Rearrangement of Arylhydrazones of Aromatic and Arylaliphatic Carbonyl Compounds to Biphenyl Derivatives. 3

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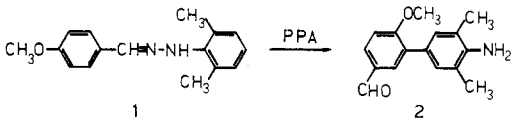
The behavior toward polyphosphoric acid of arylhydrazones of aromatic carbonyl compounds (anisaldehyde, substituted benzophenones, (4-methoxyphenyl)glyoxylic acid esters) and arylaliphatic ketones (4-methoxy- and 4-aminoacetophenone) is described. Biphenyl derivatives are formed through a [5,5] sigmatropic rearrangement, which often occurs in competition with the expected Fischer indole synthesis and, in the case of the 4-aminoacetophenone 2,6-dimethylphenylhydrazone, with a completely new [3,5] sigmatropic rearrangement.

We recently communicated[1,2] that arylhydrazones of aromatic and arylaliphatic carbonyl compounds undergo a new rearrangement promoted by polyphosphoric acid to biphenyl derivatives. In order to check the scope of this new reaction, we have tested many other substrates presenting various structural features either in the carbonyl or the hydrazinic moiety.

We now report the results we have obtained in the course of this investigation and the relative experimental details.

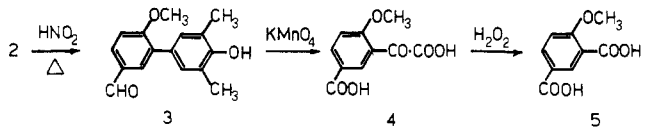
Arylhydrazones of aromatic aldehydes did not generally give encouraging results when treated with polyphosphoric acid; however, the 2,6-dimethylphenylhydrazone of anisaldehyde (1) gave in moderate yields (40%) a compound which was characterized at first chemically and spectroscopically and then by oxidative degradation.



1 2

This product was 3-(4-amino-3,5-dimethylphenyl)-4-methoxybenzaldehyde (2), as confirmed by the presence of a primary aromatic amino group and an aldehyde function and by the equivalence of the NMR signals of the two methyl groups on the aromatic ring, proving that the diphenyl system had formed at the para position of the benzene ring of the hydrazine moiety.

To determine which aromatic position of the carbonyl counterpart was the site of formation of the new bond, we converted amino aldehyde 2, via its diazonium salt, into the corresponding phenol derivative 3, which was oxidized



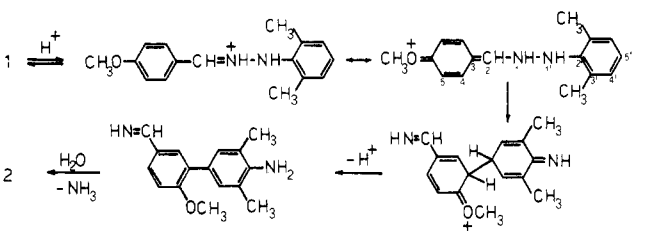
3 4 5

in turn with $KMnO_4$: the resulting α-keto carboxylic acid 4 gave the 4-methoxyisophthalic acid (5) by treatment with hydrogen peroxide in an alkaline solution.

The mechanism suggested for the formation of 2 from 1 is reported in Scheme I, and, as discussed later, it can be extended to all substrates examined so far.

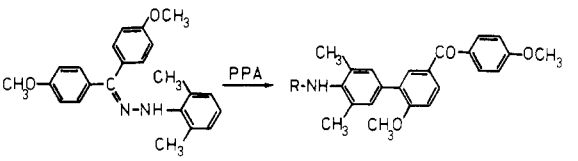
The protonated form of the substrate may be represented by a mesomeric structure with the positive charge localized on the methoxy group: two butadienylic systems would result, connected by the hydrazinic nitrogen atoms.

Scheme I



Nitrogen–nitrogen bond fission and simultaneous bond formation between carbon atoms 5 and 5′ afford **6**, from which aldimine **7** and, after hydrolysis, the final product **2** originate. According to the Woodward–Hoffmann rules,[3] this reaction can be coded as a [5,5] sigmatropic rearrangement.

The results were more satisfying in the case of the 2,6-dimethylphenylhydrazone of 4,4′-dimethoxybenzophenone (8), which gave the biphenyl derivative **9a** in a very good yield.



8

9a, R = H
b, R = COC_6H_5

Structure **9a** was deduced from spectral and chemical data, but was definitively confirmed by the independent synthesis of its benzoyl derivative **9b** starting from **2**.

Amino aldehyde **2** was subjected to the following transformations: the amino group was protected as a benzamido group and then the carbonyl function was oxidized to a carboxy group, which was converted into the acid chloride and finally condensed with anisole in the presence of $AlCl_3$.

The reaction with polyphosphoric acid has been successfully studied for the following arylhydrazones of substituted benzophenones: 4,4′-dimethoxybenzophenone phenylhydrazone (**10a**) and 4-methoxybenzophenone phenylhydrazone (**10b**), 2-methylphenylhydrazone (**10c**), and 2,6-dimethylphenylhydrazone (**10d**). The expected biphenyl derivatives **11a–d** were always isolated in good yields.

It is worth noting that, in the case of 4-methoxybenzophenone arylhydrazones, the rearrangement of the aryl

(1) R. Fusco and F. Sannicolò, *Tetrahedron Lett.*, 3163 (1977).
(2) R. Fusco and F. Sannicolò, *Tetrahedron Lett.*, 1233 (1978).
(3) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry", Academic Press, New York, 1970, p 114.

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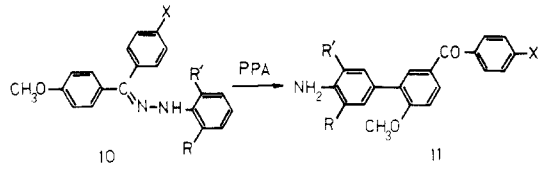


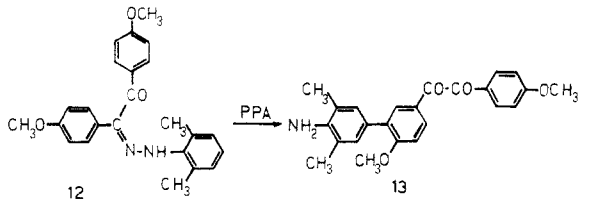
10 11

a, X = OCH_3, R = R′ = H; b, X = H, R = R′ = H; c, X = H, R = H, R′ = CH_3; d, X = H, R = R′ = CH_3

group involves the aromatic ring carrying the methoxy substituent; this result is in agreement with the mechanism proposed above which requires as the driving force for these reactions the presence of an electron-donating substituent para to the carbonyl group which is capable of allowing the delocalization of the positive charge.

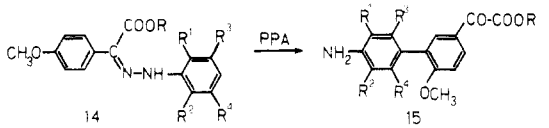
This view is strongly supported by the observation that unsubstituted arylhydrazones of benzophenone or those with electron-withdrawing substituents do not undergo this kind of rearrangement but rather undergo transformations of a different nature.[4]

The biphenyl rearrangement was observed even in the case of the 2,6-dimethylphenylhydrazone of anisil (**12**), giving the α-diketone **13**.



12 13

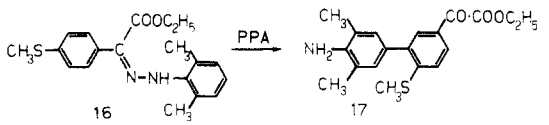
Biphenyl derivatives were obtained in excellent yields from a few arylhydrazones of (4-methoxyphenyl)glyoxylic acid esters. The following substrates were treated with polyphosphoric acid: phenylhydrazone **14a**, 2,6-dimethyl- and 3,5-dimethylphenylhydrazones **14b,c**, 2-phenylphenylhydrazone **14d**. General formula **15** summarizes the rearranged products.



