

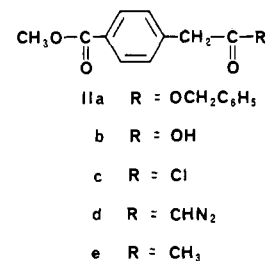
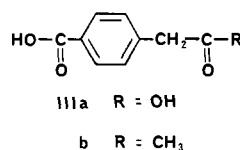
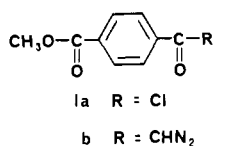
Synthetic Route to 4-Carbomethoxyphenyl-2-propanone

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A synthetic sequence starting with *p*-carbomethoxybenzoyl chloride (Ia) and leading to 4-carbomethoxyphenyl-2-propanone (IIe) is described. Per cent yields, melting points, elemental analyses, and NMR spectra for several intermediates and derivatives are given.

BECAUSE of our interest in several of the intermediates as well as the product, a somewhat lengthy route (Ia through IIe) was chosen to prepare 4-carbomethoxyphenyl-2-propanone (IIe). Some of the intermediates were new and others, previously described, showed different properties from those reported.

Addition of our starting material, *p*-carbomethoxybenzoyl chloride (Ia) (3), in benzene solution to ethereal diazomethane in the usual manner yielded *p*-carbomethoxydiazoacetophenone (Ib), but our melting point (104–05°) disagrees with that reported (ca. 135°) in the literature (3). The structure of Ib is indicated, however, by its reaction with hydriodic acid (1) and subsequent acid hydrolysis of the resulting product to form *p*-acetylbenzoic acid, melting point 206–07°. A mixed melting point of the latter product with *p*-acetylbenzoic acid prepared by a previous method (2) was not depressed. Our attempts to repeat the Wolff rearrangement of Ib, as described by Kompes, Mokry, and Tanchya (3), did not yield *p*-carbomethoxyphenylacetic acid (IIb). However, a modification of the reaction, as described by Wilds and Meader (6) in which the diazoketone is heated in benzyl alcohol and dimethylaniline, was successful. The intermediate benzyl ester (IIa) was not isolated but was hydrogenated in the crude state to yield IIb. The melting point of IIb is listed in the literature (3) as 209–11°, but our product melted at 112–13°. Acid hydrolysis of IIb yielded homoterephthalic acid (IIIa), identified by mixed melting point with homoterephthalic acid prepared as described in the literature (4).



When IIb was treated with thionyl chloride, an intermediate (IIc) was obtained which was never isolated but was treated with diazomethane to form 1-(4-carbomethoxyphenyl)-3-diazo-2-propanone (IIId). Treatment of IIId with hydriodic acid in the usual manner (1) yielded 4-carbomethoxyphenyl-2-propanone (IIe). Hydrolysis of IIe yielded 4-carboxyphenyl-2-propanone (IIIb), a compound previously listed in the literature (5) without description of physical properties.

Oxime derivatives were obtained from IIe and IIIb.

The compounds isolated from the reactions described above are listed in Table I along with pertinent data. Table II lists NMR data which further confirm the above structures. Peaks due to aliphatic protons appear in expected regions. Aromatic protons exhibit *A*₂*B*₂ patterns in all cases.

Table I. Physical Properties and Analytical Data

Compound	M.P., ° C. ^a	Yield, %	Recrystallization Solvent	Formula	Analysis					
					Calcd., %			Found, %		
					C	H	N	C	H	N
Ib	104–05.3	81.7	Benzene–pet. ether	C ₁₀ H ₉ N ₂ O ₃	58.82	3.95	13.72	58.87	4.07	13.91
IIb	112–13	68.4	Methanol–water	C ₁₀ H ₁₀ O ₄	61.85	5.19	...	61.62	5.32	...
IIId	59–61.8	71.5	Ether–pet. ether	C ₁₁ H ₁₀ N ₂ O ₃	60.55	4.62	12.84	60.33	4.80	12.82
IIe	46–49	74.8	Cyclohexane–pet. ether	C ₁₁ H ₁₂ O ₃	68.74	6.29	...	68.96	6.45	...
IIe, oxime	97–100	58.3	Ethanol–water	C ₁₁ H ₁₃ NO ₃	63.76	6.32	6.76	63.71	6.34	6.66
IIIa	235–39 ^b	83.5	Water	C ₉ H ₈ O ₄	60.00	4.48	...	59.91	4.72	...
IIIb	160–62	90.1	Water	C ₁₀ H ₁₀ O ₃	67.41	5.66	...	67.22	5.86	...
IIIb, oxime	182–85	94.6	Ethanol–water	C ₁₀ H ₁₁ NO ₃	62.17	5.74	7.25	62.13	5.89	7.06

^a Melting points of all analytical samples taken in capillary tubes and obtained with Drechsel melting point apparatus with thermometers calibrated against registered thermometers (National Bureau of Standards). ^b Literature (4), m.p. 236–37°.

