pared from trimethylhydrazine and nitrous acid.[34] A 1,4-disubstituted 2-tetrazene has been proposed as an intermediate in the reaction of *p*-toluenesulfonyl azide with a halomagnesium salt of aniline.[35] Thermally, 1-nitroso-1,4,4-trimethyl-2-tetrazene is more stable than similar 1-nitroso-1,3-diaryltriazenes.[13]

The permanganate oxidation was extended successfully to the alkyl-substituted hydronitrogen, tetramethylhydrazine. According to electron-impact studies, this material has a relatively strong nitrogen–nitrogen single bond,[21] but it is quite easily oxidized to a cation-radical.[36] This latter fact accounts for the analogous reaction. Although the permanganate oxidation of tetra-*n*-propylhydrazine to 1,2-dipropionyl-1,2-dipropylhydrazine has been reported,[37] tetra-*n*-propylhydrazine was not isolated, but was only proposed as an intermediate in the oxidation of dipropylamine, a supposition not consistent with a more recent investigation.[32]

In contrast with degradation reactions commonly associated with oxidation of amines,[38] Davis and Rosenblatt[39] recently oxidized an N-methyl to an N-formyl group in tertiary amines with oxygen and a platinum catalyst at room temperature. Tertiary amines containing aryl groups were more difficult to oxidize; under similar conditions, an N-benzyl group was not oxidized. Both the oxidizing species and the structure of the amine are especially important where dual mechanisms of electron and hydrogen abstraction are possible.[27] Dual oxidation mechanisms were discussed recently in a review of the electrochemical oxidation of amines.[40] While oxidation at low potentials forms a cation radical, at higher potentials another electron and a proton are lost rapidly to form an iminium salt. With amines, oxidants such as chlorine dioxide react according to the low-potential mechanism; oxidants such as permanganate yield products expected from oxidation at higher potentials. Since a cation radical which is more stable than the corresponding radical from amines is formed during the oxidation of the 2-tetrazenes, it is not surprising in retrospection that some chemical oxidants associated with the higher potential reaction for amines would react according to the low-potential mechanism during the oxidation of the tetrasubstituted 2-tetrazenes.

Acknowledgment.—We wish to thank Dr. Wayne Carpenter, Dr. Herman Cordes, and Dr. David Forkey for mass spectral data and Mr. Donald Moore for assistance with nmr spectra.

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(35) W. Fischer and J-P. Anselme, *J. Amer. Chem. Soc.*, **89**, 5284 (1967).
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The Fischer Indole Cyclization of Several *ortho*-Substituted Phenylhydrazones[1,2]

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Fischer indole cyclization of ethyl pyruvate *o*-methoxyphenylhydrazone in ethanolic hydrogen chloride gave 2-carbethoxy-6-chloroindole as the main product. Minor products included 2-carbethoxy-3-chloroindole, the expected 2-carbethoxy-7-methoxyindole, and several indolic dimers. Similarly, ethyl pyruvate *o*-benzyloxyphenylhydrazone gave 2-carbethoxy-6-chloroindole. Cyclization of cyclohexanone *o*-methoxyphenylhydrazone in dilute sulfuric acid yielded 8-methoxy-1,2,3,4-tetrahydrocarbazole as the major product. The only isolated by-product, previously reported to be "12-methoxy-1,2,3,4-tetrahydroisocarbazole," has now been shown to have a dimeric structure. When the reaction was run in ethanolic hydrogen chloride, the dimer hydrochloride became the main product and 8-methoxy-1,2,3,4-tetrahydrocarbazole is formed in lower yield. The structure of the dimers and the reaction mechanism are discussed.

The simplest approach to 7-methoxyindole, an intermediate in a synthetic program on indole chemistry, appeared to be the Fischer indole cyclization of ethyl pyruvate *o*-methoxyphenylhydrazone (**1**). The transformation of *o*-anisidine to 2-carbethoxy-7-methoxyindole (**2**), *via* the hydrazone (**1**), has been reported[3] to proceed in 30% over-all yield; the preparation of the ethoxy analog of **2** by cyclization of the corresponding phenylhydrazone has also been described.[4] However other workers[5] found that cyclization of **1** with ethanolic hydrogen chloride gave an unidentified indole, mp 168°, different from **2**. Our results on the Fischer cyclization of **1** and related compounds are described.