14 15

a, $R^1 = R^2 = R^3 = R^4$ = H; b, $R^1 = R^2 = CH_3$, $R^3 = R^4$ = H; c, $R^1 = R^2$ = H, $R^3 = R^4 = CH_3$; d, $R^1 = C_6H_5$, $R^2 = R^3 = R^4$ = H

Structures for these products were generally assigned on the basis of chemical and spectral data. Structure **15b** was confirmed through a few transformations which interrelated it to the amino aldehyde **2**: thus, alkaline hydrolysis of **15b** and subsequent H_2O_2 oxidation, followed by benzoylation of the amino group of the product, gave the same acid previously obtained from **2** by benzoylation and permanganic oxidation. Similar behavior was shown by the 2,6-dimethylphenylhydrazone of ethyl (4-methylthiophenyl)glyoxylate (**16**) which gave **17**, the sulfur analogue of **15b**.

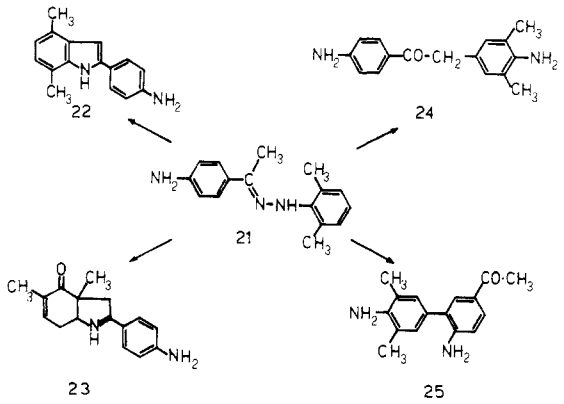


16 17

With regard to the [5,5] sigmatropic rearrangement, the importance of the electron-donating substituent "para" to the carbonyl group was confirmed even in the case of arylglyoxylic acid esters: in fact, arylhydrazones of phenylglyoxylic acid esters do not undergo this rearrangement but rather other transformations which will be reported elsewhere.[4]

(4) R. Fusco and F. Sannicolò, *Tetrahedron*, **36**, 161 (1980).

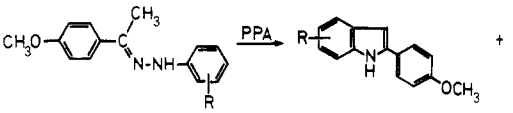
Scheme II



22 24 21 23 25

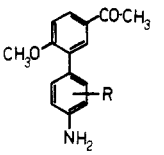
Interesting results have been obtained with arylhydrazones of 4-methoxy- and 4-aminoacetophenones, substrates with the necessary structural features for undergoing Fischer indolization.

The following reaction scheme summarizes the results obtained from 4-methoxyacetophenone phenylhydrazone (**18a**) and the 2,6- and 3,5-dimethylphenylhydrazones (**18b,c**).



18a, R = H
b, R = 2,6-Me_2
c, R = 3,5-Me_2

19a, R = H
b, R = 4,7-Me_2
c, R = 4,6-Me_2



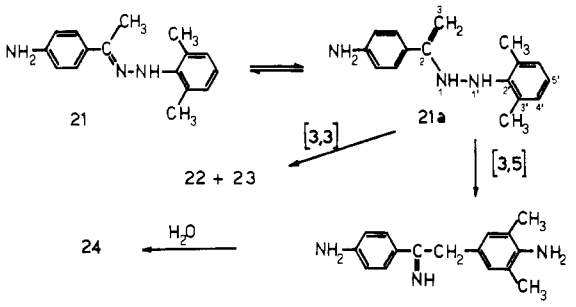
20a, R = H
b, R = 3′,5′-Me_2
c, R = 2′,6′-Me_2

As a first comment on these results, note that the new rearrangement surprisingly occurs even in the case of indolizable hydrazones. Second, the ratio in which indoles and biphenyl derivatives are formed is of interest as well.

From phenylhydrazone **18a**, much indole **19a** and little biphenyl derivative **20a** were formed. On the other hand indole **19b** was recovered in very poor yield from 2,6-dimethylphenylhydrazone **18b**, with the main product being the diphenyl derivative **20b**. In the case of substrate **18c**, the two reactions are competitive. It seems therefore that the electronic availability induced by the methyl groups in the hydrazine moiety of the substrate remarkably enhances the [5,5] sigmatropic rearrangement. Furthermore, a comparison of the results of the second and third reactions indicates that, in the case of hydrazone **18b** where the formation of indole **19b** involves a methyl group 1,2-shift, indole formation is further depressed by steric hindrance.

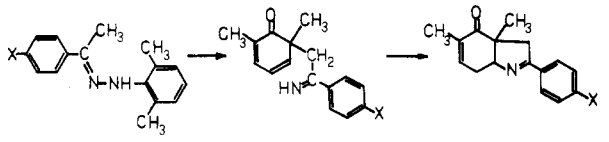
The behavior of 4-aminoacetophenone 2,6-dimethylphenylhydrazone (**21**) is more complex, with four products arising from different reaction paths. Scheme II reports

Scheme III



the structures of these compounds, as inferred from spectral data.

Biphenyl derivative **25** originates through the mechanism illustrated above involving the [5,5] sigmatropic rearrangement. Indole **22** results from Fischer indolization with a 1,2-shift of a methyl group.[5] Compound **23** arises from a reaction path hitherto recognized only by Carlin in the case of the 2,6-dimethylphenylhydrazone of acetophenone, which gave a product whose structure was proven chemically. The mechanism proposed by this author is illustrated as follows.[6]



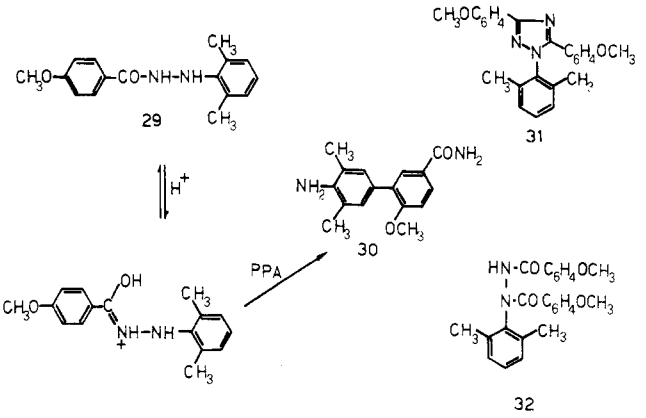
We report that this significant behavior seems to be rather general for 2,6-dimethylphenylhydrazones of acetophenones: in fact, we have provided evidence for this reaction course in the cases of 4-nitro- and 4-chloroacetophenone and even of 4-methoxyacetophenone when the rearrangement was carried out in refluxing formic acid.

Finally, diaminodimethyldesoxybenzoin **24** represents the first and hitherto unique case of a completely new rearrangement, interpreted as a deviation from Robinson's path of indole formation. The probable mechanism is reported in Scheme III.[7]

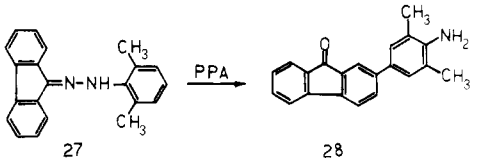
In the ene hydrazine **21a**, tautomer of the starting hydrazone, junction occurs between carbon atoms 3 and 3′ ([3,3] sigmatropic rearrangement) to give an intermediate to which two pathways are available: to the indole **22** or to the pseudoindolonic derivative **23**. However, the formation of a new bond between carbon atoms 3 and 5′ ([3,5] sigmatropic rearrangement) must be considered responsible for the formation of **24**.

