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The ultraviolet irradiation of the $\pi \rightarrow \pi^*$ transition of cocaine, *p*-anisoyl-*l*-ecognine methyl ester, *p*-toluoyl-*l*-ecognine methyl ester benzoyl tropine and benzoylpseudotropine in methanol using a Corex filter produces the corresponding *N*-demethylated products. Formaldehyde is quantitatively produced. 1-Methyl-3-piperidyl benzoate and 1-methyl-4-piperidyl benzoate yield benzoic acid under the same conditions but no demethylated products. Phenylacetyl-*l*-ecognine methyl ester gives no demethylation during irradiaiton. The phosphorescence bands of cocaine and its model compound, methyl benzoate, have been shown to be strongly dependent upon solvent polarity suggesting charge transfer in the triplet state.

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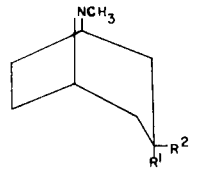
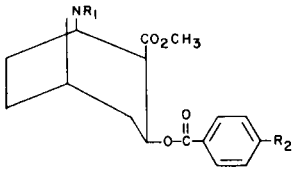
As a part of our continuing efforts towards understanding the photochemistry of alkaloids (1), the reported photochemical activity of cocaine **1** (2) was investigated to provide information on the products formed. Since cocaine is important in medicine, knowledge of the photochemical reaction which it undergoes had potential value as a source of new products and reactions. A portion of this work has been described in a preliminary communication (3). We now wish to describe the photochemical reactions of cocaine and its model compounds in detail together with the needed spectroscopic background.



4 $R_1 = CO_2Ph$, $R_2 = H$
5 $R_1 = H$, $R_2 = CO_2Ph$



1 $R_1 = CH_3$, $R_2 = H$
2 $R_1 = CH_3$, $R_2 = OCH_3$
3 $R_1 = R_2 = CH_3$
6 $R_1 = R_2 = H$

Results and Discussion.

The ultraviolet spectrum of cocaine is reproduced in Figure 1 (4). Though broad spectrum irradiation through quartz gave products, irradiation through either Corex or Vycor filters gives similar products with less polymer formation. By means of the Corex filter; these studies were restricted to the activation of the lowest energy, $\pi \rightarrow \pi^*$ transition, *i.e.*, the absorption band with λ max at 274 nm and its shoulder at 281 nm. Individually, neither the methyl ester nor the tertiary amine chromophore can account for the 274-nm transition because neither functional group, in isolation from the other, absorbs in this region of the spectrum. Further, the spectrum of cocaine in aqueous acid solution, where the amine is present as the ammonium group, varies little from that of the free base in ethanol. Hence, the 274-nm transition is best assigned to the benzoate group. The spectrum of methyl benzoate is also included in Figure 1

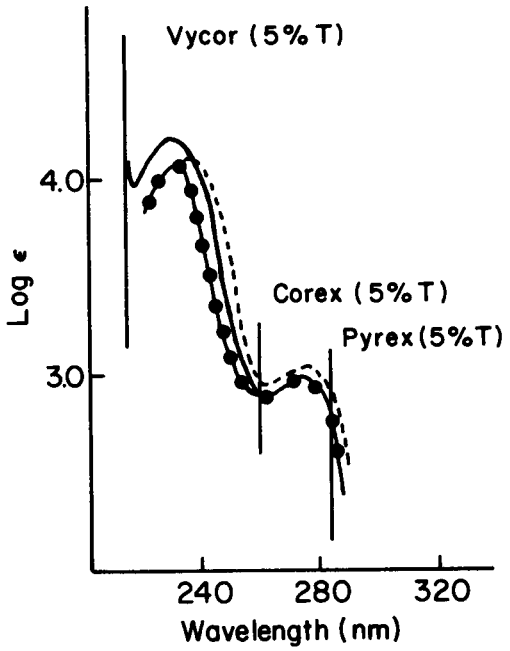


Figure 1; The ultraviolet spectra of cocaine (—) and methyl benzoate (-o-) in ethanol together with that of cocaine hydrochloride (--) in water.

to demonstrate that it coincides with the longer wavelength transition of cocaine. Therefore, when a cocaine sample is irradiated through a Corex filter, only its benzoate chromophore is being activated.

The 274-nm band is most probably a $\pi \rightarrow \pi^*$ transition, has an extinction coefficient of *ca.* 1000 which is considerably greater than that of the usual $n \rightarrow \pi^*$ transitions of carbonyl groups and corresponds both in λ max and extinction coefficient to the secondary bands (^1L_b) of monosubstituted benzenes (5). Furthermore, Kasha (6) has reported that $n \rightarrow \pi^*$ transitions disappear in acidic solvents whereas the spectrum of cocaine in aqueous acid solution varies a little from that of the free base in ethanol.