While the reaction of diazotized *o*-anisidine with ethyl α-methylacetoacetate afforded the hydrazone **1** as an oil, use of ethyl α-ethoxalylpropionate[6] yielded crystalline **1**. The latter could be separated into two forms which are presumably the *syn* and *anti* isomers as indicated by analytical and spectral properties and the fact that the mixture and both forms yielded the same product mixtures when cyclized in acid media.

Cyclization of the isomeric hydrazone mixture **1** in ethanolic hydrogen chloride gave a mixture of polar and faster moving components. Fractional crystallization yielded a single compound, mp 177–178°, whose empirical formula corresponded to $C_{11}H_{10}ClNO_2$ (yield 36%). The melting point suggested that the product was 2-carbethoxy-6-chloroindole (**3**),[7] and this was verified by comparison of the product (**3**) and its corresponding acid (**4**) with authentic samples prepared by

(1) Presented in part before the Division of Organic Chemistry of the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966.
(2) This work was carried out under Contract SA-43-ph-3021 with the Psychopharmacology Research Branch, National Institute of Mental Health, Bethesda, Md.
(3) J. B. Bell and H. G. Lindwall, *J. Org. Chem.*, **13**, 547 (1948).
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(6) R. F. B. Cox and S. M. McElvain, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p 272.
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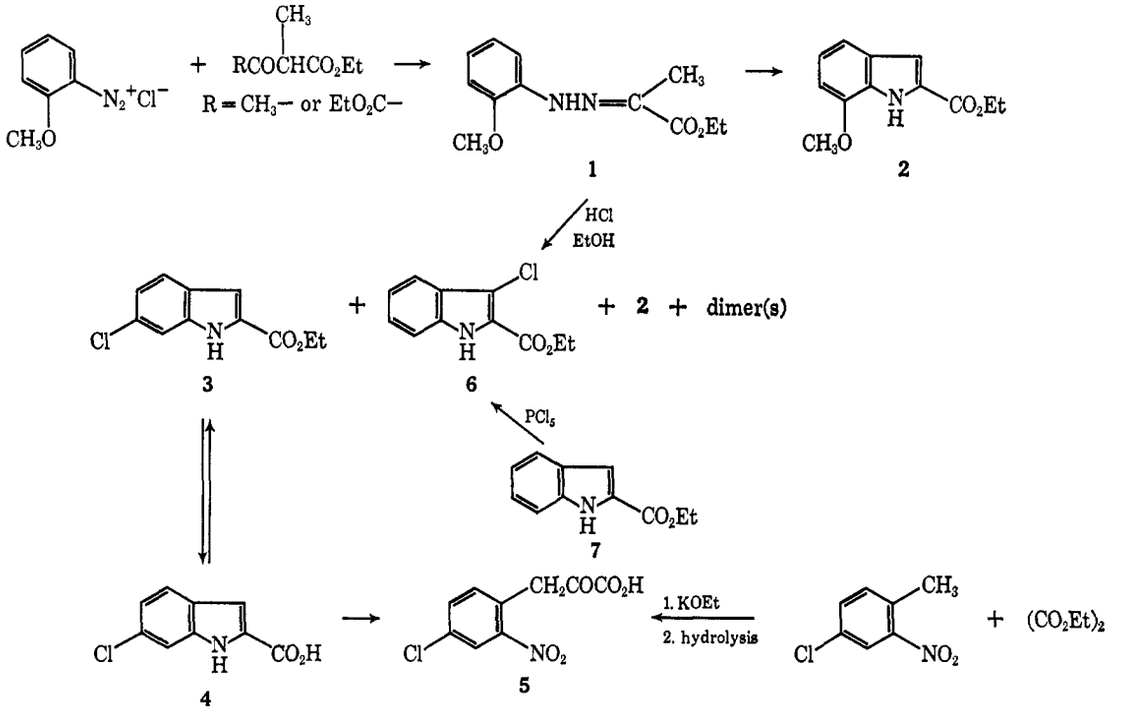
SCHEME I