The strong tendency for the [5,5] sigmatropic rearrangement to occur will now be demonstrated in the case of a few substrates which are somewhat different from those considered so far. The same product (**11a**) which was formed from 4,4′-dimethoxybenzophenone phenylhydrazone was isolated, although in poor yields, from polyphosphoric acid treatment of both the 4-chloro- and the 4-bromophenylhydrazones of 4,4′-dimethoxybenzophenone (**26a,b**). Without doubt the mechanism involved is the same in all three cases, but it is not easy to determine at which step of the reaction the reductive loss of the halogen atom occurs.[8]

Scheme IV



The same [5,5] sigmatropic rearrangement was observed even in the case of the 2,6-dimethylphenylhydrazone of fluorenone (**27**), which gave derivative **28** in low yields, whose structure was determined by oxidation to the known fluorenone-2-carboxylic acid.



In this case, the absence of any electron-donating substituent is counterbalanced by the large delocalizing ability of the fluorenyl system for the postive charge present on the protonated substrate.

The final example shows that the rearrangement under study is not confined to the field of arylhydrazones only: in fact, N^1-*p*-anisoyl-N^2-(2,6-dimethylphenyl)hydrazine (**29**) gives the biphenyl carboxyamide **30**, together with products **31** and **32** resulting from side reactions of less interest (Scheme IV).

Structure **30** was demonstrated by hydrolysis and benzoylation of the resulting amino acid to give the same product previously obtained from **2**.

The analogous structures of the protonated form of hydrazones and hydrazides account for the analogous reaction course.

Experimental Section

All melting points were determined on a Büchi apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 377 spectrophotometer: wavenumbers (ν) are given in reciprocal centimeters. NMR spectra were recorded on Varian A60 and EM-390 spectrometers with $CDCl_3$ as a solvent unless otherwise stated and tetramethylsilane as an internal standard; chemical shifts are given in δ units and refer to the center of the signal: s = singlet; d = doublet; m = multiplet; dd = double doublet. All new products gave correct elemental analyses (±0.4%).

Hydrazones. Hydrazones **10a**,[9] **b**[10] and **18a**[11] were already known in the literature and were prepared according to known routes.

2,6-Dimethylphenylhydrazone of Anysaldehyde (1). Equimolar amounts of anysaldehyde and (2,6-dimethylphenyl)-

(5) R. B. Carlin, W. O. Henley, Jr., and D. P. Carlson, *J. Am. Chem. Soc.*, **79**, 5712 (1957); R. B. Carlin, A. J. Magistro and G. J. Mains, *ibid.*, **86**, 5300 (1964); B. Healt-Brown and P. G. Philpott, *J. Chem. Soc.*, 7185 (1965).

(6) R. B. Carlin and M. S. Moores, *J. Am. Chem. Soc.*, **84**, 4107 (1962).

(7) G. M. Robinson and R. Robinson, *J. Chem. Soc.*, 639 (1918); 827 (1924).

(8) A few cases of indolization of (haloaryl)hydrazones with reductive detachment of the halogen are known: F. P. Robinson and R. K. Brown, *Can. J. Chem.*, **42**, 1940 (1964); R. B. Carlin and G. W. Larson, *J. Am. Chem. Soc.*, **79**, 934 (1957).

(9) H. Schnackenberg and R. Scholl, *Ber. Dtsch. Chem. Ges.*, **36**, 655 (1903).

(10) B. Overton, *Ber. Dtsch. Chem. Ges.*, **26**, 11 (1893).

(11) A. Koraczynsky and L. Kierzek, *Gazz. Chim. Ital.*, **55**, 361 (1925).

hydrazine[6] were reacted without solvent (exothermic reaction). The mixture was heated on a water bath for 30 min, diluted with Et_2O, washed with 5% HCl solution and 5% $NaHCO_3$ solution, and then dried (K_2CO_3). Removal of the solvent left a viscous oil which crystallized on standing; mp 50 °C (*i*-PrOH).

2,6-Dimethylphenylhydrazone of 4,4'-Dimethoxybenzophenone (8). This was prepared by refluxing a benzene solution (30 mL) of (2,6-dimethylphenyl)hydrazine[6] (1.58 g) and 4,4'-dimethoxythiobenzophenone[12] (3.0 g) in the presence of a trace of AcOH for 25 min. When the deep blue color of the solution disappeared and H_2S evolution ceased, the solvent was removed and the solid residue crystallized from hexane. Hydrazone **8** was obtained in a nearly quantitative yield as yellow crystals, mp 95–98 °C.

2-Methylphenylhydrazone of 4-Methoxybenzophenone (10c). This was prepared by refluxing a solution of 4-methoxybenzophenone (21.2 g), (2-methylphenyl)hydrazine hydrochloride (16 g),[3] and $AcONa{\cdot}3H_2O$ (15.0 g) in EtOH (150 mL) for 16 h. Hydrazone **10c** separated on cooling as a brown paste which crystallized when treated with warm AcOH: mp 91 °C; 25.5 g; ^1H NMR spectrum shows that the product is an about 1:1 mixture of two geometric isomers, 3.87 and 3.78 (2 s, OCH_3), 1.88 and 1.82 (2 s, CH_3).

2,6-Dimethylphenylhydrazone of 4-Methoxybenzophenone (10d). A mixture of 4-methoxybenzophenone (18.4 g), (2,6-dimethylphenyl)hydrazine hydrochloride[6] (15 g), $AcONa{\cdot}3H_2O$ (12 g), and EtOH (150 mL) was refluxed for 8 h. Hydrazone **10d** crystallized on cooling of the mixture: mp 120 °C (*i*-PrOH); 5 g.

2,6-Dimethylphenylhydrazone of Anisil (12). An ice-cold solution of 2,6-dimethylbenzenediazonium chloride, prepared from 2,6-dimethylaniline (2.0 g), 10% HCl solution (14 mL), and $NaNO_2$ (1.2 g), was poured into a stirred solution of 1,2-bis(4-methoxyphenyl)-1,3-propanedione[14] (4.8 g) and $AcONa{\cdot}3H_2O$ (4.5 g) in dioxane (100 mL) and water (25 mL). The resulting mixture was stirred at room temperature for 2 h, the dioxane was distilled at reduced pressure, and the product was extracted with ether. Removal of the solvent left a yellow residue (5.5 g) which was chromatographed on a silica gel column (150 g) by using a $CHCl_3$–MeOH (95:5) mixture as eluent. The final fractions gave the hydrazone **12** in a pure state: mp 94 °C (diisopropyl ether); 2.0 g.

Arylhydrazones of (4-Methoxyphenyl)glyoxylic Acid Esters (14), of Ethyl [4-(Methylthio)phenyl]glyoxylate (16), and of 4-Methoxy- (18) and 4-Aminoacetophenone (21). These substrates were usually prepared by refluxing equimolar amounts of the carbonyl compound and the proper hydrazine in alcoholic solution in the presence of traces of AcOH for 1 h. In the case of the phenylglyoxylic acid esters, two isomeric hydrazones, one yellow and one colorless, were generally formed, which could be separated by careful column chromatography (eluent $CHCl_3$). Both isomers gave the same rearranged products by treatment with PPA. Physical and spectral data are reported.

Phenylhydrazone of Methyl (4-Methoxyphenyl)glyoxylate (14a). Yellow isomer: mp 54 °C (*i*-PrOH); yield 62%; ^1H NMR 12.21 (1 H, s, NH), 7.2 (9 H, m, aromatic), 3.80 and 3.78 (2 × 3 H, 2 s, OCH_3 and $COOCH_3$). Colorless isomer: mp 125 °C (*i*-PrOH); yield 10%; ^1H NMR 8.14 (1 H, s, NH), 7.1 (9 H, m, aromatic), 3.84 (6 H, s, OCH_3 and $COOCH_3$).

