

the reciprocal of an intercept and  $\beta$  can be evaluated from the slope.

A visual observation of the intercepts of a Langmuir isotherm (Fig. 2, Ref. 5) shows the order of adsorbents according to  $\alpha$  to be charcoal > talc > kaolin > magnesium trisilicate. The calculated values (Table II, Ref. 5) show the order to be charcoal > kaolin > talc > magnesium trisilicate. The discrepancy arises because the calculated value of  $\alpha$  for talc is in error<sup>1</sup> and should be  $\sim 71.4$  (based on an estimated  $1/\alpha$  value of  $1.4 \times 10^{-2}$  from Fig. 2, Ref. 5). The corrected values will show that the order coincides well with visually observed intercept values.

It should be noted that, for Langmuir plots, the use of units other than moles/liter for  $C$  will not change the order of adsorbents according to  $\alpha$  values, since  $\alpha$  is evaluated when  $C$  equals zero. However, numerical values of  $\alpha$  will change.

It is to be expected that the order of adsorbents would be retained regardless of the equation utilized. This would be true if the adsorption isotherms did not cross over, as in this case. The difference in order is due to the fact that the Freundlich constant  $k$  is evaluated at unit equilibrium concentration and the Langmuir constant  $\alpha$  is evaluated at zero equilibrium concentration. If the isotherms crossed over between zero and a unit concentration, the order of adsorbents would be different.

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<sup>1</sup> There is also a typographical error in Table II, Ref. 5. Units of  $\alpha$  should be given (adsorbed) per gram (adsorbent) and not gram (adsorbed) per milligram (adsorbent).

## Potential Errors in Determining Freundlich and Langmuir Constants from Adsorption Isotherms: A Response

**Keyphrases** □ Adsorbents—determination of Freundlich and Langmuir constants, potential errors, reply □ Freundlich constants—potential errors in determination, reply □ Langmuir constants—potential errors in determination, reply

### To The Editor:

In a recent publication (1) we calculated Freundlich and Langmuir constants for the adsorption of cimetidine on various adsorbents. A number of points in this article have been criticized by Hajratwala (2) and we wish to respond to some of these criticisms.

We believe the author has incorrectly assumed that the

intercepts on which our values were based were read directly from the graph. Actually, both intercepts and slopes were calculated using standard linear regression methods. We also fail to see why 6-cycle paper would be necessary in any case. In addition, we feel that the calculation of the parameters based on a single point, as the author has done, is inappropriate. The accuracy of the values obtained is questionable given the closeness of the logarithmic values employed.

With respect to the use of units, we wish to point out that physical chemistry texts (3, 4) employ molarity as the unit for concentration in determining Freundlich parameters, not milligrams percent or grams percent as suggested by Hajratwala. Indeed, we are puzzled as to why this should make a difference in any case. We agree that utilizing different units will yield different values for the constants. However, one need only state which units are used and this should not affect the relative order of constants.

Finally, we acknowledge the error in Table II as pointed out by the author. The value for  $\alpha$  is indeed 70.4 (the intercept being  $1.42 \times 10^{-2}$ ) and the correct value of  $\beta$  is  $15.2 \times 10^4 M^{-1}$ . We regret the miscalculation. There is a typographical error in Table II as Hajratwala notes; however, we feel that this was a misreading. The correct units are neither g(adsorbed)/mg(adsorbent) as printed nor g(adsorbed)/g (adsorbent) as stated by Hajratwala, but g(adsorbed)/M-g(adsorbent). The capital "M" (for molarity) was obviously misread as a lower case "m."

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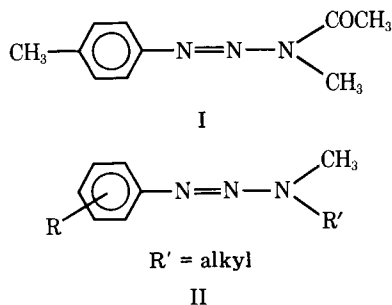
## 1-Aryl-3,3-dialkyltriazenes with Antitrypanosomal Activity

**Keyphrases** □ Antitrypanosomal agents—1-aryl-3,3-dialkyltriazenes □ Antitumor agents—1-alkyl-3,3-dialkyltriazenes □ Triazenes, substituted—antitrypanosomal and antitumor activity

### To the Editor:

We recently reported the activity of 1-(*p*-tolyl)-3-acetyl-3-methyltriazene (I), against *Trypanosoma rhodensiense* in the mouse (1). We now wish to report that a number of 1-aryl-3-alkyl-3-methyltriazenes (II) have shown significant activity against these parasites in the mouse model.