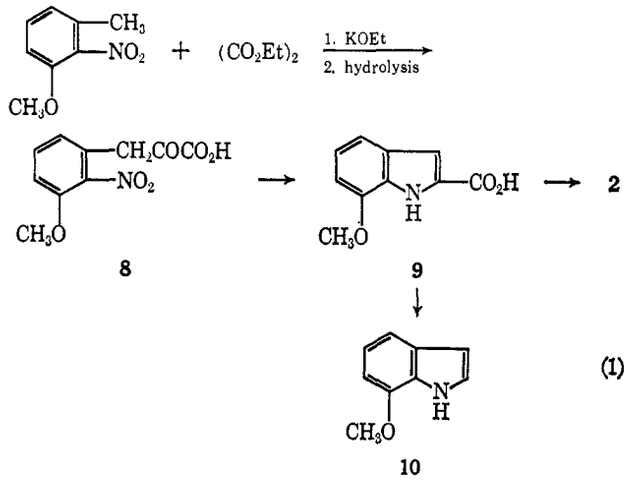
cyclization of the Reissert product (**5**) obtained from 4-chloro-2-nitrotoluene[8] (see Scheme I). It now seems reasonable to assume that the unknown indole obtained previously[5] under these conditions is in fact 2-carbethoxy-6-chloroindole.

Chromatography of the recrystallization mother liquors separated the indolic materials from more polar substances (total yield of indoles was 53%). Examination (tlc) of the indolic mixture indicated the presence of additional 2-carbethoxy-6-chloroindole (**3**), the expected 2-carbethoxy-7-methoxyindole (**2**), and an unknown compound. Fractional crystallization first yielded a mixture of only **3** and the unknown. Further treatment allowed the isolation of a 0.9% yield of the unknown which was shown to be 2-carbethoxy-3-chloroindole (**6**) by comparison with an authentic sample.[9] Comparison of the nmr spectra of the pure 3-chloro compound and the mixture of the 3- and 6-chloro compounds showed that the 3-chloro isomer was present in the greater amount.

The combined mother liquors from the recrystallizations gave an oily solid which showed only 2-carbethoxy-7-methoxyindole (**2**) and 2-carbethoxy-3-chloroindole (**6**) by tlc. The mass spectrum of this solid confirmed these assignments, but in addition showed a parent peak at *m/e* 233 for which we suggest 2-carbethoxy-6-ethoxyindole. The nmr spectrum of this mixture is consistent with these structures. Further attempts to isolate individual components were unsuccessful.

The polar mixture obtained from the alumina column was rechromatographed, whereby a single component, mp 233–235°, was isolated. The nmr spectrum of this compound indicated the presence of CO_2Et, OCH_3, and aromatic protons. The mass spectrum showed a parent peak at *m/e* 406. Lack of material precluded further work on this compound, but the data available, together with results to be discussed later, prompt us to suggest a dimeric structure consisting of 2-carbethoxy-7-methoxyindole coupled to a molecule of the same type wherein the methoxy group has been lost.

The authentic 7-methoxyindole (**10**) was eventually prepared *via* the Reissert synthesis illustrated in eq 1.[10] Conversion of the intermediate acid (**9**) into the ester (**2**) provided comparison material used in the Fischer study.



(1)

Cyclization of the hydrazone mixture **1** in mixed acetic and sulfuric acids gave a 4.2% yield of 2-carbethoxy-7-methoxyindole (**2**) as the only isolable indolic product (similar to the previously described results[5]). Attempted cyclization with polyphosphoric acid gave no indication of reaction up to 95°, at which point extensive darkening occurred. No products could be isolated.

