[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF FURMAN UNIVERSITY]

Effect of Iodine as Carrier on the Rates of Dark Room Bromination of Condensed Ring Compounds[1]

BY JOHN R. SAMPEY, ANNE B. KING AND JESSIE M. COX

The enhanced effect of iodine as carrier in the bromination of fluorene[2] has been extended to determine the carrier effect in the dark room bromination of other condensed ring compounds. Since iodine acts as such a rapid carrier, the usual potassium iodide method for determining the extent of the bromination could not be employed; a standard solution of sodium sulfite has been used to stop the bromination, and the excess sulfite has been titrated with a standard iodine solution. The results with the sodium sulfite solutions have been compared with those from sodium iodide analyses described in a previous communication.[3]

Experimental

Development of a Sodium Sulfite Method of Analysis.—Bunsen[4] was the first to carry out the titration of sulfite with iodine. In our procedure we found a sharp end-point was produced when a molar sodium sulfite solution was shaken in a glass-stoppered Erlenmeyer flask with a known concentration of bromine dissolved in carbon tetrachloride, and the excess sulfite was titrated with a standard iodine solution. In order to decrease the pressure of sulfur dioxide in the flask, one mole of sodium acetate was added to the sulfite solution. The ease of oxidation of this sulfite solution by atmospheric oxygen was checked: when 10.00 ml. of the molar sulfite–acetate solution was shaken vigorously for forty-five seconds in a glass-stoppered flask, from 0.3 to 0.6% of the sulfite was oxidized; on shaking for ninety seconds, there was 1.0% oxidation. When the temperature was raised to 41° (that used later in some brominations), the amount of oxidation was 2.0 to 2.5% in forty-five seconds; the addition of carbon tetrachloride increased the rate of atmospheric oxidation to 2.5 to 3.5% with forty-five seconds of vigorous shaking. The molar sodium sulfite–sodium acetate solution was stable when not shaken; standard solutions have been kept for weeks. By reducing the agitation to a minimum the sulfite titration gave a rapid method of determining the rates of bromination which was sufficiently accurate for the purposes of the present investigation.

As a further check on the values of the sodium sulfite analyses, samples of fluorene were brominated photochemically, and after the sulfite titrations, the carbon tetrachloride layers were washed with water to remove inorganic bromides, and the carbon tetrachloride evaporated, the residue dried, and then dissolved in a saturated sodium iodide-acetone solution; the precipitated sodium bromide was analyzed as described previously.[3]

Two comparisons with the solution at 3 in. distance from the lamp gave in a four-minute exposure 72 and 72% photobromination by the sodium sulfite method and 70 and 71% by the sodium iodide method of analysis. Two other comparisons at a distance of 1 in. gave in two minutes 76 and 76, and 76 and 75% bromination, respectively, by the two methods. Two further comparisons at 3 and 6 in. distance gave in three minutes 66 and 44, and 62 and 43% bromination, respectively. It is evident, therefore, that the two methods give closely checking results.

Rates of Dark Room Bromination.—Brominations were carried out at constant temperature in an Erlenmeyer flask fitted with a short ground-glass condenser closed with a calcium chloride tube in a darkened laboratory. To 0.01 mole of the hydrocarbon in 20.00 ml. of the carbon tetrachloride, 0.01 mole of bromine in 20.00 ml. of the same solvent was added. The reaction was stopped by the addition of 15.00 ml. of standard sodium sulfite solution and the amount of bromination was determined by titration of the excess sulfite with iodine solution. After a sixty minute-period of reaction the following percentage brominations were obtained: *fluorene*, 51 ± 5, *phenanthrene*, 26 ± 1, *diphenylmethane*, 18 ± 1, and *naphthalene*, 4 ± 1. No bromination was obtained under these conditions with toluene, diphenyl- or triphenylmethane.

Carrier Effect of Iodine.—To 0.01 mole of the condensed ring compound in 10.00 ml. carbon tetrachloride and 10.00 ml. of a saturated solution of iodine in the same solvent in a darkened laboratory at 41°, there was added 10.00 ml. of molar bromine–carbon tetrachloride solution; the reaction was stopped and the extent of the bromination determined by the sulfite titration method, a correction being made for the iodine added as carrier; titration of the iodine in the 10.00 ml. of saturated iodine solution showed 0.2899 g. of iodine present. For further study three other concentrations of iodine were prepared by diluting the saturated solution one to ten, one to one hundred, and one to one thousand with the same solvent.

TABLE I

CARRIER EFFECT OF IODINE ON DARK ROOM BROMINATION IN CCl_4, 41°

I_2 concn. =	0.2899		0.0289		0.0029		0.0003	
	Time, min.	%	Time, min.	%	Time, min.	%	Time, min.	%
Fluorene	1	77 ± 1	10	50 ± 2	60	84	20	29 ± 1
Phenanthrene	1	66 ± 1	20	54 ± 2	20	21 ± 2	20	15 ± 1
Naphthalene	20	81 ± 2	60	21 ± 1	60	4	..	....
Diphenyl	60	21 ± 1	60	1 ± 1	..	....	..	....
Triphenylmethane	60	12 ± 1	60	1 ± 1	..	....	..	....
Diphenylmethane	60	7 ± 1	60	6	60	4	..	....
Toluene	60	6 ± 1	60	0	..	....	..	....

All the above compounds show marked increased rates of bromination under the influence of iodine, except diphenylmethane. The several substances have been listed in the decreasing order of the rapidity of their bromination in the presence of iodine, and the results show an enormous decrease in the rapidity as, for instance,

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(1) Presented before the Division of Organic Chemistry at the 114th A. C. S. Meeting, Washington, August 30, 1948.