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Compd.	Solvent	Chemical Shifts of Aliphatic Protons ^b , δ				Chemical Shifts of Aromatic Protons ^c , δ (J) ^d
		CH ₃ O	CH ₂	CHN ₂	COCH ₃	
Ib	CDCl ₃	3.93	...	5.94	...	8.10, 7.78 (8.5)
IIb	CDCl ₃	3.89	3.68	7.97, 7.31 (8.5)
IIId	CDCl ₃	3.89	3.64	5.21	...	7.96, 7.28 (8.5)
IIe	CDCl ₃	3.90	3.75	8.02, 7.28 (8.0)
IIIb	DMS-D ₆	...	3.88	7.91, 7.30 (8.0)

^aAll spectra run on Varian A-60 spectrophotometer. Chemical shifts given in parts per million relative to tetramethylsilane as internal standard. ^bAll peaks are singlets. Relative peak areas correspond to number of protons in each group. ^cAll doublets; area = 2. ^dCoupling constants (J) in cps. J values are $J_{\text{H}^{\text{a}}\text{H}^{\text{b}}} = J_{\text{H}^{\text{b}}\text{H}^{\text{a}}}$ where aromatic rings are numbered starting with carbon bearing carbomethoxy or carboxy substituent in all cases.

ACKNOWLEDGMENT

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Synthesis of Some Phenyl *N*-Arylcarbamates

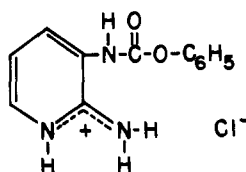
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Eight phenyl *N*-(substituted phenyl)carbamates, the three isomeric phenyl *N*-pyridylcarbamates, five diphenyl *N,N'*-arylenedicarbamates, and diphenyl *N,N'*-2,6-pyridylenedicarbamate were prepared by the reaction of the appropriate amine and phenyl chloroformate. All of the new compounds were purified, characterized, and converted into derivatives, where possible. Infrared and NMR spectral data are reported, as well as some thermal data.

USING the method described by Raiford *et al.* (8, 9) (with minor modifications) a series of phenyl *N*-arylcarbamates was prepared by reaction of phenyl chloroformate and an aryl amine in dioxane in the presence of an acid acceptor; where tertiary amines were present as part of the molecular structure, no added base was required. To ensure completeness of reaction, stoichiometric amounts of added tertiary amine are required in the syntheses of dicarbamates which contain pyridyl or dialkylamino groups. In these latter cases, *N,N*-dimethylaniline was used as the acid acceptor. Addition of triethylamine to the mixture of hydrochlorides yielded the desired product. The reactivity of triethylamine with phenyl chloroformate (4) necessitated the two-step synthesis.

Reaction of excess phenyl chloroformate with 2,3-diaminopyridine produced good yields of 2(3)-amino-3(2)-carbophenoxyaminopyridine hydrochloride.



The above structure is postulated for this hydrochloride because of resonance stabilization of the cation. Analogous structures have been postulated for 2,3-diaminopyridine

hydrochloride to explain its inability to form a dihydrochloride. Neutralization with a strong base yielded the cyclic 1*H*,2*H*-2-oxo-imidazo[4,5-*b*]pyridine (XIX).

The addition of 1 mole of phenyl chloroformate to 1 mole of 2,6-diaminopyridine (in water), followed by neutralization with strong base and the subsequent addition of another mole of phenyl chloroformate, resulted in a 49% yield of 2,6-bis-(carbophenoxyamino)pyridine (XVIII). No isolation of the intermediate, 2-amino-6-carbophenoxyaminopyridine hydrochloride, was attempted.

The properties and analytical data for all of the compounds synthesized are listed in Tables I, II, and III.

The NMR spectra for each compound are in agreement with the protons of the group characteristic of the particular structure positively identified. The characteristic chemical shift, δ , for the phenyl group occurs at about 7.3 p.p.m. and exists as a multiplet. The chemical shifts and splitting patterns associated with the NH and aromatic protons are characteristic of each particular structure and also are listed in the tables.

The infrared spectra for all the phenyl carbamates investigated exhibit characteristic absorption bands as follows: medium intensity bands at 2.89 to 3.16 microns for NH; medium intensity bands at 5.65 to 5.80 microns for C=O; strong intensity bands at 6.42 to 6.57 microns for —CONH; and two bands (6.13 to 6.27, medium, and 6.65 to 6.73, strong) for the phenyl group. Other distinguishing bands peculiar to each particular structure are also present. The thermal data, including the melting range and the heats of fusion, were determined on the differential scanning calorimeter (10) using the Perkin-Elmer DSC-1.