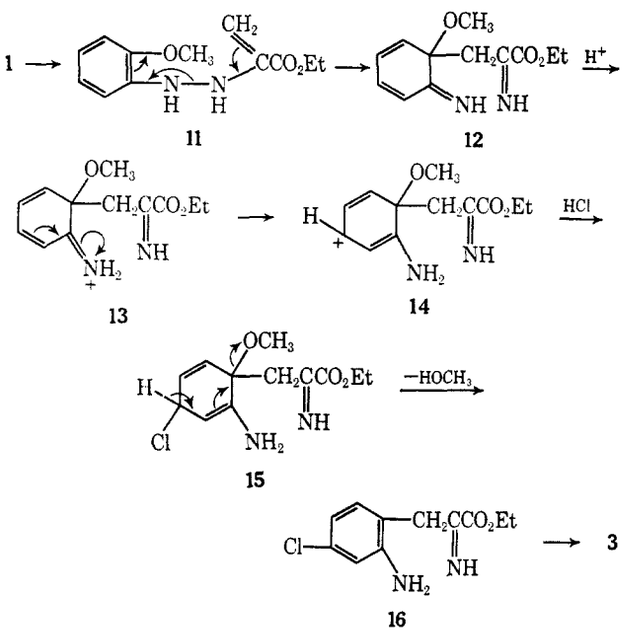
We also attempted the cyclization of ethyl pyruvate *o*-benzyloxyphenylhydrazone in ethanolic hydrogen chlo-

(8) H. N. Rydon and J. C. Tweddle, *J. Chem. Soc.*, 3499 (1955).
(9) S. Gabriel, W. Gerhard, and R. Wolter, *Ber.*, **56B**, 1024 (1923).
(10) K. G. Blaike and W. H. Perkin, *J. Chem. Soc.*, **125**, 29 (1924).

ride. Ek and Witkop[11] abandoned attempts to prepare analogs of this compound when they found that ethyl pyruvate *o*-tosyloxyphenylhydrazone "could not be brought to cyclize." Our reaction became quite dark and was quenched shortly after starting. Tlc of the reaction mixture showed a complex mixture which contained hydrazones and 2-carbethoxy-6-chloroindole (**3**). Column chromatography yielded a solid which was shown to be one of the hydrazone isomers.

We have subjected 2-carbethoxy-7-methoxyindole to refluxing ethanolic hydrogen chloride and recovered it unchanged, implying that the novel reaction leading to the main product (**3**) occurs prior to indole formation. A possible interpretation is illustrated below (Scheme II). Carbon–carbon bond formation of the ene–hydrazine intermediate (**11**) at the occupied *ortho* position gives **12** which by protonation of the ring imino nitrogen and shift of the double bonds subsequently leads to the introduction of chlorine as in **15**. Loss of methanol produces **16** which can then cyclize in normal fashion[12] to give 2-carbethoxy-6-chloroindole (**3**). Admittedly an additional shift of the second ring double bond in species **13** would lead to a carbonium ion in the incipient 4-indole position, but we have been unable to detect any 2-carbethoxy-4-chloroindole in the reaction mixture. Further, it is noteworthy that attack at an occupied site predominates over normal Fischer cyclization at the unoccupied position.

