NMR ($CDCl_3$) δ 9.75 (s, 1 H), 7.78 (m, 2 H), 7.42 (m, 8 H), 2.10 (br, s, 3 H).

***2-Benzoyl-1-butyryl-1-phenylhydrazine* (*IIg*).** Mp 173.5–174 °C; IR (KBr) 3275, 2975, 1670, 1600 cm^{-1}; NMR ($CDCl_3$) δ 7.72 (m, 2 H), 7.32 (m, 8 H), 2.32 (br, t, 2 H), 1.70 (q, 2 H).

***2-Benzoyl-1-isobutyryl-1-phenylhydrazine* (*IIh*).** Mp 192 °C; IR (KBr) 3260, 2960, 1680, 1615 cm^{-1}; NMR ($CDCl_3$) δ 7.63 (m, 2 H), 7.35 (m, 8 H), 2.72 (m, 1 H), 1.15 (d, 6 H).

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Registry No. Ia, 114-83-0; Ib, 20730-02-3; Ic, 20730-03-4; Id, 5461-50-7; Ie, 532-96-7; If, 2719-07-5; Ig, 6561-63-3; Ih, 6561-60-0; Ii, 7461-93-0; Ij, 6947-29-1; Ik, 79984-65-9; Il, 92186-54-4; Im, 22207-29-0; In, 22207-30-3; Io, 17473-76-6; Ip, 65763-66-8; IIa, 38604-74-9; IIb, 92186-55-5; IIc, 92186-56-6; IId, 92186-57-7; IIe, 23459-55-4; IIf, 67491-56-9; IIg, 92186-58-8; IIh, 92186-59-9; $PhNHNH_2$, 100-63-0; $2,4-(NO_2)_2C_6H_3NHNH_2$, 119-26-6; $4-ClC_6H_4NHNH_2 \cdot HCl$, 1073-70-7; $4-MeC_6H_4NHNH_2 \cdot HCl$, 637-60-5; $(MeCO)_2O$, 106-24-7; $(EtCO)_2O$, 123-62-6; $(PrCO)_2O$, 106-31-0; $(i\text{-}PrCO)_2O$, 97-72-3; $(PhCO)_2O$, 93-97-0.

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Synthesis of *O*-Carbanilinobenzamidoximes

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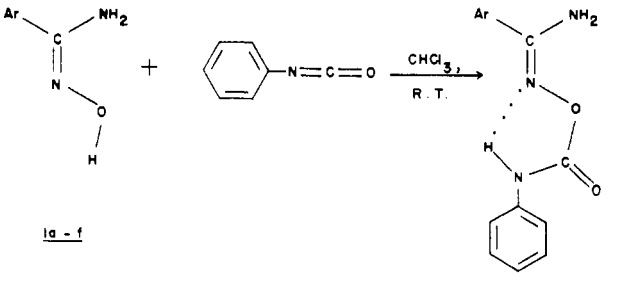
Preparation of six *O*-carbanilinobenzamidoximes, 2a–f, starting from benzamidoximes, 1a–f, is described. Spectroscopic results are in accord with the structure assignment. Compounds 2a–f were tested against bacteria and fungi. Only two, viz., *O*-carbanilinobenzamidoxime, 2a, and *O*-carbanilino-*o*-toluamidoxime, 2b, showed activity. The former inhibited the growth of *Escherichia coli* and *Neurospora crassa* whereas the latter stopped the growth of *N. crassa* only.

Introduction

So far, two publications (*1*, *2*) have appeared regarding the reaction of phenyl isocyanate with benzamidoxime. In the first report (*1*), *N*-carbanilinobenzamidoxime was proposed for the reaction product, while in the second one (*2*) the structure was assigned as *O*-carbanilinobenzamidoxime based on the infrared absorption results. Recently, the configuration and conformation of **2a** have also been studied (*3*). Reaction of *p*-toluamidoxime and phenyl isocyanate was reported (*4*) to yield *N*-carbanilino-*p*-toluamidoxime. Since, only two compounds, **2a** and **2b**, are known in this series and no other work except infrared spectroscopy (for **2a**) has been done, we thought it to be interesting to prepare some ring-substituted *O*-carbanilinobenzamidoximes and test their physiological activity. This paper reports the synthesis of six such compounds, **2a–f**, from **1a–f**

[†]Taken in part from the M.S. thesis of Maryone Borba Brito, Universidade Federal de Pernambuco, Recife, PE, 1982.

Scheme I



1a - f

2a - f

a : Ar = Ph
b : Ar = o-Tolyl
c : Ar = m-Tolyl
d : Ar = p-Tolyl
e : Ar = p-Chlorophenyl
f : Ar = p-Bromophenyl

(Scheme I) and their preliminary test for pharmacological activity.

Results and Discussion

Benzamidoximes, **1a–f** were allowed to react with phenyl isocyanate in alcohol-free chloroform at room temperature for an extended period of time. After purification, compounds **2a–f** were obtained in crystalline forms.

The infrared spectra of all *O*-carbanilinobenzamidoximes displayed strong absorption at 1715–1740 cm^{-1} (ν(–O–CO–)). Since no other product was detected on TLC, it is obvious that these are single compounds.