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Cocaine **1**, *p*-anisoyl-*l*-ecgonine methyl ester **2**, *p*-toluoyl-*l*-ecgonine methyl ester **3**, benzoyltropine **4** and benzoylpseudotropine **5** all gave the corresponding *N*-demethylated products when their methanolic solutions were irradiated through Corex glass using the 300-nm lamps of the Rayonet reactor. The photoproducts were isolated from their reaction mixtures by neutral alumina chromatography.

The *N*-methyl groups of the bicycloamines **1-5** appeared in the reaction solutions as formaldehyde. Formaldehyde was identified in the reaction solutions of **1-5** by directly preparing its dimedone derivative and quantitatively determined to be present in equimolar ratios of the demethylated products by means of the Nash reagent.

The bicyclococaine structure appears essential to the photochemical reaction because 1-methyl-3-piperidyl benzoate and 1-methyl-4-piperidyl benzoate yield benzoic acid and polymers and no demethylated products on irradiation under identical conditions to the cocaine reaction. When the nitrogen is not included or bound in the reactant structure, neither demethylation nor benzoic acid formation occurs. Cyclohexylbenzoate and cocaine hydrochloride were found to be photochemically stable. When the benzoate chromophore is changed to that of phenyl acetate, the demethylation reaction also fails to happen. Phenylacetyl-*l*-ecgonine methyl ester gives no demethylation and only polymer formation upon irradiation at 253.7 nm. Thus the bridged nitrogen and the benzoate chromophore are essential to the demethylation reaction.

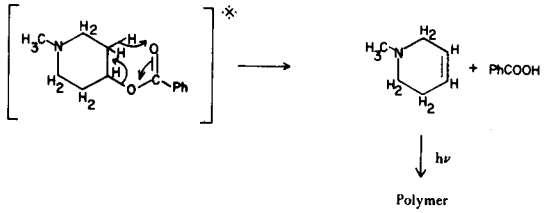
The retention of sterochemistry on the equilibratable centers, C-2 and C-3, during irradiation of cocaine was demonstrated in two ways. First, the photoproduct, norcocaine, was identical to that prepared by an independent synthesis of it from cocaine by permanganate oxidation. Second, the recovered cocaine from the reaction solution did not contain pseudococaine.

The methoxycarbonyl substituent on C-2 of cocaine is not essential to the photoreaction of cocaine since benzoylpseudotropine **5** also gives the corresponding demethylated product under identical irradiation conditions. Since the demethylation also occurs for benzoyltropine, where the benzoyl group does not come in close proximity to the N-methyl reaction center in any conformer, the reaction must be at least partially intermolecular in character.

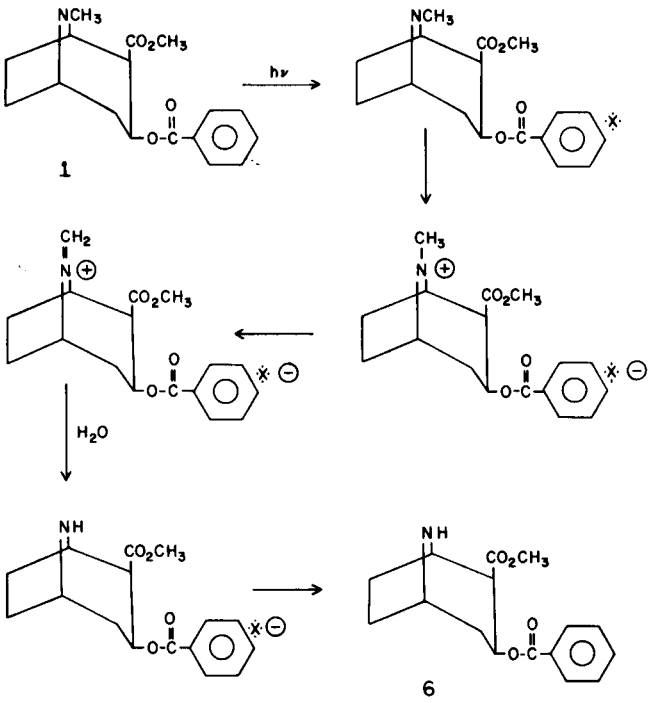
Neither the *p*-methyl group nor the methoxy substituent on the benzoate enhances the demethylation process. *p*-Anisoyl-*l*-ecgonine methyl ester **2** and *p*-tolyoyl-*l*-ecgonine methyl ester **3** both undergo the photochemical demethylation reaction. In these cases, the yield of demethylated products as well as the quantum yields based on formaldehyde formation are less than that of cocaine.

On the other hand, 1-methyl-3-piperidyl benzoate and 1-methyl-4-piperidyl benzoate both give benzoic acid and polymers, but no demethylated products. A Norrish Type II mechanism as illustrated in Scheme I accounts for the formation of both the benzoic acid and the polymer formed.