The synthesis and characterization of the 1-aryl-3-



alkyl-3-methyltriazenes were reported previously (2, 3). The triazenes were tested against *T. rhodesiense* (Wellcome CT strain) in the mouse (ICR/HA Swiss) (4). Test and control mice were 6 weeks old and weighed 28–30 g. No differences in response between male and female mice have been reported. Each mouse was infected with an intraperitoneal injection of 0.05 ml of a 1:50,000 dilution of heparinized heart blood drawn from donor mice infected 3 days earlier.

Drugs were administered subcutaneously as a single dose in peanut oil 2 hr after injection. Untreated mice died between 4.2 and 4.5 days after injection. Surviving animals were observed for 30 days and mice surviving after this time were considered cured. The surviving mice were not checked for parasitemia. Test data are given in Table I. The activities of some of the compounds against Sarcoma-180 in the mouse are also included.

The activities reported in Table I suggest that triazenes have curative effects against *T. rhodesiense* in mice. However, high doses are required to produce these effects. It has been suggested that similarities exist between some metabolic pathways of the predominant bloodstream form of the African trypanosome and tumor cells (5) and it was shown that a number of anticancer agents are active against *T. rhodesiense* (6). This correlation was also suggested by the data in Table I when a comparison was made of those activities for the compounds on which both types of data were determined. Compounds 2 and 4 are active in both test systems. Compounds 1 and 3 also were reported

**Table I—Activity of II against *T. rhodesiense* Infection in Mice**

R	R'	Dose, mg/kg ip	Antitrypanosomal Activity <sup>a</sup>	Anticancer Activity <sup>b</sup>	
1	<i>p</i> -COOH	CH <sub>3</sub>	424	4/5	
			424 <sup>c</sup>	5/5	
2	<i>m</i> -COOH	CH <sub>3</sub>	424	1/5	3.01 <sup>d</sup>
			424	2/5	
3	<i>p</i> -NHCO-CH <sub>3</sub>	CH <sub>3</sub>	212	1/5	
			424 <sup>c</sup>	2/5	
4	<i>p</i> -NO <sub>2</sub>	CH <sub>3</sub>	424	3/5	3.43 <sup>d</sup>
			212	1/5	
			424 <sup>c</sup>	3/5	
5	<i>p</i> -C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	424	Inactive	Inactive
6	<i>m</i> -CF <sub>3</sub>	CH <sub>3</sub>	424	Inactive	3.18 <sup>e</sup>
7	<i>m</i> -Cl	CH <sub>3</sub>	424	Inactive	3.16 <sup>e</sup>
8	<i>p</i> -COOH	CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	424	Inactive	Inactive <sup>e</sup>
9	<i>p</i> -COOH	CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -CH <sub>3</sub>	424	Inactive	3.25 <sup>e</sup>
10	<i>p</i> -COOH	CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -OCH <sub>3</sub>	424	Inactive	Inactive <sup>e</sup>
11	<i>p</i> -COOH	CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -NO <sub>2</sub>	424	Inactive	Inactive <sup>e</sup>
12	<i>p</i> -COOH	CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -CN	424	Inactive	Weakly active <sup>e</sup>
13	<i>p</i> -CN	CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -CH <sub>3</sub>	424	Inactive	Inactive <sup>e</sup>
14	<i>p</i> -CN	CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -Cl	424	Inactive	Inactive <sup>e</sup>

<sup>a</sup> Cures per five treated animals. <sup>b</sup> Activity is given as  $-\log C$ ;  $C$  is the moles/kg required to give an increase life span of 130% of control. Tumor was S-180 in the mouse. <sup>c</sup> Duplicate. <sup>d</sup> From reference 2. <sup>e</sup> From reference 3.

to be active against murine leukemia L-1210 in the mouse while the *p*-phenyl analog of II (compound 5) is inactive against *T. rhodesiense*, S-180, and L-1210 (7).

The exact mechanism of the anticancer action of the triazenes is not known but it is known that the 3,3-dialkyltriazenes undergo extensive metabolic *N*-dealkylation to produce alkylating intermediates (8). This metabolic pathway to activation could be host-mediated or it could also be present in the African trypanosome and be involved in the mechanism of action of the triazenes against this parasite. The antitrypanosomal activities of triazenes are being studied further.

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## Comparison of Equilibrium Times in Dialysis Experiments Using Spiked Plasma or Spiked Buffer

**Keyphrases** □ Equilibrium dialysis—comparison of spiked plasma and spiked buffer □ Protein binding—effect of spiked plasma and spiked buffer on equilibrium dialysis

### To the Editor:

When the plasma protein binding of a drug is to be determined using equilibrium dialysis *in vitro*, the drug can be added to either the buffer side or the plasma side of a dialysis cell. Adding drug to the plasma will dilute the plasma proteins if the drug has to be added as a solution. Adding the drug solution to the buffer avoids this difficulty. However, the approach to equilibrium is slower when the buffer is spiked than when the plasma is spiked. Under conditions where the equilibrium conditions can change