(2) J. R Sampey and A. B. King, THIS JOURNAL, **70**, 2606 (1948).

(3) J. R. Sampey, B. C. Blitch and A. B. King, *ibid.*, **70**, 2606 (1948)

(4) Bunsen, *Ann.*, **86**, 265 (1853).

between fluorene on the one hand and toluene on the other.

Since anthracene is insoluble in carbon tetrachloride a series of experiments was made in carbon disulfide. Only 0.005 mole of the hydrocarbon is dissolved in 50.00 ml. of carbon disulfide, and the previous experimental procedure repeated at 26°. To make the iodine effects comparable, iodine–carbon disulfide solutions were prepared containing the same amount of iodine as in Table I. Only 0.005 mole of fluorene in 50.00 ml. of solvent was used also.

TABLE II

CARRIER EFFECT OF IODINE ON DARK ROOM BROMINATION IN CS_2, 26°

I_2 concn. =	0.290		0.029		0.000	
	Time, min.	%	Time, min.	%	Time, min.	%
Fluorene	10	31 ± 2	10	5 ± 1	60	6 ± 2
Anthracene	1	76 ± 1	..	...	1	60 ± 1

Anthracene is so rapidly brominated even in the absence of iodine that it is possible to determine only from Table II that the effect is positive.

In a final series of brominations when the experiments were run overnight in a darkened laboratory at room temperature with and without iodine in carbon tetrachloride solution, the results were as follows: In the absence of iodine there was no perceptible bromination with toluene, dibenzyl, fluorenone, 9,10-anthraquinone and 2-methyl-9,10-anthraquinone; in the presence of iodine toluene showed a bromination of 55, dibenzyl, 51, and fluorenone, 5%, respectively, while the others were unaffected.

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Summary

1. An approximate method has been developed for measuring the rate of bromination of condensed ring compounds, using standard sodium sulfite solution.

2. Rates of dark room bromination, both with and without iodine as carrier, have been measured for the following compounds: fluorene, fluorenone, naphthalene, anthracene, phenanthrene, dibenzyl, diphenyl, diphenylmethane, triphenylmethane and toluene. 9,10-Anthraquinone and 2-methyl-9,10-anthraquinone are not brominated in overnight experiments at room temperature, either with or without iodine.

3. Fluorene, phenanthrene, anthracene and naphthalene all show an enhanced effect of iodine as carrier.

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Histamine Antagonists. VI. Pyrrolidylethylamine Derivatives

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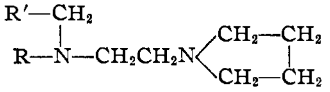
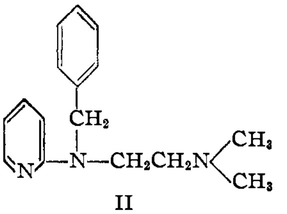
In the course of an extensive investigation of histamine antagonists being conducted in this Laboratory[1-5] a number of tertiary pyrrolidylethylamine derivatives of general structure I have been prepared and their antihistaminic activity determined.



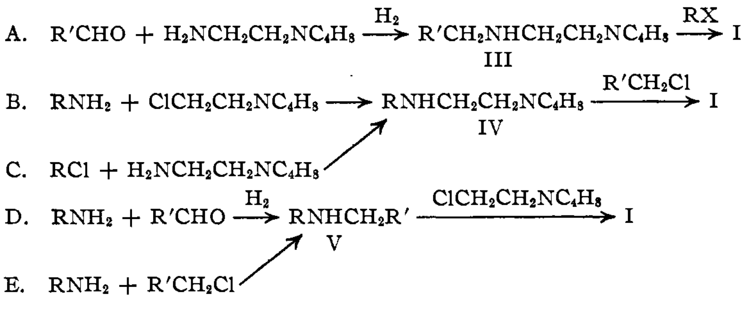
I



II

The groups R and R′ were varied widely, as indicated in Table II. In general, the order of activity of these pyrrolidylethylamine compounds is low[6]; the most active members, N-(2-pyridyl)-N-(*p*-methoxybenzyl)-β-(1-pyrrolidyl)-ethylamine and N-(2-pyridyl)-N-(5-chloro-2-thenyl)-β-(1-pyrrolidyl)-ethylamine, had an effectiveness equal to approximately one-fourth that of II.

The tertiary amines were prepared via the corresponding secondary amino compounds by one of the following procedures.



A. $R'CHO + H_2NCH_2CH_2NC_4H_8 \xrightarrow{H_2} \underset{III}{R'CH_2NHCH_2CH_2NC_4H_8} \xrightarrow{RX} I$

B. $RNH_2 + ClCH_2CH_2NC_4H_8 \longrightarrow \underset{IV}{RNHCH_2CH_2NC_4H_8} \xrightarrow{R'CH_2Cl} I$

C. $RCl + H_2NCH_2CH_2NC_4H_8 \nearrow$

D. $RNH_2 + R'CHO \xrightarrow{H_2} \underset{V}{RNHCH_2R'} \xrightarrow{ClCH_2CH_2NC_4H_8} I$

E. $RNH_2 + R'CH_2Cl \nearrow$

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[1] Wright, Kolloff and Hunter, THIS JOURNAL, **70**, 3098 (1948).

[2] Reid, Wright, Kolloff and Hunter, *ibid.*, **70**, 3100 (1948).

[3] Reitsema and Hunter, *ibid.*, **70**, 4009 (1948).

[4] Wright, *ibid.*, **71**, 1028 (1949).

[5] Wright, *ibid.*, **71**, 2035 (1949).

[6] The assays were carried out under the direction of Dr. Milton J. Vander Brook of our Pharmacology Department.