Scheme I



Scheme II illustrates a suggested mechanism for the demethylation consistent with the experimental data and photochemical theory (7). The reaction can proceed intermolecularly as well. The benzoate group absorbs the light and causes the amine to react, when and how the benzoate radical anion loses the extra electron is a matter of speculation. Though Scheme II illustrates the mechanism for an intramolecular reaction, only a trivial modification would be necessary to make it intermolecular. Both direct and sensitized irradiations of amines are known to give imine intermediates (8,9). In the case of cocaine, the imine intermediate is reactive and with the water present in methanol gives norcocaine **6** and formaldehyde. The fact that both direct and sensitized irradiations of amines are known to give imines complements the Scheme. To give partial experimental evidence on the charge transfer, fluoresence and phosphore-



Insert Scheme II

Table 1

Total Emission Spectra of Cocaine and Methyl Benzoate in Various Polar and Non-Polar Solvents (a).

	Methyl benzoate		Cocaine	
Solvent	Fluorescence	Phosphorescence	Fluorescence	Phosphorescence
n-Hexane	298	367, 382, 394 (b), 422	297	369, 384, 393 (b), 409
Carbon tetrachloride	300	367, 382, 390 (b), 406, 415	300	367, 383, 390 (b), 407
Ether	298	368, 382, 393 (b), 408, 417	300	369, 383, 394 (b), 408, 417
Tetrahydrofuran	298	368, 382, 392 (b), 407, 417 (sh)	300	369, 382, 394 (b), 408, 417 (sh)
Dimethyl-sulphoxide	299	371, 396 (b), 409 (sh)	300	372, 397, 412 (b), 420 (sh)
Acetonitrile	298	398, 425 (b), 457	300	433 (no fine structure)
Methanol	299	366, 380, 391 (b), 405, 414	300	367, 382, 392 (b), 406, 415

(a) Cocaine and Methyl benzoate were used at a concentration of 1 x 10^{-3} *M* in all solvents. The emission spectra were recorded at liquid nitrogen temperatures. Excitation and emission band pass were 2 nm and λ ex (excitation) was 277 nm. (b) λ max in emission, sh = shoulder.

sence studies were undertaken (10).

The absorption spectra of cocaine and methyl benzoate exhibit virtually no band shift over a wide range of solvent polarity: cyclohexane, carbon tetrachloride, dimethyl-sulfoxide and acetonitrile, at least not in the magnitude of several kcal/mole change in the excited state energies. In a similar manner, the fluorescence bands were also virtually independent of solvent polarity, *cf.* Table 1. Hence, there is no solvent effect evident on the excited singlet state.

However, there is a significant solvent effect on the phosphoresence bands of cocaine and methyl benzoate, *cf.*, Table 1. For cocaine, there is an apparent dividing line between its spectra in the nonpolar solvents, carbon tetrachloride and cyclohexane, and the polar, non-hydrogen-bonding solvents, acetonitrile and dimethyl-sulfoxide. Tetrahydrofuran, of intermediate polarity, gives a phosphoresence band similar to those in the nonpolar solvents. Between *n*-hexane and acetonitrile, the band has "shifted" 40 nm. This is appropriate for inter- and intramolecular charge transfer complexes where the donor and acceptor are separated or the chromophores are isolated from one another such as in the cocaine molecule.

Closer examination of the carbon tetrachloride, acetonitrile and combination solvent spectra illustrates that though there is some band shifting occurring, the primary event is the reduction in intensity of the longer wavelength bands, which can now be assigned to have charge

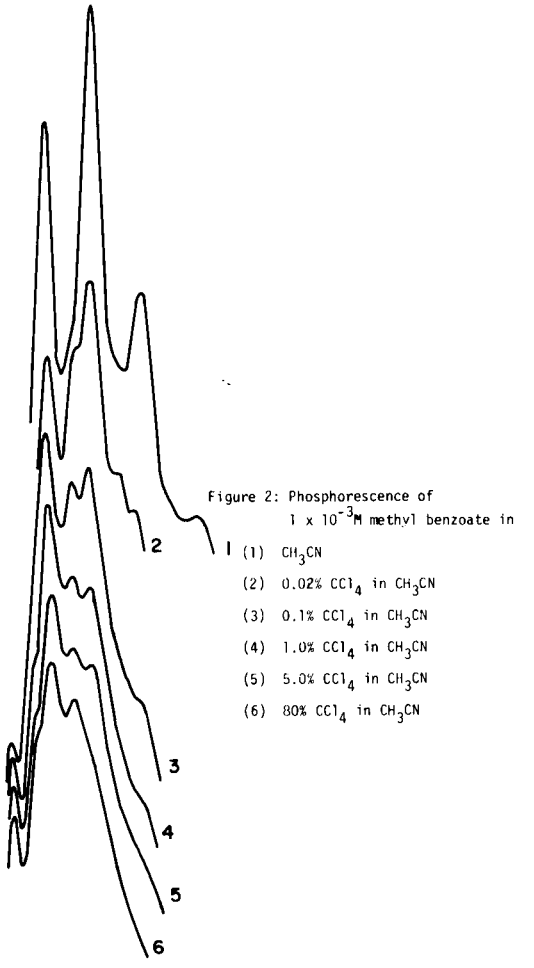


Figure 2: Phosphorescence of 1 x 10^{-3}M methyl benzoate in
(1) CH_3CN
(2) 0.02% CCl_4 in CH_3CN
(3) 0.1% CCl_4 in CH_3CN
(4) 1.0% CCl_4 in CH_3CN
(5) 5.0% CCl_4 in CH_3CN
(6) 80% CCl_4 in CH_3CN

