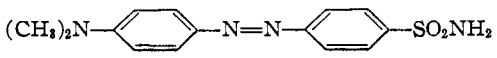
tensity of color. A control gel containing no dye was prepared simultaneously with the other samples. The dyes used were methyl and ethyl orange (I), and *p*-diamino-*p'*-sulfonamidoazobenzene (II).



II

Tables I and II summarize the results of adsorption measurements on extracted gels, for three independent investigations (those of Dickey (A), Emmett (B), and the present work (C)). The concentrations of dye and amounts of gel were as follows: A, dye concn. = $1.5 \times 10^{-5}$ *M* in 5% acetic acid, 1 g. gel; B, dye concn. = $3.0 \times 10^{-5}$ *M* in 5% acetic acid, 1 g. gel; C, dye concn. = $0.5 \times 10^{-5}$ *M* in 0.1 *N* hydrochloric acid, 0.25 g. gel.

Ten ml. of dye solution was used in each case. In the present investigation samples were shaken 24 hours on a high speed shaker. Longer shaking periods did not affect the results. All readings were made on a Beckman spectrophotometer at 5100 Å. In Table I

$$\text{Adsorption Power} = \frac{\text{Moles of dye adsorbed/g. of gel}}{\text{Moles of dye in solution/g. of solution}}$$

and in Table II

$$\%\ \text{excess adsorption} = \frac{\text{Adsorption power of gel-adsorption power of control}}{\text{Adsorption power of control}} \times 100$$

TABLE I

ADSORPTION POWER

| Investigation | Gel prepared with | Adsorption power for Methyl orange | Ethyl orange | II |
|---|---|---|---|---|
| (A) | Control | 84 | 80 | ... |
| | Methyl orange | 300 | 128 | ... |
| | Ethyl orange | 230 | 740 | ... |
| (B) | Control | 5.6 | 5.2 | ... |
| | Methyl orange | 11 | 7.2 | ... |
| | Ethyl orange | 8.0 | 10 | ... |
| This paper | Control | 18 | 9.2 | 31 |
| | Methyl orange | 100 | 32 | 144 |
| | Ethyl orange | 90 | 74 | 120 |
| | II | 106 | 34 | 168 |

TABLE II

% EXCESS ADSORPTION

| Investigation | Gels prepared with | % Excess adsorption of Methyl orange | Ethyl orange | II |
|---|---|---|---|---|
| (A) | Methyl orange | 250 | 60 | ... |
| | Ethyl orange | 150 | 800 | ... |
| (B) | Methyl orange | 100 | 40 | ... |
| | Ethyl orange | 40 | 90 | ... |
| This paper[a] | Methyl orange | 450 | 250 | 370 |
| | Ethyl orange | 380 | 700 | 290 |
| | II | 480 | 280 | 450 |

[a] In a previous experiment in this Laboratory, when the present techniques were not as yet developed, two gels prepared in the presence of methyl orange and II gave the following % excess adsorption for methyl orange, ethyl orange and II, respectively: Methyl orange gel, 80, 50, 90; gel (II), 90, 50, 120; each sample contained 10 ml. of $2.5 \times 10^{-5}$ *M* dye and 0.5 g. of gel.

The new data are in agreement with the observations of Dickey.

It is of interest to note that specificity for II and methyl orange are closely parallel, indicating that a negative charge at the *p'*-substituent is not a requirement for specificity. Since the sulfonate and sulfonamido groups are nearly the same size, stereochemical specificity for the *p'*-substituent could not be investigated in this experiment. None of the gels would measurably adsorb methyl orange at *p*H 7.0.

The number of moles of methyl orange adsorbed onto the methyl orange gel was calculated, and the same quantity of dye was then adsorbed onto a control gel (by suitable increase of the initial dye concentration in solution). The intensity of color of the control gel after adsorption of the dye was qualitatively noted to be much less than that of the original methanol-extracted methyl orange dye, indicating that under the conditions of the adsorption experiments reported here less dye was adsorbed than was originally present in the gel, even under the most favorable conditions for adsorption.

Specific adsorbants for dyes of the methyl orange type can be readily prepared by a method similar to that of Dickey.[1] The dyes must contain a cationic center in order that the adsorption be measurable. The specificity of the gels has again been shown to be dependent on the stereochemical constitution of the *p*-substituent (dialkylamino group) of the dye. Although no stereochemical investigation of the *p'*-substituent has been made, the specificity has been found to be independent of a negative charge on this group.