2,6-Dimethylphenylhydrazone of Methyl (4-Methoxyphenyl)glyoxylate (14b). Yellow isomer: mp 64 °C (EtOH); yield 61%; ^1H NMR 12.18 (1 H, s, NH); 7.50 (2 H, d, aromatic ortho to the hydrazone function), 6.86 (5 H, m, aromatic), 3.85 and 3.78 (2 × 3 H, 2 s, OCH_3 and $COOCH_3$), 2.44 (6 H, s, $2CH_3$). Colorless isomer: mp 108 °C (diisopropyl ether); yield 10%; ^1H NMR 7.77 (1 H, s, NH), 7.29 (2 H, d, aromatic ortho to the hydrazone function), 6.97 (2 H, d, aromatic ortho to the OCH_3 group), 6.9 (3 H, s, aromatic of hydrazine moiety), 3.85 and 3.80 (2 × 3 H, 2 s, OCH_3 and $COOCH_3$), 2.25 (6 H, s, 2 CH_3).

3,5-Dimethylphenylhydrazone of Methyl (4-Methoxyphenyl)glyoxylate (14c). The yellow isomer directly crystallized from the reaction mixture: mp 100 °C (EtOH); yield 37%; ^1H NMR 12.17 (1 H, s, NH), 7.53 (2 H, d, aromatic ortho to the hydrazone function), 6.88 (4 H, m, aromatic), 6.60 (1 H, s, aromatic in position 4 of the hydrazine moiety), 3.8 (6 H, s, OCH_3 and $COOCH_3$), 2.29 (6 H, s, 2 CH_3).

2-Phenylphenylhydrazone of Ethyl (4-Methoxyphenyl)glyoxylate (14d). The yellow isomer directly crystallized from the reaction mixture: mp 105–107 °C (EtOH); yield 73%; ^1H NMR 11.78 (1 H, s, NH), 7.2 (13 H, m, aromatic), 4.09 (2 H, q, OCH_2CH_3), 3.75 (3 H, s, OCH_3), 1.16 (3 H, t, OCH_2CH_3).

2,6-Dimethylphenylhydrazone of Ethyl [4-(Methylthio)phenyl]glyoxylate (16). Yellow isomer: mp 74–76 °C (EtOH); yield 69%; ^1H NMR 7.7 (1 H, s, NH), 7.20 and 7.60 (2 × 2 H, AA'–BB' system, aromatic of ketone moiety), 6.80 (3 H, s, aromatic of hydrazine moiety), 4.20 (2 H, q, OCH_2CH_3), 2.45 (3 H, s, SCH_3), 2.20 (6 H, s, 2 CH_3), 1.25 (3 H, t, OCH_2CH_3). The colorless isomer was obtained only in a very small amount: ^1H NMR 7.7 (1 H, s, NH), 7.70 and 7.30 (2 × 2 H, AA'–BB' system, aromatic of ketone moiety), 7.05 (3 H, s, aromatic of hydrazine moiety), 4.40 (2 H, q, OCH_2CH_3), 2.50 (3 H, s, SCH_3), 2.45 (6 H, s, 2 CH_3), 1.35 (3 H, t, OCH_2CH_3).

2,6-Dimethylphenylhydrazone of 4-methoxyacetophenone (18b): mp 52–54 °C (EtOH).

3,5-Dimethylphenylhydrazone of 4-methoxyacetophenone (18c): mp 94 °C (MeOH).

2,6-Dimethylphenylhydrazone of 4-Aminoacetophenone (21). This substrate was obtained as an oxalate in 95% yield by addition of an equimolar amount of oxalic acid to the alcoholic solution of crude hydrazone; mp 180 °C dec.

2,6-Dimethylphenylhydrazone of 4-Chloroacetophenone. A solution of 4-chloroacetophenone (4.0 g), (2,6-dimethylphenyl)hydrazine hydrochloride[6] (4.5 g), and $AcONa{\cdot}3H_2O$ (4.0 g) in 50% AcOH (30 mL) was refluxed for 30 min. The title hydrazone separated when the mixture was cooled: 5.4 g; mp 60 °C (*i*-PrOH); ^1H NMR 7.68 and 7.33 (2 × 2 H, AA'–BB' system, aromatic of 4-chlorophenyl group), 6.97 (3 H, m, aromatic), 5.82 (1 H, br s, exchangeable with D_2O, NH), 2.43 (6 H, s, 2 CH_3), 2.26 (3 H, s, $CH_3C{=}N$).

2,6-Dimethylphenylhydrazone of 4-Nitroacetophenone. It was obtained in a 90% yield through the procedure described above for the analogous derivative of 4-chloroacetophenone: mp 104 °C; ^1H NMR 8.20 and 7.87 (2 × 2 H, AA'–BB' system, aromatic of 4-nitrophenyl group), 7.05 (3 H + 1 H exchangeable with D_2O, m, aromatic and NH), 2.42 (6 H, s, 2 CH_3), 2.31 (3 H, s, $CH_3C{=}N$).

4-Chloro- and 4-Bromophenylhydrazones of 4,4'-Dimethoxybenzophenone (26a,b). Equimolar amounts of 4,4'-dimethoxythiobenzophenone[12] and (4-chlorophenyl)-[15] or (4-bromophenyl)hydrazine[16] were refluxed in EtOH solution in the presence of a trace of AcOH until the blue color of starting thioketone completely disappeared, and EtOH was then distilled from the mixture under reduced pressure. Hydrazone **26a** was purified by crystallization from *i*-PrOH: mp 89–92 °C; yield 84%. Hydrazone **26b** was obtained as a brown viscous oil after column chromatography (eluent benzene) and was directly submitted to the reaction with PPA without further purification: yield 46%; ^1H NMR 7 (13 H, m, 12 aromatic and 1 NH), 3.78 (3 H, s, OCH_3), 3.70 (3 H, s, OCH_3).

2,6-Dimethylphenylhydrazone of Fluorenone (27). A solution of fluorenone (18 g), (2,6-dimethylphenyl)hydrazine hydrochloride[6] (17.3 g), and $AcONa{\cdot}3H_2O$ (13.6 g) in EtOH (180 mL) was refluxed for 3 h. Hydrazone **27** crystallized when the mixture cooled: mp 95 °C; 25.0 g (yield 83%).

Reaction of Hydrazones with Polyphosphoric Acid (PPA). This reaction was generally performed by addition of solid hydrazones in portions with stirring to a 10-fold excess by weight of PPA preheated to 80 °C on an oil bath. Sometimes an exothermic reaction was observed. The temperature was then increased to 100–120 °C and maintained there for 0.5–1 h to complete the reaction. The still warm mass was poured onto ice, and the resulting mixture, made basic with ammonia, was extracted

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with $CHCl_3$. Basic products were generally separated from the neutral fraction through the usual procedures and purified by careful column chromatography (silica gel).

Reaction of 1 with PPA (Exothermic Reaction). 3-(4-Amino-3,5-dimethylphenyl)-4-methoxybenzaldehyde (**2**) was obtained after chromatography (eluent $CHCl_3$) as a viscous oil in a 35% yield: ^1H NMR 9.52 (1 H, s, CHO), 7.7 and 7.0 (2 H and 3 H, respectively, 2 m, aromatic), 5.84 (3 H, s, OCH_3), 3.5 (2 H, br s exchangeable with D_2O, NH_2), 2.20 (6 H, s, 2 CH_3). Aldehyde **2** immediately reacts with (4-nitrophenyl)hydrazine in 50% AcOH solution to give an orange hydrazone (mp 226 °C) and with benzoyl chloride in pyridine solution to give a benzoyl derivative, mp 221 °C.

Reaction of 8 with PPA. The phosphoric acid salt of **9a** separated when the reaction mixture was poured onto water; it gave the 3-(4-amino-3,5-dimethylphenyl)-4,4′-dimethoxybenzophenone (**9a**) in a pure state: 32% yield; mp 149 °C; ^1H NMR 7.7 and 7.0 (4 H and 5 H, respectively, 2 m, aromatic), 3.82 (6 H, s, 2 OCH_3), 3.60 (2 H, br s, exchangeable with D_2O, NH_2), 2.19 (6 H, s, 2 CH_3).