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Table I. ^{1}H NMR Data (τ) of *O*-Carbanilinobenzamidoximes, 2a–f

	τ			
compd	aromatic	$-NH_2$	>NH	$-CH_3$
2a[a]	2.2–3.0 (10 H, m)	4.6 (2 H, b)	1.37 (1 H, b)	
2b[a]	2.4–3.0 (9 H, m)	4.67 (2 H, b)	1.48 (1 H, b)	7.51 (3 H, s)
2c[a]	2.3–3.0 (9 H, m)	4.6 (2 H, b)	1.30 (1 H, b)	7.62 (3 H, s)
2d[a]	2.3–3.0 (9 H, m)	4.6 (2 H, b)	1.30 (1 H, b)	7.64 (3 H, s)
2e[b]	1.82–2.93 (9 H, m)	3.5 (2 H, b)	0.88 (1 H, b)	
2f[b]	1.92–2.92 (9 H, m)	3.45 (2 H, b)	1.11 (1 H, b)	

[a] In $CDCl_3$. [b] In CD_3COCD_3.

The 60-MHz NMR spectrum of **2a** showed a multiplet at τ 2.2–3.0 (10 H, Ar protons), a broad signal at τ 1.37 (1 H, >NH), and another broad signal at τ 4.6 (2 H, $-NH_2$). Table I lists the chemical shifts of various protons of **2a–f**.

Activity Testing

Preliminary tests of **2a–f** have been performed against bacteria and fungi. Only two of them, viz., **2a** and **2b**, showed positive activity. The former inhibited the growth of *E. coli* (S IA–27) and *N. Crassa* (IA-2038) in the concentration range of 100–300 μg/mL. The individual substance was dissolved in a mixture of Tween 80–ethanol–water in the ratio of 0.5:1.0:1.0. No pharmacological test has yet been reported in the literature on this series of compounds.

Experimental Section

The melting points were obtained on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infared spectra were measured (Nujol mull) on a Perkin-Elmer Model 467 Infracord and NMR spectra on a A-60 Varian Associates spectrometer using Me_4Si as internal reference. Satisfactory elemental analyses were made by Dr. Riva Mascovici, Instituto de Química, Universidade de São Paulo, S. P., and these were submitted for review. Thin-layer chromatography was done on plates coated with silica gel G (Merck) using benzene–ethyl acetate (7:3) for development and iodine for detection of the spots.

***Benzamidoximes* (1a–f).** Compound **1a** was prepared by the method given in the literature (*5*). Benzamidoximes **1b,d–f** were synthesized as reported (*6*), while **1c** was obtained according to the procedure of Andrade (*7*).

***O*-Carbanilinobenzamidoximes (2a–f).** Amidoxime (3.7 mmol) in alcohol-free chloroform (10 mL) was taken in a 100-mL two-neck round-bottom flask fitted with an addition funnel and protected by a drying tube. Phenyl isocyanate (3.7 mmol) dissolved in chloroform (10 mL) was dropped in about 0.5 h to this solution under constant stirring at room temperature. After addition, the contents were left under agitation between 5 and 9 h at ambient temperature. Removal of the solvent left a residue. Thin-layer chromatography in all preparations showed that a small quantity of amidoxime remained unreacted and therefore liquid chromatography was necessary to obtain the pure material. The purification process and physical constants of each compound are described below.

***O*-Carbanilinobenzamidoxime (2a).** The material obtained after the reaction was chromatographed on silica gel by using benzene–chloroform (1:1) as eluent. The fast-moving spot (R_f = 0.64) after crystallization from chloroform–petroleum ether (40–60 °C) provided crystals in about 80% yield: mp 124 °C [lit. (*2*) mp 123–125 °C (yield 75–100%)].

***O*-Carbanilino-*o*-toluamidoxime (2b).** In this case, the product was chromatographed on silica gel by employing ethyl acetate–benzene (1:9) as solvent. The fractions having R_f values of 0.7 were combined and the solvent was evaporated to give pure **2b** (80%). Crystallization from $CHCl_3$–petroleum ether (40–60 °C) afforded crystals with mp 126–128 °C.

***O*-Carbanilino-*m*-toluamidoxime (2c).** After chromatography and workup, **2c** crystallized from ethyl acetate and petroleum ether (40–60 °C), R_f = 0.67, and the yield was 89%. It melted at 134 °C.

***O*-Carbanilino-*p*-toluamidoxime (2d).** Repeated crystallizations from chloroform and petroleum ether (40–60 °C) afforded 74% of **2d** (R_f = 0.66), mp 156 °C; ref *4* and *5* cited mp 155 °C but did not mention the yield.

***O*-Carbanilino-*p*-chlorobenzamidoxime (2e).** The reaction product was chromatographed on a column containing silica gel. The fractions with R_f values of 0.63 were combined and the solvent was evaporated. The solid residue on crystallization from ethanol provided **2e** (61%), mp 176–178 °C.

***O*-Carbanilino-*p*-bromobenzamidoxime (2f).** Liquid chromatography of the reaction product on silica gel followed by the workup of the fractions with R_f values 0.62 gave crystals (77%). Recrystallization from methanol afforded crystals, mp 182–184 °C.

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Registry No. **1a**, 613-92-3; **1b**, 40312-14-9; **1c**, 40067-82-1; **1d**, 19227-13-5; **1e**, 5033-28-3; **1f**, 19227-14-6; **2a**, 93474-34-1; **2b**, 93474-35-2; **2c**, 93474-36-3; **2d**, 93474-37-4; **2e**, 93474-38-5; **2f**, 93474-39-6; phenyl isocyanate, 103-71-9.

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