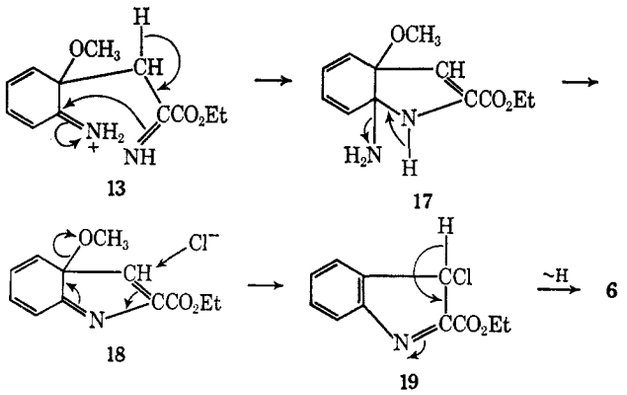
SCHEME II



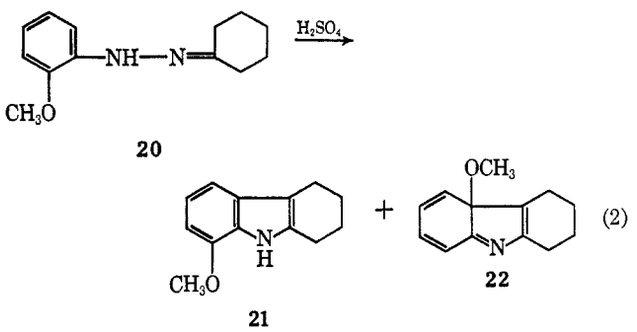
The formation of the by-product **6** may be visualized as shown in Scheme III. Cyclization of structure **13** (see Scheme II) in the "abnormal" Fischer sense[12] would give **17** which, by loss of ammonia, could give rise to structure **18**. Attack of chloride, concurrent with the loss of methanol, and subsequent aromatization could lead to 2-carbethoxy-3-chloroindole (**6**).

While there has been a report[13] of a Fischer indolization wherein a by-product containing a new aromatic substituent was obtained in low yield, the reaction shown in Scheme I is, to our knowledge, the first reported instance of such an exchange determining the main product.

SCHEME III



In connection with these studies we noted that the cyclization of cyclohexanone *o*-methoxyphenylhydrazone (**20**) in dilute sulfuric acid has been reported[13a] to give as major products the normal Fischer product, 8-methoxy-1,2,3,4-tetrahydrocarbazole (**21**) and the unlikely 12-methoxy-1,2,3,4-tetrahydroisocarbazole (**22**) (eq 2). We repeated the published procedure and did indeed obtain compound **21** in 64% crude yield and a quantity (now considered to be 20%) of a solid (A) whose melting point was close to that reported for structure **22**.



Initial evidence indicated that neither compound **22** nor any simple tetrahydrocarbazole structure could fit the data for the reaction by-product. Analysis is consistent with the empirical fromula $C_{25}H_{26}N_2O$ and the mass spectrum displays a parent peak at m/e 370. The nmr spectrum shows one NH, one OCH_3, six to seven aromatic protons in a complex system, and an unresolved area of multiplets in the aliphatic region.

When the cyclization of **20** was conducted in ethanolic hydrogen chloride, the normal product (**21**) was isolated in only 9% yield and a new compound (B) was obtained as the major product (28%), $C_{25}H_{29}ClN_2O$. The spectral data are reminiscent of, but not identical with, the first product (A). Treatment of the latter with ethanolic hydrogen chloride gave the new compound B; conversely passage of the chloro compound B over an alumina column or treatment with base returned A. While B appears to be a hydrochloride hydrate of A it is noteworthy that A failed to form a crystalline derivative with picric, sulfuric, or fumaric acids.

(11) A. Ek and B. Witkop, *J. Amer. Chem. Soc.*, **76**, 5579 (1954).

(12) For a review of the Fischer indole synthesis, see B. Robinson, *Chem. Rev.*, **63**, 373 (1963).

(13) (a) C. S. Barnes, K. H. Pausacker, and C. I. Schubert, *J. Chem. Soc.*, 1381 (1949); (b) A. H. Milne and M. L. Tomlinson, *ibid.*, 2789 (1952).

While the data rule out structure 22 for the reaction by-product A, they do not permit an unambiguous structural assignment. Similar to the polar compound isolated from the cyclization of ethyl pyruvate *o*-methoxyphenylhydrazone, we suggest for compound A a dimeric structure composed of 8-methoxy-1,2,3,4-tetrahydrocarbazole (21) coupled to a molecule of 21 which has lost the methoxy group. However additional information would be required to determine the point at which the two ring systems are joined and the disposition of double bonds.

Experimental Section[14]

Ethyl Pyruvate 2-Methoxyphenylhydrazone (1).—To a solution of 28.5 g (0.23 mol) of *o*-anisidine in 46 ml of hydrochloric acid and 68 ml of water cooled to 5–7° was added a solution of 16.8 g (0.24 mol) of sodium nitrite in 30 ml of water. The addition took 20 min, and the resulting solution was stirred for an additional 20 min.

This diazonium solution was added dropwise below the surface at 5–7° over 25 min with stirring to a solution of 174 g (2.10 mol) of sodium acetate, 460 ml of water, and 70 ml of alcohol. To the resulting suspension was added 50 g (0.25 mol) of ethyl α-ethoxalylpropionate dropwise over a period of 1.0 hr at 5–7°, and the suspension was stirred at 7–10° for 2 hr. After the water had been decanted the resulting oil was crystallized from 50% aqueous ethanol to give 44.0 g (82.2%) of product, mp 66–80°.