Reaction of 10a with PPA. 3-(4-Aminophenyl)-4,4′-dimethoxybenzophenone (**11a**) was obtained in a pure state through column chromatography (eluent C_6H_6): 39% yield; mp 120 °C ($EtOH–H_2O$); ^1H NMR 7.72 (4 H, m, aromatic adjacent to CH_3O groups), 7.30 (2 H, m, aromatic adjacent to the NH_2 group), 6.80 (5 H, m, aromatic), 3.85 (6 H, s, 2 OCH_3), 3.67 (2 H, br s, exchangeable with D_2O, NH_2).

Reaction of 10b with PPA. 3-(4-Aminophenyl)-4-methoxybenzophenone (**11c**) was isolated either as the free base [mp 154 °C (*i*-PrOH)] or as its *N*-acetyl derivative: mp 221 °C; ^1H NMR 6.90 (2 H, d, aromatic ortho to the nitrogen atom), 8.1–7.0 (10 H, m, aromatic), 3.95 (5 H, s and br s exchangeable with D_2O, OCH_3 and NH_2).

Reaction of 10c with PPA. 3-(4-Amino-3-methylphenyl)-4-methoxybenzophenone (**11c**) was obtained in a pure state as a viscous oil through a column chromatography (eluent benzene): 41% yield; ^1H NMR 6.60 (1 H, d, aromatic in position ortho to the CH_3O group), 6.90 (1 H, d, aromatic in position ortho to the NH_2 group), 7.10–7.90 (9 H, m, aromatic), 3.84 (3 H, s, OCH_3), 3.50 (2 H, br s, exchangeable with D_2O, NH_2), 2.18 (3 H, s, CH_3).

Reaction of 10d with PPA. 3-(4-Amino-3,5-dimethylphenyl)-4-methoxybenzophenone (**11d**) was obtained in a pure state through column chromatography (eluent benzene): 37% yield; mp 114 °C; ^1H NMR 7.5 (7 H, m, aromatic), 7.1 (2 H, s, aromatic of xylidine ring), 6.9 (1 H, d, AB system, aromatic in position meta to the CO group), 3.80 (3 H, s, OCH_3), 3.56 (2 H, br s, exchangeable with D_2O, NH_2), 2.15 (6 H, s, 2 CH_3).

Reaction of 12 with PPA. 3-(4-Amino-3,5-dimethylphenyl)anisil (**13**) was obtained in a pure state as a yellow solid by column chromatography (eluent $CHCl_3$–AcOEt, 9:1): 33% yield; mp 170 °C (*i*-PrOH); ^1H NMR 8.9 (4 H, m, aromatic in position ortho to the CO groups), 7.0 (5 H, m, aromatic), 3.88 (6 H, s, 2 OCH_3), 3.60 (2 H, br s, exchangeable with D_2O, NH_2), 2.20 (6 H, s, 2 CH_3).

Reaction of 14a with PPA (Exothermic Reaction). A phosphoric acid salt precipitated when the mixture was poured onto water; it was filtered and suspended in water, and then a 35% NaOH solution was added; the insoluble compounds were filtered off, and the clear solution was made acidic with 35% HCl solution. The [3-(4-aminophenyl)-4-methoxyphenyl]glyoxylic acid was obtained in a 82% yield; mp 250 °C (AcOH). A solution of the latter (2.3 g) in MeOH (40 mL) was saturated with dry HCl and refluxed for 2 h. Two products were obtained, after the usual treatment, which were separated through column chromatography (eluent C_6H_6). Compound **15a** was first eluted (1.22 g) and refluxed in AcOH solution (10 mL) in the presence of Ac_2O (0.2 mL) to give the methyl [3-(4-acetaminophenyl)-4-methoxyphenyl]-glyoxylate: mp 177 °C (*i*-PrOH); ^1H NMR (Me_2SO) 10.43 (1 H, s, exchangeable with D_2O, NH), 7.6 (7 H, m, aromatic), 3.94 (2 × 3 H, 2 s, OCH_3 and $COOCH_3$), 1.63 (3 H, s, $COCH_3$). The second product eluted (0.55 g; eluent C_6H_6–AcOEt, 4:1) was refluxed with Ac_2O (0.4 mL) in acetic acid solution (15 mL) and gave the methyl [3-(4-acetaminophenyl)-4-methoxyphenyl]glyoxylate dimethyl ketal: mp 210 °C (*i*-PrOH); ^1H NMR (Me_2SO) 9.93 (1 H, s, exchangeable with D_2O, NH), 7.4 (7 H, m, aromatic), 3.79 and 3.69 (2 × 3 H, 2 s, $ArOCH_3$ and $COOCH_3$), 3.18 (6 H, s, 2 OCH_3 of the ketal group); 2.1 (3 H, s, OCH_3). Both the *N*-acetyl derivatives described above gave the same 4-nitrophenylhydrazone (mp 204 °C).

Reaction of 14b with PPA (Exothermic Reaction). A phosphoric acid salt separated when the mixture was poured into water; it was filtered, washed with water and acetone, and then decomposed with diluted ammonia to give methyl [3-(4-amino-3,5-dimethylphenyl)-4-methoxyphenyl]glyoxylate (**15b**): 85% yield; mp 124 °C (MeOH); ^1H NMR 7.92 (2 H, m, aromatic in position ortho to the carbonyl group), 6.98 (3 H, m, aromatic), 3.93 and 3.87 (2 × 3 H, 2 s, OCH_3 and $COOCH_3$), 3.53 (2 H, s exchangeable with D_2O, NH_2), 2.2 (6 H, s, 2 CH_3).

Reaction of 14c with PPA (Exothermic Reaction). A phosphoric acid salt separated when the mixture was poured into water; it was separated by decantation and treated with 5% $NaHCO_3$ solution. The free base was extracted with Et_2O, and the solid residue resulting from removal of the solvent was crystallized first from a cyclohexane–benzene (1:1) mixture and then from *i*-PrOH to give the methyl [3-(4-amino-2,6-dimethylphenyl)-4-methoxyphenyl]glyoxylate (**15c**): 85% yield; mp 138 °C; ^1H NMR 8.05 (1 H, m, aromatic in position 2), 7.08 (1 H, d, aromatic in position 6), 6.35 (2 H, s, aromatic of the aniline ring), 3.92 and 3.82 (2 × 3 H, 2 s, OCH_3 and $COOCH_3$), 3.38 (2 H, s, exchangeable with D_2O, NH_2), 1.90 (6 H, s, 2 CH_3).

Reaction of 14d with PPA. Ethyl [3-(6-aminobiphen-3-yl)-4-methoxyphenyl]glyoxylate (**15d**) was isolated after two subsequent column chromatographies (eluent $CHCl_3$–AcOEt, 95:5) and purified by crystallization of its hydrochloride ($EtOH–H_2O$): mp 112 °C (EtOH); yield 19%; ^1H NMR 7.7 (2 H, m, aromatic in position ortho to the carbonyl group), 7.1 (7 H, m, C_6H_5 and aromatics in positions 2 and 4 of the biphenyl group), 6.80 and 6.60 (2 × 1 H, 2 d, aromatic in position ortho to the CH_3O group and in position 5 of the biphenyl group), 4.26 (2 H, q, OCH_2CH_3), 3.75 (3 H, s, OCH_3), 3.48 (2 H, br s, exchangeable with D_2O, NH_2), 1.32 (3 H, t, OCH_2CH_3).

Reaction of 16 with PPA. Ethyl [3-(4-amino-3,5-dimethylphenyl)-4-(methylthio)phenyl]glyoxylate (**17**) was purified through its hydrochloride and isolated in about a 10% yield after crystallization from a diisopropyl ether–benzene mixture: mp 121 °C; ^1H NMR 7.80 (2 H, m, aromatic in positions 2 and 4), 7.15 (1 H, d, AB system, aromatic in position 5), 6.88 (2 H, s, aromatic in position meta to the NH_2 group), 4.35 (2 H, q, OCH_2CH_3), 3.50 (2 H, br s, exchangeable with D_2O, NH_2), 2.40 (3 H, s, SCH_3), 2.20 (6 H, s, 2 CH_3), 1.35 (3 H, t, OCH_2CH_3).