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## *p*-Amino- and *p*-Fluoro-β-phenylalanine

BY ERNST D. BERGMANN[1]

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Convenient methods are described for the preparation of *p*-amino- and *p*-fluorophenylalanine, which were required for biochemical experiments. *p*-Aminophenylalanine has been prepared by reduction of the easily available[2] *p*-nitro compound with stannous chloride and hydrochloric acid,[1] or from diethyl *p*-nitrobenzylacetamidomalonate.[3] Both by catalytic hydrogenation of *p*-nitrophenylalanine (yield 87%) and by reduction of the azlactone[4] from *p*-nitrobenzaldehyde and hippuric acid (yield 78%, calculated on the aldehyde), the amino acid is obtained in pure form.

For the preparation of *p*-fluorophenylalanine, the azlactone synthesis[5] and the condensation of diethyl acetamidomalonate with *p*-fluorobenzyl chlo-

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ride[6] has been used before; the application of diethyl phthalimidomalonate gives an over-all yield of 50% (calculated on *p*-fluorobenzyl chloride).

### Experimental Part

**p-Amino- from p-Nitrophenylalanine.**—When 8 g. of the nitro compound[1] (from *t*-butyl alcohol, m.p. 240–245° (dec.)) in 150 ml. of water, was hydrogenated at room temperature and atmospheric pressure, in the presence of 0.8 g. of 5% palladium–barium sulfate as catalyst, the theoretical amount of hydrogen was absorbed rapidly. The filtered solution was concentrated at 50° *in vacuo*, until crystallization set in. Upon cooling, 5.9 g. (87%) of the amino acid was obtained in form of fine needles.

**Azlactone of α-Benzoylamino-p-nitrocinnamic Acid.**—A mixture of 40 g. (1/6 mole) of hippuric acid, 82 g. (1/6 mole) of anhydrous sodium acetate, 25 g. (1/6 mole) of *p*-nitrobenzaldehyde and 102 g. (1 mole) of acetic anhydride was heated on the steam-bath for 45 minutes, with occasional shaking. The excess of the acetic anhydride was destroyed by treatment with water and the product filtered, thoroughly washed with hot water, and dried at 100°. It was recrystallized from toluene, forming yellow needles of m.p. 242° (lit. 233°,[4a] 239°,[4b] yield 45 g. (91.8%, lit. 76%[4a]).

**p-Aminophenylalanine.**—The mixture of 29.4 g. of the azlactone, 200 ml. of glacial acetic acid, 500 g. of hydriodic acid (sp. gr. 1.7) and 20 g. of red phosphorus was refluxed for 6 hours, and the hot solution filtered (glass filter) and evaporated *in vacuo* to dryness. The residue was taken up in 200 ml. of water and evaporated again *in vacuo* to dryness; during these operations, part of the benzoic acid formed, sublimed over. The residue was dissolved in 100 ml. of water and this solution extracted twice with ether, concentrated *in vacuo* to about 50 ml. and made alkaline (litmus) by the slow addition of concentrated ammonia solution. Crystallization started at once and was completed by cooling. The crystals were collected and washed with 10 ml. of ice-cold water. Recrystallization from boiling water gave colorless needles of the hydrate which lost its water at 140° (*in vacuo*) and showed a m.p. (dec.) of 265° on quick, and of 254° on slow heating (lit. 245–250°[2]); yield 16.9 g. (85.3%).

*Anal.* Calcd. for $C_9H_{12}O_2N_2 + 1H_2O$: $H_2O$, 9.1; C, 54.5; H, 7.1; N, 14.1. Found: $H_2O$, 9.2; C, 54.3; H, 7.0; N, 14.0.

**p-Fluorophenylalanine.** (a) **Ethyl p-Fluorobenzyl-phthalimidomalonate.**—An intimate mixture of 6.7 g. of *p*-fluorobenzyl chloride[7] (b.p. 75–77° (14 mm.)) and 11.7 g. of ethyl sodiophthalimidomalonate[8] was heated for six hours at 160° and subsequently for 15 minutes at 200°. The product was digested with hot water, cooled and extracted with ether; it formed an oil (15 g., 72%) which could be purified by distillation *in vacuo*: b.p. 245–250° (13 mm.).