Table 2

Quantum Yield for Formaldehyde Formation

Compound	ϕ HCHO
Cocaine	0.01
p-Anisoyl-*l*-ecgonine methyl ester	0.0086
p-Toluoyl-*l*-ecgonine methyl ester	0.008

transfer characters. With decreasing solvent polarity, there is a concomittant intensity increase in the short wavelength bands, *cf.* Figure 2. Thus, the longer wavelength bands are assigned to have a charge transfer character and the shorter ones, a non-charge transfer nature. Thus, the triplet state has a charge transfer component and a non-charge transfer component in equilibrium with one another as predicted in Scheme II, and the two states are separated by about 7.3 kcal/mole based on the separation of λ max in carbon tetrachloride and acetonitrile.

EXPERIMENTAL

Melting points and mixed melting points were obtained on a Fisher-Johns melting point apparatus and are corrected. Ultraviolet (uv) spectra were obtained with a Cary Model 14 spectrophotometer. A Perkin-Elmer MPF-44A spectrophotofluorometer with phosphorescence attachment was used for the measurement of fluorescence and phosphorescence spectra. Infrared (ir) spectra were recorded with IR-12 spectrophotometer. Nuclear magnetic resonance spectra were recorded with a Varian Associate A-60 instrument using tetramethylsilane as an internal standard and carbon tetrachloride as the solvent. The chemical shifts are given in δ values. Mass spectra (70 eV) were obtained on DuPont model 21-491 mass spectrometer. A Beckman model 25 spectrophotometer was used for measuring the ferrous ion concentration as well as formaldehyde concentration during quantum yield determination. Microanalyses were performed by Chemalytics, Inc., Tempe, Arizona. Thin layer chromatography was done on glass plates coated with aluminium oxide G (E. Merck AG. Darmstadt, Germany). The neutral alumina (Brockman Activity I, 80-200 mesh) for column chromatography was purchased from Fisher Scientific Company, Fair Lawn, New Jersey. All the spectrograde solvents were purchased from Burdick and Jackson Laboratories, Inc., Muskegon, Michigan.

Chemicals.

Tropine, tropinone, cyclohexanol, 3-hydroxy and 4-hydroxy-*N*-methylpiperidines and 1:10-phenanthroline monohydrate were purchased from Aldrich Chemical Company, Inc., Milwaukee, Wisconsin. Acetylacetone was supplied by British Drug House, Ltd., Poole, England. Cocaine hydrochloride was obtained form Merck and Co., Inc., Rahway, New Jersey.

1-Methyl-3-piperidyl Benzoate.

To a solution of 3-hydroxy-*N*-methylpiperidine (11.5 g., 0.1 mole) in 50 ml. of dry *n*-hexane was added dropwise benzoyl chloride (14 g., 0.1 mole) and the reaction mixture was stirred for 2 hours. The solid compound obtained by filtration of *n*-hexane, was neutralized with sodium carbonate solution and extracted with ether. The ether layer was washed with water, dried over anhydrous sodium sulphate and evaporated to yield a yellowish liquid. This liquid was distilled at 158-160°/11 mm [lit. (12) 94-97°/0.05 mm] to yield 16.64 g. (76%) of 1-methyl-3-piperidyl benzoate; uv (methanol): 270 nm (ε, 2,000), 280 (1,500) and 282 (1,300); ir (carbon tetrachloride): C=O 1710 cm^{-1}; nmr (carbon tetrachloride): δ 2.25 (S, 3H, N-CH_3), 5.00 (m, 1H, *CH*OCOC_6H_5), 7.4 (m, 3H, C_6H_5), and 8.03 (m, 2H, C_6H_5).

1-Methyl-4-piperidyl Benzoate.

As described above, 14 g. (0.1 mole) of benzoyl chloride was added dropwise to a solution of 11.5 g. (0.1 mole) of 4-hydroxy-*N*-methylpiperidine in 50 ml. of dry *n*-hexane with constant stirring. The resulting mixture was stirred for 2 hours. After work-up the resultant liquid was distilled at 161-163°/10 mm [lit. (13) hydrochloride, m.p. 219-220°] to yield 18.4 g. (84%) of 1-methyl-4-piperidyl benzoate; uv (methanol): 274 mm (ε, 1,000) and 282 (800); ir (carbon tetrachloride): C=O 1710 cm^{-1}; nmr (carbon tetrachloride): δ 2.25 (S, 3H, N-CH_3), 5.00 (m, 1H, *CH*OCOC_6H_5), 7.4 (m, 3H, C_6H_5), 8.03 (m, 2H, C_6H_5).