Reaction of Hydrazone 18a with PPA. 2-(4-Methoxyphenyl)indole (**19a**) separated in an 80% yield when the reaction mixture was poured into water; mp 225 °C[11] (AcOH). The basic fraction could be directly crystallized from *i*-PrOH to give the 3-(4-aminophenyl)-4-methoxyacetophenone (**20a**) in a pure state: mp 131 °C; ^1H NMR 7.9 (2 H, m, aromatic in position ortho to the carbonyl group), 7.33 (2 H, d, aromatic in position meta to the NH_2 group), 6.95 (1 H, d, aromatic in position ortho to the CH_3O group), 6.72 (2 H, d, aromatic in position ortho to the NH_2 group), 3.87 (3 H, s, OCH_3), 3.67 (2 H, br s, exchangeable with D_2O, NH_2), 2.57 (3 H, s, $COCH_3$).

Reaction of Hydrazone 18b with PPA. 3-(4-Amino-3,5-dimethylphenyl)-4-methoxyacetophenone (**20b**) was obtained in a 45% yield by direct crystallization of the basic fraction from a diisopropyl ether–benzene mixture: mp 110 °C; ^1H NMR 7.9 (2 H, m, aromatic in position ortho to the carbonyl group), 7.15 (2 H, s, aromatic of the xylidine group), 6.98 (1 H, d, aromatic in position ortho to the CH_3O group), 3.89 (3 H, s, OCH_3), 3.57 (2 H, br s, exchangeable with D_2O, NH_2), 2.58 (3 H, s, $COCH_3$), 2.24 (6 H, s, 2 CH_3). Only traces of the indole **19b** could be detected by TLC.

Reaction of Hydrazone 18c with PPA. The 4,6-dimethyl-2-(4-methoxyphenyl)indole (**19c**) separated when the reaction mixture was poured into water in a 35% yield: mp 130 °C (EtOH); ^1H NMR 7.9 (1 H, br s, NH), 7.40 (2 H, d, aromatic in position meta to the CH_3O group), 6.85 (3 H, m, aromatics in position ortho to the CH_3O group and in position 5), 6.62 and 6.55 (2 × 1 H, 2 s, aromatic), 3.75 (3 H, s, OCH_3), 2.48 and 2.35 (2 × 3 H, 2 s, 2 CH_3). The solid basic fraction was crystallized from EtOH to give 3-(4-amino-2,6-dimethylphenyl)-4-methoxyacetophenone (**20c**): about 60% yield; mp 139 °C (diisopropyl ether); ^1H NMR 7.7 (2 H, m, aromatic in position ortho to the carbonyl group), 7.0 (1

H, d, aromatic in position ortho to the CH_3O group), 7.47 (2 H, s, aromatic), 4.80 (3 H, s, OCH_3), 4.63 (2 H, br s, exchangeable with D_2O, NH_2), 2.54 (3 H, s, $COCH_3$), 1.91 (6 H, s, 2 CH_3).

Reaction of Hydrazone 21 with PPA. The reaction (10 g of **21**) was exothermic enough to increase the temperature from 80 to 100 °C. The acidic aqueous solution obtained when the reaction mixture was poured into water was filtered and made strongly alkaline with 35% NaOH solution was then extracted with CH_2Cl_2. The organic extract was dried over Na_2SO_4 and after removal of the solvent gave a residue (10 g) which was treated with AcOEt. Insoluble 2-(4-aminophenyl)-3a,5-dimethyl-3a,4,7,7a-tetrahydro-3*H*-pseudoindol-4-one (**23**) was recovered by filtration: yield 4.5 g; mp 217–218 °C (*i*-PrOH); ^1H NMR 6.70 (1 H, m, vinylic CH=), 7.70 and 6.75 (2 × 2 H, AA′–BB′ system, aromatic), 4.55 (2 H, br s, exchangeable with D_2O, NH_2), 4.20 (1 H, br s, CH_2CH), 2.95 (2 H, m, CH_2CH), 3.75 and 2.70 (2 H, dd, CH_2 of nitrogenated ring), 1.75 (3 H, m, CH_3 on unsaturated carbon), 1.37 (2 H, s, CH_3 on saturated carbon). The mother liquors from the crystallization of **23** gave, on being allowed to stand, the ω-(4-amino-3,5-dimethylphenyl)-4-aminoacetophenone (**24**): mp 214 °C; yield 0.20 g; ^1H NMR (Me_2SO) 6.70 (2 H, s, aromatic of xylidine ring), 7.70 and 6.55 (2 × 2 H, AA′–BB′ system, aromatic of acetophenone ring), 6.0 (2 H, br s, exchangeable with D_2O, NH_2), 4.35 (2 H, br s, exchangeable with D_2O, NH_2), 3.90 (2 H, s, CH_2), 2.03 (6 H, s, 2 CH_3). The AcOEt solution was evaporated to dryness and the residue (5.0 g) chromatographed on a silica gel column (150 g) with a $CHCl_3$–MeOH (95:5) mixture as an eluent. The first fractions eluted gave a solid which was crystallized from diisopropyl ether. 3-(4-Amino-3,5-dimethylphenyl)-4-aminoacetophenone (**25**, 1.0 g) was obtained in a pure state as a light brown solid: mp 193 °C; ^1H NMR (Me_2SO) 7.75 (1 H, s, aromatic in position 6), 6.95 (2 H, s, aromatic of the xylidine ring), 6.65 and 7.70 (2 H, dd, AB system, aromatic in positions 3 and 4), 4.25 (2 H, br s, exchangeable with D_2O, NH_2), 3.65 (2 H, br s, exchangeable with D_2O, NH_2), 2.50 (3 H, s, $COCH_3$), 2.25 (6 H, s, 2 CH_3).

The mother liquors from the crystallization of **25** were evaporated to dryness, and the brown residue (0.7 g) was chromatographed on a silica gel column (1.5 g) with Et_2O as an eluent. The initial fractions eluted afforded a solid which was crystallized from diisopropyl ether to give the 2-(4-aminophenyl)-4,7-dimethylindole (**22**) monohydrate: yield 0.4 g; mp 217–219 °C; ^1H NMR 8.20 (1 H, s, NH), 7.80 and 7.50 (2 H, dd, AB system, aromatic in position 5 and 6), 6.75 (4 H, m, aromatic), 3.90 (2 H, br s, exchangeable with D_2O, NH_2), 2.55 and 2.50 (2 × 3 H, 2 s, 2 CH_3). The final fractions eluted from the first column chromatography gave a second crop of **24** (0.2 g) which was crystallized from *n*-PrOH.

Reaction of the (2,6-Dimethylphenyl)hydrazone of 4-Nitroacetophenone with PPA (Exothermic Reaction). The basic fraction was treated with Et_2O to dissolve the impurities and then crystallized from *n*-PrOH to give 2-(4-nitrophenyl)-3a,5-dimethyl-3a,4,7,7a-tetrahydro-3*H*-pseudoindol-4-one: mp 145–146 °C; yield 50%; ^1H NMR 8.50 and 8.12 (2 × 2 H, AA′–BB′ system, aromatic of 4-nitrophenyl group), 6.75 (1 H, m, vinylic CH=), 4.20 (1 H, m, CH_2CH), 3.85 and 2.85 (2 × 1 H, d and m, CH_2 of nitrogenated ring), 3.08 (2 H, m, CH_2CH), 1.78 (3 H, m, CH_3 on unsaturated carbon), 1.44 (3 H, s, CH_3 on saturated carbon).