*Anal.* Calcd. for $C_{22}H_{20}NO_6F$: C, 64.2; H, 4.9; N, 3.4. Found: C, 64.2; H, 5.0; N, 3.6.

(b) **N-(o-Carboxybenzoyl)-p-fluorobenzyl-aminomalonic Acid.**—A mixture of 5 g. of the (crude) ester, 5 ml. of alcohol and 14 ml. of 5 *N* sodium hydroxide solution was refluxed for 2 hours; a solid salt precipitated. Addition of 20 ml. of water, and of 2 *N* hydrochloric acid to neutrality, gave a viscous precipitate, which crystallized upon trituration with 30 ml. of concentrated hydrochloric acid; yield 4 g. (87%); from 50% acetic acid, m.p. 165°.

*Anal.* Calcd. for $C_{18}H_{14}NO_7F$: C, 57.9; H, 3.8; N, 3.8. Found: C, 57.5; H, 4.0; N, 4.1.

(c).—The foregoing acid (4.2 g.) was heated at 100° with 120 ml. of 5 *N* hydrochloric acid for 45 minutes and, after addition of 60 ml. of 10 *N* hydrochloric acid, for two more hours. The filtered solution was evaporated to dryness *in vacuo*, the residue dissolved in a little hot water and ammonia solution added. Upon addition of some alcohol, the amino acid crystallized. From a water–alcohol mixture (3:1), well-shaped needles, m.p. 238–242° (dec.) upon slow heating; when the substance was heated rapidly, the m.p. was higher (previous authors: 263.5–264°,[5] 259–261[6]); yield 1.7 g. (80%).

*Anal.* Calcd. for $C_9H_{10}NO_2F$: C, 59.7; H, 5.5; N, 7.7. Found: C, 59.6; H, 5.5; N, 7.8.

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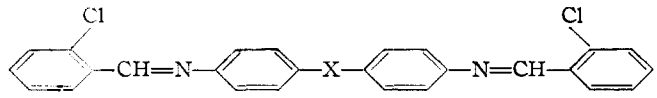
## Three Analogs of Bis-(*o*-chlorobenzylidene)-4,4′-diaminodiphenyl Sulfone

BY ERNST D. BERGMANN AND D. LAVIE

RECEIVED MAY 28, 1952

Sah, Oneto, Rohrmann and Kleiderer[1] have shown that the product mentioned in the title (I, X = $SO_2$) is effective against tuberculosis and have stressed the analogy with the anti-tubercular activity of *o*-chloro substituted benzophenones.[2]

The bis-(*o*-chlorobenzylidene) derivatives of 4,4′-diaminobenzophenone (I, X = CO), 4,4′-diaminodiphenylmethane (I, X = $CH_2$) and 1,1-di-(*p*-aminophenyl)-2,2,2-trichloroethane (I, X = $CH{\cdot}CCl_3$) were prepared and their anti-tubercular activity was tested. The selection of these materials was guided not only by the structural similarity




I

with the substituted sulfone, but also by the fact that 1,1-di-(*p*-aminophenyl)-2,2,2-trichloroethane itself inhibits the growth of *M. tuberculosis*[3] and that 4,4′-diaminobenzophenone has been shown by Auhagen[4] and by Kuhn and co-workers[5] to be bacteriostatic against *Streptobacterium plantarum*.

The three substances were tested against a human strain of *Mycobacterium tuberculosis* (Dubos liquid medium No. 2) and proved inactive in the concentration of $10^{-5}$ g./l.; at $10^{-4}$ g./l. they showed slight activity.[6]

### Experimental

**Bis-(o-chlorobenzylidene)-4,4′-diaminodiphenylmethane** (I, X = $CH_2$).—A mixture of 1.5 g. of 4,4′-diaminodiphenylmethane[7] and 2.5 g. of *o*-chlorobenzaldehyde was subjected to azeotropic distillation with 50 cc. of benzene. When no more water appeared in the trap, the solvent was evaporated and the residue recrystallized from glacial acetic acid or butanol; needles, m.p. 135°, yield 3 g.

*Anal.* Calcd. for $C_{27}H_{20}N_2Cl_2$: N, 6.3. Found: N, 6.5.

**Bis-(o-chlorobenzylidene)-4,4′-diaminobenzophenone** (I, X = CO).—The mixture of 2.1 g. of the ketone,[8] 2.8 g. of *o*-

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(6) We are indebted to Dr. David Nachtigall, Tel-Aviv, for these tests.

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