Pseudotropine.

Commercial tropinone was distilled to get a pure compound which melted at 41-43° [lit. (14) m.p. 42°]. Dry toluene (5 ml.) and 1.2 g. of sodium metal were placed in a three-necked flask fitted with reflux condenser carrying a guard tube, magnetic stirrer and a separatory funnel. The separatory funnel was charged with 2.5 g. of tropinone dissolved in 5 ml. of dry toluene and 3 ml. of isobutyl alcohol. The flask was heated to boiling and the solution in the separatory funnel was added slowly (10 minutes) with stirring. After addition, the reaction mixture was further refluxed for 3 hours, cooled and 30 ml. of water was added to decompose the sodium isobutoxide. The aqueous layer was separated and extracted with toluene (100 ml.). A red layer was separated from the combined toluene layer and discarded. Removal of the toluene gave a reduction product which was recrystallized from benzene-petroleum ether (35-49°) in 87% (2.5 g.) yield, m.p. 108-109° [lit. (15) m.p. 106-108°].

Benzoyl Pseudotropine (Tropacocaine).

Pseudotropine (1.412 g., 0.01 mole) and 11.25 g. (0.08 mole) of freshly distilled benzoyl chloride were placed in a 50-ml. flask fitted with a reflux condenser and guard tube. The reaction mixture was refluxed gently with continuous stirring for 2 hours.

On cooling, white crystals of benzoyl pseudotropine hydrochloride separated out which were filtered and washed with 20 ml. of dry benzene. The hydrochloride was placed in a separatory funnel containing 100 ml. of ether and extracted with 10% sodium carbonate solution. The ether layer was washed with water, dried over anhydrous sodium sulphate. Removal of ether yielded benzoyl pseudotropine which was recrystallized from ethanol, m.p. 49° [lit. (16) m.p. 49°], yield 79% (1.95 g.); uv (methanol): 275 nm (ε, 880) and 281 (710); ir (carbon tetrachloride): C=O 1722 cm^{-1}; nmr (carbon tetrachloride): δ 2.3 (s, 3H, N-CH_3); 5.18 (m, 1H, *CH*OCOC_6H_5), 7.47 (m, 3H, C_6H_5) and 8.15 (m, 2H, C_6H_5).

Benzoyl Tropine (**4**).

In a similar manner to the above, 1.412 g. (0.01 mole) of tropine and 11.25 g. (0.08 mole) of benzoyl chloride was refluxed in a 50-ml. flask for 2 hours. On work-up, the ether layer gave a white solid which was recrystallized from ethanol, to yield 2.07 g. (89%) of the hydrochloride of **4**, m.p. 274-275° [lit. (17) m.p. 275°]; uv (methanol): 273 nm (ε, 700) and 280 (530); ir

(carbon tetrachloride): C=O 1718 cm^{-1}; nmr (carbon tetrachloride): δ 2.3 (s, 3H, N-CH_3), 5.25 (m, 1H, C*H*OCOC_6H_5), 7.5 (m, 3H, C_6H_5), and 8.15 (m, 2H, C_6H_5).

l-Ecgonine Hydrochloride.

A solution of cocaine hydrochloride 10.2 g. (0.03 mole) in 100 ml. of 2*N* hydrochloric acid was refluxed for 8 hours. The reaction mixture was cooled and extracted with ether to remove benzoic acid. The white solid was obtained on the evaporation of acidic layer on rotatory evaporator and recrystallized from ethanol, m.p. 246° [lit. (18) m.p. 246°], yield 90% (6 g.).

l-Ecgonine Methyl Ester.

To a solution of *l*-ecgonine hydrochloride (5.525 g., 0.025 mole) in 100 ml. of absolute methanol was added 10 ml. of concentrated sulfuric acid slowly and the solution was refluxed on water bath for 6 hours. The reaction mixture was cooled and methanol was removed under reduced pressure. The residue was neutralized with 10% sodium carbonate solution and extracted with chloroform. The chloroform layer was dried over anhydrous sodium sulphate and filtered. The chloroform was removed from filtrate to yield 3.9 g. (78%) of *l*-ecgonine methyl ester; hydrochloride, m.p. 210-212° dec. [lit. (19) m.p. 212° dec.]; ir (carbon tetrachloride): C=O 1720 and OH 3530 cm^{-1}; nmr (carbon tetrachloride): δ 2.15 (s, 3H, N-CH_3) and 3.7 (s, 3H, $COOCH_3$).

p-Anisoyl-*l*-ecgonine Methyl Ester (**2**).