Reaction of 2,6-Dimethylphenylhydrazone of 4-Chloroacetophenone with PPA (Exothermic Reaction). The neutral fraction consisted chiefly of 2-(4-chlorophenyl)-4,7-dimethylindole: mp 115 °C (*i*-PrOH); yield 37%; ^1H NMR 8.05 (1 H, br s, NH), 7.57 and 7.35 (2 × 2 H, AA′–BB′ system, aromatic of the 4-chlorophenyl group), 6.86 (2 H, s, aromatics in positions 5 and 6), 6.80 (1 H, s, aromatic in position 3), 2.53 and 2.47 (2 × 3 H, 2 s, 2 CH_3). The 2-(4-chlorophenyl)-3a,5-dimethyl-3a,4,7,7a-tetrahydro-3*H*-pseudoindol-4-one was the main constituent of the basic fraction: mp 108 °C (diisopropyl ether); yield 36%; ^1H NMR 7.73 and 7.37 (2 × 2 H, AA′–BB′ system, aromatic of 4-chlorophenyl group), 6.67 (1 H, m, vinylic CH=), 4.15 (1 H, m, CH_2CH), 3.75 and 2.75 (2 H, d and m, CH_2 of nitrogenated ring), 3.0 (2 H, m, CH_2CH), 1.77 (3 H, m, CH_3 on unsaturated carbon), 1.40 (3 H, s, CH_3 on saturated carbon).

Reaction of Hydrazone 26a with PPA. The basic fraction (0.8 g) obtained from the reaction of hydrazone **26a** (5.2 g) with PPA was chromatographed on a silica gel column with C_6H_6 as an eluent. 4-Chloroaniline was first eluted (0.4 g), and then, by increasing the AcOEt percentage in the eluent, the amino ketone **11a** was obtained: 0.25 g (5% yield); mp 119–120 °C. Analytic and spectral data were identical with those shown by the product of the reaction of **10a** with PPA.

Reaction of Hydrazone 26b with PPA. The basic fraction was treated with Ac_2O in AcOH solution and the solid product crystallized from EtOH to give the acetyl derivative of **11a**: mp 180–182 °C; ^1H NMR (Me_2SO) 10.60 (1 H, s, exchangeable with D_2O, NH), 7.4 (10 H, m, aromatic), 3.90 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3), 2.09 (3 H, s, $COCH_3$).

Reaction of Hydrazone 27 with PPA. Reaction of hydrazone **27** (24 g) with PPA was carried out at 170 °C. The red basic fraction (13 g) was purified by precipitating yellow hydrochlorides from an Et_2O solution and chromatographing the bases obtained from them (3.0 g). By use of C_6H_6 as an eluent, fluorenone was first eluted, and then 2-(4-amino-3,5-dimethylphenyl)fluorenone (**28**) was obtained by adding AcOEt to the eluent: red crystals; mp 152 °C (*i*-PrOH); yield (1.3 g); ^1H NMR 8.0–7.0 (9 H, m, aromatic), 5.70 (2 H, br s, exchangeable with D_2O, NH_2), 2.22 (6 H, s, 2 CH_3); mol wt (mass spectroscopy) 299.

Oxidation of 28 to Fluorenone-2-carboxylic Acid. Amino ketone **28** (0.45 g) was added portionwise to a hot solution (90 °C) of $Na_2Cr_2O_7 \cdot 2H_2O$ (2.0 g) in water (11 mL) and 96% H_2SO_4 (2.5 mL). The resulting solution was diluted with water, and the precipitated solid was filtered by suction and suspended in a hot 4% NaOH solution (20 mL). A saturated 5% aqueous solution of $KMnO_4$ (10 mL) was then added and the resulting mixture refluxed for few minutes. The excess oxidizing agent was then destroyed with EtOH and the MnO_2 filtered off. A yellow acid separated upon acidification, which was extracted with AcOEt. Evaporation of the solvent left a solid residue which gave the fluorenone-2-carboxylic acid[17] (0.14 g) in a pure state, mp 260 °C (MeOH). The corresponding methyl ester was obtained by reaction of the acid with CH_2N_2: mp 184 °C;[18] ^1H NMR 8.8–7.3 (7 H, m, aromatic), 3.92 (3 H, s, OCH_3). Spectral and analytical data are identical with those obtained from an authentic sample synthesized by a known route.

3-(3,5-Dimethyl-4-hydroxyphenyl)-4-methoxybenzaldehyde (3). Amino aldehyde **2** (2.5 g) was dissolved in a warm 20% H_2SO_4 solution (20 mL); an amorphous sulfate precipitated on cooling of the solution. A $NaNO_2$ (1 g) solution in water (5 mL) was then added with stirring to the slurry cooled at 5 °C. The starting solid rapidly dissolved, and a diazonium sulfate separated; urea was first added to destroy HNO_2 excess and then a trace of $CuSO_4$. When the mixture was heated at 50 °C, nitrogen evolved, and the brown solid phenol **3** separated (2.0 g). It gave a *p*-nitrophenylhydrazone, mp 219 °C (AcOH).

(5-Carboxy-2-methoxyphenyl)glyoxylic Acid (4). A 2% $KMnO_4$ solution in water (about 500 mL) was added to a hot solution of phenol **3** (1.8 g) in a 10% NaOH solution (80 mL). EtOH (2 mL) was added to destroy excess oxidizing agent, and the clear solution was acidified with 35% HCl solution. A solid acid separated which was extracted with Et_2O. Insoluble impurities were removed by filtration, and the solid obtained after evaporation of the solvent was crystallized from dioxane to give (5-carboxy-2-methoxyphenyl)glyoxylic acid (**4**): yield 0.3 g; mp 130 °C dec. This acid gave a yellow 4-nitrophenylhydrazone [mp 260 °C (AcOH)] and 4-methoxyisophthalic acid (**5**, mp 155 °C) by treatment with H_2O_2 in hot 10% NaOH solution.[19] Both the acid and its methyl ester (CH_2N_2) (mp 96 °C) were identical with authentic samples obtained by following known methods.

Reaction of Hydrazone 18b with HCOOH. A solution of hydrazone **18b** (1.0 g) in 99% HCOOH (10 mL) was refluxed for 2 h. Removal of the solvent left a residue which was purified through an acid–base treatment. The basic fraction gave the 2-(4-methoxyphenyl)-3a,4,7,7a-tetrahydro-3*H*-pseudoindol-4-one (0.54 g) in a pure state: mp 121 °C (diisopropyl ether); ^1H NMR 7.60 and 6.74 (2 × 2 H, AA′–BB′ system, aromatic of 4-methoxyphenyl group), 6.51 (1 H, m, vinylic CH=), 4.06 (1 H, m,

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CH_2CH), 3.74 (3 H, s, OCH_3), 3.68 and 2.67 (2 × 1 H, d and m, CH_2 of nitrogenated ring), 2.87 (2 H, m, CH_2CH), 1.71 (3 H, m, CH_3 on unsaturated carbon), 1.33 (3 H, s, CH_3 on saturated carbon).

N^1-(4-Methoxybenzoyl)-N^2-(2,6-dimethylphenyl)-hydrazine (29). A solution of anisoyl chloride (12.0 g) in dry $CHCl_3$ (70 mL) was carefully added to a stirred solution of (2,6-dimethylphenyl)hydrazine (9.7 g) and triethylamine (7.2 g) in dry $CHCl_3$ (80 mL). The mixture was stirred for an additional 30 min at room temperature and then water was added (150 mL). Hydrazine **29** separated as a white crystalline mass, which was filtered and crystallized from ethanol: 13.3 g (yield 70%); mp 187 °C.

