho* substituents such as *o*-NO_2 do not exert any steric influence on the rate of the reaction. These observations are in favour of Scheme 1, *i.e.* *N*-bromate ester formation is the rate-determining step. Both schemes can account for 11–12 equivalents of Br^V consumed by one equivalent of thiosemicarbazone.

Table 3 Stoichiometric data in the Br^V oxidation of thiosemicarbazones[a]

$10^5[\mathrm{Ph{-}\overset{R}{\overset{\vert}{C}}{=}N{-}\overset{H}{\overset{\vert}{N}}{-}\overset{S}{\overset{\Vert}{C}}{-}NH_2}]$/ mol dm^{-3}		$10^4[Br^V]$/ mol dm^{-3} (initial)	$10^4[Br^V]$/ mol dm^{-3} (final)	$10^4\Delta[Br^V]$/ mol dm^{-3} [b]	$\frac{\Delta[Br^V]}{[\text{substrate}]}$	$10^5[\mathrm{-\overset{O}{\overset{\Vert}{C}}-}]$/ mol dm^{-3}
R = H	6.5	18.7	17.3	1.40	2.1	4.4(68)
	10.0	18.7	17.0	1.70	1.70	7.0(70)
	20.0	18.7	15.1	3.6	1.8	13.4(67)
R = Me	7.0	18.7	15.0	1.5	2.1	5.7(82)
	10.0	18.7	16.6	2.1	2.1	8.4(84)
	20.0	18.7	17.2	3.7	1.85	16.4(82)
R = Ph	7.0	18.7	17.2	1.50	2.1	5.7(82)
	10.0	18.7	16.6	2.1	2.1	8.4(84)
	20.0	18.7	15.0	3.7	1.85	16.4(82)

[a] These reactions were carried out in 50% aq. acetic acid in 0.20 mol dm^{-3} $HClO_4$ and 0.010 mol dm^{-3} $Hg(OAc)_2$ at 31 ± 0.2 °C. [b] The change in concentration of Br^V due to its reaction with thiosemicarbazone was calculated after applying due blank corrections for self-decomposition/disproportionation of Br^V at this concentration, which comes to nearly 6.5% of $[Br^V]_{initial}$. The yield of carbonyl compounds by the Br^V reaction with thiosemicarbazones is of the same order as that observed in Br^V reaction with semicarbazones.[3]



Scheme 2

Experimental

The benzaldehydes, acetophenones and benzophenones used for the preparation of the thiosemicarbazones were extrapure (Fluka AG and K-Aldrich) and the corresponding thiosemicarbazones were prepared by a procedure similar to that used for the corresponding semicarbazones.[8] Potassium bromate, perchloric acid, acetic acid and mercury(II) acetate were of reagent grade (BDH).

The rate of disappearance of Br^V was followed iodimetrically[9a] to a starch end-point. The specific rates evaluated using integrated rate equations from duplicate runs agreed to within ±7%, and these values were also in agreement with those obtained from graphs of the logarithm of change in bromate concentration *versus* time.

Product Analysis and Stoichiometry.—To a thiosemicarbazone dissolved in 50% aq. acetic acid at 31 ± 0.2 °C in 0.20 mol dm^{-3} $HClO_4$ was added a solution of potassium bromate (~1–2 mmol) in 50% aq. acetic acid was added. After *ca.* 9 half-lives, the mixture was diluted with an equal volume of ice-water and extracted with $CHCl_3$, in three portions. Extracts were dried ($MgSO_4$), then filtered, and acetic acid was neutralised with saturated aq. $NaHCO_3$. The organic product was extracted (Et_2O) and, from UV and IR spectra, was identified as the corresponding aldehyde or ketone. The amount of benzaldehyde, acetophenone or benzophenone formed was determined by measurement of the absorbance of the ethereal extracts at 250 (ε = 11 400 dm^3 mol^{-1} cm^{-1}), 246 (12 600) or 257 (18 500)[10,11] nm respectively. The other products (sulphate and cyanate) were detected by standard tests,[12] and sulphate was quantitatively estimated by gravimetric procedure.[9b]

The stoichiometric results are summarised in Table 3. The yield of benzaldehyde is only 70% as it is partly oxidised to benzoic acid under the reaction conditions. As Br^V does not oxidise ketones under these conditions, the yield of acetophenone or benzophenone is ~80%.

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