A mixture of *l*-ecgonine methyl ester (0.995 g., 0.005 mole) and *p*-anisoyl chloride (6.816 g., 0.04 mole) in a 50-ml. round bottom flask was refluxed gently with constant stirring for 4 hours, poured in 30 ml. of water, neutralized with 10% sodium carbonate solution and extracted with 100 ml. of ether. The ether layer was dried over anhydrous sodium sulphate. Removal of ether under reduced pressure yielded crude **2** The crude *p*-anisoyl-*l*-ecgonine methyl ester was purified by column chromatography (neutral alumina, benzene) to give 0.70 g. (42%) colorless liquid **2** The hydrochloride melted at 185°; uv (methanol): 272 nm (ε, 7,200) and 282 (2,400); ir (carbon tetrachloride): C=O 1715 and 1755 cm^{-1}; nmr (carbon tetrachloride): δ 2.2 (s, 3H, N-CH_3), 3.66 (s, 3H, $COOCH_3$), 3.83 (s, 2H, OCH_3), 5.2 (m, 1H, C*H*O$COC_6H_4OCH_3$), 6.88 (d, 2H, J = 8 cps, C_6H_4) and 8.00 (d, 2H, J = 10 cps, C_6H_4).

Anal. Calcd. for $C_{18}H_{23}NO_5 \cdot HCl$: C, 58.45; H, 6.49; N, 3.78. Found: C, 58.37; H, 6.30; N, 3.50.

p-Toluoyl-*l*-ecgonine Methyl Ester (**3**).

l-Ecgonine methyl ester (0.995 g., 0.005 mole) and *p*-toluoyl chloride (6.182 g., 0.04 mole) were placed in a 50-ml. round bottomed flask fitted with reflux condenser carrying a guard tube. The reaction mixture was refluxed on a hot plate with constant stirring for 4 hours. The reaction mixture was cooled and worked up as in case of **2** to get crude product **3** Finally the purification of crude product was achieved by column chromatography (neutral alumina, benzene) to yield 0.64 g. (40%) of **3** The hydrochloride of *p*-toluoyl-*l*-ecgonine methyl ester melted at 162°; uv (methanol): 270 nm (ε, 1,020) and 282 (540); ir (carbon tetrachloride): C=O 1722 and 1720 cm^{-1}; nmr (carbon tetrachloride): δ 2.2 (s, 3H, N-CH_3), 2.4 (s, 3H, CH_3) 3.66 (s, 3H, $COOCH_3$), 5.2 (m, 1H, C*H*O$COC_6H_4 \cdot CH_3$), 7.2 (d, 2H, J = 8 cps, C_6H_4) and 7.94 (d, 2H, J = 9 cps, C_6H_4).

Anal. Calcd. for $C_{18}H_{23}NO_4 \cdot HCl$: C, 61.05; H, 6.78; N, 3.96. Found: C, 60.79; H, 6.78; N, 4.01.

Phenylacetyl-*l*-ecgonine Methyl Ester.

In a 50-ml. round bottomed flask 0.796 g. (0.004 mole) of *l*-ecgonine methyl ester and 4.95 g. (0.032 mole) of phenylacetyl chloride was refluxed (19). The mixture was stirred throughout the reaction time. After 4 hours refluxing, the reaction mixture was cooled and worked up as in case of **2** The pure phenylacetyl-*l*-ecgonine methyl ester was isolated by column chromatography (neutral alumina, benzene), yielding 0.77 g. (60%). Its hydrochloride was very hydroscopic. This compound was further characterized by its spectral data; uv (methanol): 254 nm (ε, 285), 259 (300) and 265 (230); ir (carbon tetrachloride): C=O 1730 and 1745 cm^{-1}; nmr (carbon tetrachloride): δ 2.15 (s, 3H, N-CH_3), 3.45 (s, 2H, O$COCH_2C_6H_5$), 3.53 (s, 3H, $COOCH_3$) 4.83 (m, 1H, C*H*O$COCH_2C_6H_5$) and 7.23 (s, 5H, C_6H_5).

Cocaine (**1**).

Free cocaine was obtained by neutralization of cocaine hydrochloride with 10% sodium carbonate followed by extraction with ether and recrystallization from ethanol, m.p. 98-99° [lit. (20) m.p. 98° [lit. (20) m.p. 98°]; uv (methanol): 274 nm (ε, 1,860) and 282 (ε, 1,540); ir (carbon tetrachloride): C=O nmr (carbon tetrachloride): δ 2.21 (s, 3H, N-CH_3), 3.71 (s, 3H, $COOCH_3$), 5.5 (m, 1H, C*H*OCOC_6H_5), 7.6 (m, 3H, C_6H_5) and 8.2 (m, 2H, C_6H_5).

Determination of Emission Spectra.

The total emission spectra of cocaine and methyl benzoate in various solvents were measured at liquid nitrogen temperature on a Perkin-Elmer MPF-44A spectrofluorometer and recorded in Table 1.