Separation of Isomers.—The crude hydrazone was recrystallized twice from ethanol to give a solid: mp 87–90°; tlc (silica gel, benzene), single spot, R_f 0.52; ir ($CHCl_3$) 5.99 μ (ester carbonyl).

Anal. Calcd for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83; N, 11.86. Found: C, 60.94; Y, 6.76; N, 12.16.

The mother liquors were concentrated and cooled slowly to return 5.8 g of the other isomer: mp 68–70° (recrystallization from alcohol did not raise the melting point); tlc (silica gel, benzene), single spot, R_f 0.61; ir ($CHCl_3$) 5.95 μ (ester carbonyl).

Anal. Found: C, 60.76; H, 6.55; N, 11.81.

Fischer Cyclization of 1 (Mixture).—A solution of 50.0 g (0.212 mol) of 1 in 1.0 l. of saturated ethanolic hydrogen chloride was heated to reflux for 25 min. The mixture was cooled and poured into ice–water; the resulting solid was collected, washed well with water, and dried to give 35.3 g of material melting at 115–145°. The solid was recrystallized from benzene–hexane (9:5) to give in two crops 17.2 g (36.1%) of 2-carbethoxy-6-chloroindole, mp 169–173°. The product was recrystallized from benzene–hexane to a constant melting point of 177–178° (lit.[5] mp 177–178°). It was found to be identical with authentic 2-carbethoxy-6-chloroindole prepared as previously described[8] with respect to melting point, mixture melting point, tlc, and ir.

Saponification of the ester obtained from the reaction in the usual manner yielded 64.4% 2-carboxy-6-chloroindole, which, after purification, melted at 244–245° dec: ir (KBr) 5.97 μ (C=O of acid); tlc [silica gel H, methanol–water (1:1)], single spot, R_f 0.75. This compound was identical with authentic 2-carboxy-6-chloroindole prepared as previously described[8] with respect to melting point, mixture melting point, tlc, and ir.

Anal. Calcd for $C_9H_6ClNO_2$: C, 55.26; H, 3.09; N, 7.16. Found: C, 55.41; H, 3.32; N, 7.23.

The mother liquors were taken to dryness, and the resulting 17 g of oil was dissolved in 30 ml of benzene–hexane (3:1) and chromatographed through a dry packed alumina column 1 × 24 in. The column was eluted with benzene–hexane (3:1). Thin layer chromatography (silica Gel H, benzene) showed the first 10 fractions of 80 ml to be identical, a mixture of 2-carbethoxy-6-chloroindole and two other compounds having lower R_f values. The combined fractions were taken to dryness to yield 7.8 g of solid, which was recrystallized from hexane–benzene (9:1) to yield 3.2 g of solid, mp 130–145°. Thin layer chromatography showed the presence of 2-carbethoxy-6-chloroindole and only one other compound having a lower R_f value.

The solid was dissolved in 27 ml of methanol and cooled very slowly to room temperature. There resulted 0.42 g of crystals, mp 153–156°, which was recrystallized from methanol and then from hexane to give long white needles: mp 156–157°; ir ($CHCl_3$) 2.98 (NH) and 5.89 μ (C=O); tlc (silica gel, benzene), single spot, R_f 0.52. This compound was identical with authentic 2-carbethoxy-3-chloroindole prepared by the literature method[9] with respect to melting point, mixture melting point, tlc, and ir.

Anal. Calcd for $C_{11}H_{10}ClNO_2$: C, 59.07; H, 4.51; N, 6.23; Cl, 15.86. Found: C, 59.19; H, 4.67; N, 6.32; Cl, 15.72.