Reaction of Hydrazide 29 with PPA. Reaction of hydrazide **29** (4.8 g) with PPA was carried out at 110 °C for 30 min; the basic fraction (1.92 g) obtained by following the usual procedure was a brown syrup which became solid on treatment with a little C_6H_6. 3-(4-Amino-3,5-dimethylphenyl)-4-methoxybenzamide (**30**) was obtained in a 10% yield (0.52 g): mp 168 °C (*i*-PrOH); mol wt (mass spectroscopy) 270; ^1H NMR 7.05 (2 H, s, aromatics in positions 2 and 6 of the xylidine ring), 7.55 and 6.85 (2 H and 1 H, 2 m, aromatic), 6.65 (2 H, br s, exchangeable with D_2O, NH_2), 2.20 (6 H, s, 2 CH_3). The benzene solution gave a residue (0.68 g) which was chromatographed on a silica gel column (12 g) with $CHCl_3$ as an eluent. 1-(2,6-Dimethylphenyl)-3,5-bis(4-methoxyphenyl)-1,2,4-triazole (**31**, 0.21 g) was first eluted: yield 4%; mp 135 °C (diisopropyl ether); mol wt (mass spectroscopy) 385; ^1H NMR 8.1 and 7.0 (2 H and 9 H, d and m, aromatic), 3.80 and 3.73 (2 × 2 H, 2 s, 2 OCH_3), 2.0 (6 H, s, 2 CH_3). From the subsequent fractions the N^1,N^2-dianisoyl(2,6-dimethylphenyl)hydrazine (**32**, 0.21 g) was obtained: yield 3%; mp 158 °C; ^1H NMR 9.24 (1 H, br s, exchangeable with D_2O, NH), 7.78 (2 H, d, aromatic in position ortho to the carbonyl group), 3.1 (9 H, m, aromatic), 3.75 and 3.70 (2 × 3 H, 2 s, 2 OCH_3), 2.30 (6 H, s, 2 CH_3). Analytical and spectral data were identical with those obtained from an authentic sample prepared from (2,6-dimethylphenyl)hydrazine, a double molar amount of anisoyl chloride, and triethylamine in dry $CHCl_3$ solution. Hydrolysis of amide **30** (0.24 g) in refluxing 20% HCl solution (5 mL) was complete in 1 h. Treatment of the precipitated solid with BzCl in dry pyridine solution gave the benzoylamino acid **9b** as colorless crystals [mp 250 °C (AcOH)] identical in every respect with the benzoyl derivative of the product obtained by oxidation of amino aldehyde **2**.

3-(4-Benzamino-3,5-dimethylphenyl)-4-methoxybenzoic Acid. Method A. A pyridine (20 mL) solution of the benzamide of **2** (2.76 g) described above was treated with a 2% $KMnO_4$ solution at 45–50 °C until the violet color of $KMnO_4$ persisted. The excess oxidizing agent was destroyed with $Na_2S_2O_5$, and then a 10% HCl solution was added. The precipitated 3-(4-benzamino-3,5-dimethylphenyl)-4-methoxybenzoic acid was purified through an acid–base process and then crystallized from diluted AcOH: mp 250 °C; yield 0.95 g.

Method B. The benzamide of **15b** described above (0.5 g) was refluxed in a 5% NaOH ethanolic solution (20 mL) for 10 min. The solvent was distilled off and water added to dissolve the residue. A 35% (w/v) H_2O_2 solution (2 mL) was added, and the resulting mixture was refluxed for a few minutes, filtered, and acidified with a 10% HCl solution to give the 3-(4-benzamino-3,5-dimethylphenyl)-4-methoxybenzoic acid: yield 0.40 g; mp 250 °C (AcOH).

4,4′-Dimethoxy-3-(4-benzamino-3,5-dimethylphenyl)-benzophenone (9b). A solution of 3-(4-benzamino-3,5-dimethylphenyl)-4-methoxybenzoic acid described above (0.48 g) in $SOCl_2$ (2.3 g) was refluxed for 30 min. The excess $SOCl_2$ was distilled and the crude acid chloride dissolved in anisole. $AlCl_3$ (0.50 g) was added, and the resulting mixture was left to stir at 40 °C for 1 h and then poured onto a 5% HCl solution. The product was extracted with ether, and the organic layer was washed (5% $NaHCO_3$) and dried (Na_2SO_4). Removal of the solvent left a residue which was dissolved in hot *i*-PrOH. The solution was filtered and the solvent distilled to give a residue (0.35 g) which was chromatographed on a silica gel column. The main product eluted (0.27 g) was 4,4′-dimethoxy-3-(4-benzamino-3,5-dimethylphenyl)benzophenone [**9b**, mp 215 °C (C_6H_6)], identical with the compound obtained by benzoylation of the product resulting from the rearrangement of hydrazone **8** in PPA.

Registry No. 1, 65814-11-1; 2, 65814-14-4; 3, 65814-21-3; 4, 65814-18-8; 5, 2206-43-1; 8, 65814-12-2; 9a, 65814-15-5; 9b, 65814-19-9; 10a, 75600-85-0; 10b, 75600-86-1; 10c, 75600-87-2; 10d, 75600-88-3; 11a, 75626-85-6; 11a·acetyl derivative, 75601-21-7; 11b, 75600-89-4; 11c, 75600-90-7; 11d, 75600-91-8; 12, 75600-92-9; 13, 75600-93-0; 14a, 75600-94-1; 14b, 75626-86-7; 14c, 75600-95-2; 14d, 75600-96-3; 15a, 75600-97-4; 15b, 75600-98-5; 15c, 75600-99-6; 15d, 75601-00-2; 15d·*x*HCl, 75601-17-1; 16, 75601-01-3; 17, 75601-02-4; 17·*x*HCl, 75601-18-2; 18a, 24310-46-1; 18b, 67658-98-4; 18c, 67658-99-5; 19a, 5784-95-2; 19b, 67659-03-4; 19c, 67659-04-5; 20a, 67659-01-2; 20b, 67659-00-1; 20c, 67659-02-3; 21, 75601-03-5; 22, 75601-04-6; 23, 75601-05-7; 24, 75601-06-8; 25, 75601-07-9; 26a, 75601-08-0; 26b, 75601-09-1; 27, 65814-13-3; 28, 65814-23-5; 29, 75601-10-4; 30, 75601-11-5; 31, 75601-24-0; 32, 75601-25-1; anisaldehyde, 50984-52-6; 2,6-dimethylphenylhydrazine, 603-77-0; 4,4′-dimethoxythiobenzophenone, 958-80-5; 4-methoxybenzophenone, 611-94-9; 2-methylphenylhydrazine·HCl, 27110-36-7; 2,6-dimethylbenzenediazonium chloride, 75601-12-6; 2,6-dimethylaniline, 87-62-7; 1,2-bis(4-methoxyphenyl)-1,2-ethanedione, 1226-42-2; 4-chloroacetophenone-2,6-dimethylphenylhydrazone, 75601-13-7; 4-chloroacetophenone, 99-91-2; 4-nitroacetophenone-2,6-dimethylphenylhydrazone, 75601-14-8; PPA, 75601-15-9; 3-(4-aminophenyl)-4-methoxyphenylglyoxylic acid, 75601-15-9; 3-(4-acetaminophenyl)-4-methoxyphenylglyoxylate, 75626-87-8; 4-nitrophenylhydrazone-3-(4-acetaminophenyl)-4-methoxyphenylglyoxylate, 75601-16-0; 2-(4-nitrophenyl)-3a,5-dimethyl-3a,4,7,7a-tetrahydro-3*H*-pseudoindol-4-one, 75626-88-9; 2-(4-chlorophenyl)-4,7-dimethylindole, 75601-19-3; 2-(4-chlorophenyl)-3a,5-dimethyl-3a,4,7,7a-tetrahydro-3*H*-pseudoindol-4-one, 75601-20-6; fluorenone-2-carboxylic acid, 784-50-9; methylfluorenone-2-carboxylate, 3096-45-5; 3·*p*-nitrophenylhydrazone, 65814-17-7; 4·4-nitrophenylhydrazone, 65814-22-4; 2-(4-methoxyphenyl)-3a,4,7,7a-tetrahydro-3*H*-pseudoindol-4-one, 75601-22-8; 3-(4-benzamino-3,5-dimethylphenyl)-4-methoxybenzoic acid, 75601-23-9.