Irradiation of Cocaine.

Cocaine (0.4545 g., 0.0015 mole) was dissolved in 12 ml. of freshly distilled methanol and placed in a cylindrical quartz vessel inside a Corex filter sleeve, purified nitrogen was bubbled for 20 minutes. The sample was irradiated for 43 hours in a Rayonet reactor fitted with 300 nm lamps. The removal of solvent under vacuum left a yellow oil. The oil was dissolved in 20 ml. of chloroform and extracted with 10% sodium carbonate solution. The basic layer was neutralized with dilute hydrochloric acid and extracted with ether to get benzoic acid. The removal of ether yielded white solid which on recrystallization from hot water gave 0.0128 g (7%) benzoic acid m.p. 121-122°, mixed m.p. 121-122° [lit. (21) m.p. 122°]. After drying the chloroform layer over anhydrous sodium sulphate, the chloroform was removed to give yellow oil. This oil was purified by column chromatography (neutral alumina, 3:2 benzene-chloroform) to yield 0.087 g. (20%) norcocaine, m.p. 80-82°, [lit. (22) m.p. 82°] and 0.340 g. of cocaine. Further norcocaine was identified by its mass spectrum m/e 289 (M^+) and the absence of the *N*-methyl proton signal (at δ 2.21) in the nmr spectrum. Formaldehyde was identified in the reaction mixture by directly preparing its dimedone derivative, m.p. 188-189° [lit. (23) m.p. 189°] and quantitative determination by the Nash reagent (24).

Irradiation of Cocaine Hydrochloride.

Cocaine hydrochloride (0.509 g., 0.0015 mole) in 12 ml. of methanol was irradiated under identical conditions of cocaine and worked up. There was no reaction.

Irradiation of Cyclohexyl Benzoate.

A solution of cyclohexyl benzoate (1.836 g., 0.009 mole) in 12 ml. of freshly distilled methanol was irradiated for 43 hours in a Rayonet reactor fitted with 300-nm lamps. After removal of solvent, a colorless liquid was obtained which was taken in chloroform and extracted with 10% sodium carbonate solution.

The basic layer on neutralization with dilute hydrochloric acid and extraction with ether did not yield benzoic acid. The chloroform layer after removal of solvent yielded a colorless liquid which infrared and nmr spectrum were identical to the spectrum of cyclohexylbenzoate.

Irradiation of 1-Methyl-3-piperidyl Benzoate.

1-Methyl-3-piperidyl benzoate (1.2172 g., 0.0055 mole) in 12 ml. of methanol was placed in a quartz vessel inside a Corex filter sleeve. After bubbling nitrogen free from oxygen for 20 minutes, the sample was irradiated for 43 hours in a Rayonet reactor fitted with 300-nm lamps. Removal of solvent yielded a light yellow oil which was taken in 20 ml. of chloroform and extracted with 10% sodium carbonate solution. The basic layer was neutralized with dilute hydrochloric acid and extracted with ether. The ether extract, after drying over anhydrous sodium sulphate and removing solvent, gave white solid. This solid was recrystallized from hot water to yield 0.110 g. (15%) benzoic acid, m.p. 122°. The removal of solvent from chloroform layer under reduced pressure left a light yellow oil. The thin layer chromatography of this oil showed the starting material and a polymer. Nash reagent test of irradiated solution did not show formaldehyde formation.

Irradiation of 1-Methyl-4-piperidyl Benzoate.

A solution of 1-methyl-4-piperidyl benzoate (1.54 g., 0.007 mole) in 12 ml. of freshly distilled methanol was irradiated under the similar experimental conditions of 1-methyl-3-piperidyl benzoate. After work up, 0.109 g. (13%) of benzoic acid was obtained, m.p. 122°. The thin layer chromatography of irradiated product after removal of benzoic acid showed the starting material and a polymer. The irradiated solution did not contain formaldehyde.

Irradiation of 1-Methyl-4-piperidyl Benzoate.

A solution of 1-methyl-4-piperidyl benzoate (1.54 g., 0.007 mole) in 12 ml. of freshly distilled methanol was irradiated under the similar experimental conditions of 1-methyl-3-piperidyl benzoate. After work up, 0.109 g. (13%) of benzoic acid was obtained, m.p. 122°. The thin layer chromatography of irradiated product after removal of benzoic acid showed the starting material and a polymer. The irradiated solution was tested against Nash reagent for the formaldehyde formation during irradiation of 1-methyl-4-piperidyl benzoate and was found to be devoid of formaldehyde.

Irradiation of Benzoyl Pseudotropine (**5**).

A solution of benzoyl pseudotropine (0.7566 g., 0.0031 mole) in 12 ml. of methanol was irradiated for 43 hours under the above described conditions. The work up of the irradiated solution gave (< 2%) benzoic acid and a yellow oil. This oil on purification by column chromatography (neutral alumina, chloroform, yielded 0.106 g. (15%) of benzoyl norpseudotropine, while 0.590 g. of benzoyl pseudotropine was recovered from the column. The hydrochloride of the demethylated product melted at 232° [lit. (15) m.p. 232-233°]. This compound was further characterized by its mass spectrum m/e 231 (M^+) and the absence of the *N*-methyl proton signal at (δ 2.3) in the nmr spectrum.

Irradiation of Benzoyl Tropine (**4**).

Benzoyl tropine (0.490 g., 0.002 mole) was dissolved in 12 ml. of methanol and the resulting solution was irradiated for 43 hours in a quartz vessel inside a Corex filter sleeve using Rayonet reactor fitted with 300-nm lamps. Nitrogen free from oxygen was bubbled in the reaction solution for 20 minutes before irradiation. Similar work up of the reaction mixture yielded benzoic acid (<1%) and a yellow oil. The isolation of demethylated product from the yellow oil was achieved by column chromatography (neutral alumina, 1:4 benzene-chloroform) to yield 0.0483 g. (13%) of benzoyl nortropine, m.p. 166-168°, while benzoyltropine, 0.410 g. was recovered from the column. This product was also identified by its mass spectrum m/e 231 (M^+) and the absence of the *N*-methyl proton signal at (δ 2.3) in the nmr spectrum.

Irradiation of *p*-Anisoyl-*l*-ecgonine Methyl Ester (**2**).

p-Anisoyl-*l*-ecgonine methyl ester (0.10 g., 0.0003 mole) was dissolved in 12 ml. of methanol and placed in a quartz vessel inside a Corex filter sleeve. Nitrogen free from oxygen was bubbled for 20 minutes and the solution was irradiated using 300-nm lamps. After 43 hours irradiation, the reaction mixture was worked up and a viscous yellow liquid was obtained. Finally the demethylated product of **2** was isolated by column chromatography (neutral alumina, 3:2 benzene-chloroform)' The yield of *p*-anisoylnor-*l*-ecgonine methyl ester was 0.0112 g. (11%) along with 0.073 g. of recovered starting material. The structure of the demethylated product of **2** was confirmed by its mass spectrum m/e 319 (M^+) and the absence of the *N*-methyl proton signal at (δ 2.2) in the nmr spectrum.

Irradiation of *p*-Toluoyl-*l*-ecgonine Methyl Ester (**3**).

A solution of *p*-toluoyl-*l*-ecgonine methyl ester 0.117 g. (0.00037 mole) in 12 ml. of freshly distilled methanol was irradiated under similar experimental conditions to those used for **2** The irradiated reaction mixture was worked up to yield a viscous yellow liquid. The *p*-toluylnor-*l*-ecgonine methyl ester was separated from this yellow liquid by column chromatography (neutral alumina, 3:2 benzene-chloroform) in 6% (0.007 g.) yield along with 0.090 g. of recovered starting material. The structure of this demethylated product was assigned by its mass spectrum, m/e 303 (M^+), and the absence of the *N*-methyl proton signal at (δ 2.2) in the nmr spectrum.

Irradiation of Phenylacetyl-*l*-ecgonine Methyl Ester.

Dissolved 0.192 g. (0.0006 mole) of phenylacetyl-*l*-ecgonine methyl ester in 12 ml. of methanol and placed in a quartz tube. Nitrogen gas free from oxygen was bubbled into the reaction solution for 20 minutes. The sample was irradiated for 43 hours in a Rayonet reactor fitted with 253.7-nm lamps. The thin layer chromatography showed the presence of starting material along with polymer. Nash reagent test also showed that there was no formaldehyde formation during irradiation of phenylacetyl-*l*-ecgonine methyl ester.

Determination of Quantum Yields.

A methanol solution of cocaine ($10/3 \times 10^{-3}$ *M*), *p*-anisoyl-*l*-ecgonine methyl ester ($10/3 \times 10^{-3}$ *M*) or *p*-toluoyl-*l*-ecgonine methyl ester ($10/3\ 10^{-3}$ *M*) were transferred into quartz tubes which were constructed to facilitate sealing. These tubes were degassed and sealed (three freeze-pump-thaw cycles). The samples were irradiated in a Southern New England ultraviolet merry-go-round apparatus (24) fitted with a medium pressure Hg arc employing $NiSO_4$-$CoCl_2$-$BiCl_3$ filter (25). Potassium ferrioxalate actinometry was employed (26). Quartz tubes containing potassium ferrioxalate (0.006 *M*) in 0.1 *N* sulphuric acid were irradiated prior to and at the end of each experiment. The production of ferrous ion was determined by measuring the optical density of its complex with 1:10-phenanthroline at 510 nm and using a calibration graph for ferrous ion (26). The quantum yield for ferrous ion at 282 nm was taken as 1.24 (26). The formaldehyde produced during irradiation of **1**, **2** or **3** was measured by Nash reagent (27). The results are given in Table 2.

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