The mother liquors, from which the mixture of the two esters was taken, was concentrated to dryness. Tlc showed the presence of 2-carbethoxy-3-chloroindole, 2-carbethoxy-6-chloroindole, and 2-carbethoxy-7-methoxyindole. Continued crystallization from benzene–hexane left a near-solid which showed only 2-carbethoxy-3-chloroindole and 2-carbethoxy-7-methoxyindole by tlc: nmr δ 1.42 and 1.52 (overlapping triplets, CH_3 of ester), 3.93 (s, OCH_3), 4.38 (q, CH_2) 6.62–7.67 ppm (m, aromatic); mass spectrum *m/e* 223, 229 ($C_{11}H_{10}ClNO_2$), 219 ($C_{12}H_{13}NO_3$), and 233 ($C_{13}H_{15}NO_3$).

The chromatography column was finally eluted with ethanol to give 7.5 g of semisolid which was rechromatographed. Elution with chloroform–benzene (9:1) gave 0.04 g, which was recrystallized from benzene: mp 233–235°; nmr δ 1.35 (broad m, ester CH_3), 4.09 (s, OCH_3), 4.34 (broad m, CH_2 of ester), and 7.13–7.55 ppm (broad m, aromatic); mass spectrum *m/e* 406–407.

Fischer Cyclization of *syn*- and *anti*-Hydrazones Separately.—A solution of 5.0 g (0.21 mol) of ethyl pyruvate *o*-methoxyphenylhydrazone (mp 68–70°) in 200 ml of alcoholic hydrogen chloride was heated to 50° for 30 min. Tlc showed that the starting material had been completely consumed. The mixture was concentrated to half its volume, cooled, and poured into cold water. The resultant solid was collected, air dried, and recrystallized from benzene–hexane to give 1.1 g (23.2%) of 2-carbethoxy-6-chloroindole, mp 166–171°. A sample was recrystallized to a constant melting point of 177–178°, and was identical in all respects with the authentic sample of 2-carbethoxy-6-chloroindole.

Concentration of the filtrate gave an oil which could not be induced to crystallize; tlc [silica gel, benzene–ethyl acetate (19:1)] shows additional 2-carbethoxy-6-chloroindole at R_f 0.52 as well as several other components.

When a 5.0-g sample of the second hydrazone isomer (mp 88–90°) was subjected to the same conditions, a 1.18-g (24.7%) yield of 2-carbethoxy-6-chloroindole was obtained; tlc of these mother liquors was essentially the same as that described above.

2-Carbethoxy-7-methoxyindole (2).—Authentic 2-carboxy-7-methoxyindole prepared by the literature method[10] was treated with ethanol and sulfuric acid in the usual manner to give a 62% yield of product: mp 114–115° (recrystallization from hexane did not change the melting point); tlc [silica gel, benzene–ethyl acetate (19:1)], single spot, R_f 0.47.

Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.91; N, 6.39. Found: C, 66.01; H, 6.17; N, 6.66.

The indole itself was prepared by decarboxylation of the 2-carboxy derivative.[10]

Attempted Reaction of 2 under Fischer Cyclization Conditions.—A solution of 0.25 g (0.0011 mol) of 2 in 10 ml of ethanolic hydrogen chloride was stirred and heated at 50° for 0.5 hr. The solvent was removed and the residue was recrystallized from alcohol to give 0.18 g (72%) of unchanged ester, mp 114–115°. The mother liquors showed no trace of 2-carbethoxy-6-chloroindole by tlc.

Ethyl Pyruvate 2-Benzyloxyphenylhydrazone.—A mixture of 50.0 g (0.25 mol) of *o*-benzyloxyaniline,[11] 50 ml of concentrated hydrochloric acid, and 50 ml of water was heated and stirred at 70° for 10 min. The suspension was cooled to 7° and to the mixture was added dropwise over 10 min a solution of 18.3 g (0.265 mol) of sodium nitrite in 50 ml of water. Stirring and cooling were continued for 0.5 hr.

To a slurry made from 190 g (2.26 mol) of sodium acetate, 75 ml of alcohol, and 500 ml of water at 5–7°, a 54.0-g (0.267 mol) portion of ethyl α-ethoxalylpropionate was added. To the

(14) Melting points were taken on a Thomas–Hoover Uni-Melt capillary apparatus and are corrected. Ultraviolet spectra were measured on a Perkin-Elmer recording spectrophotometer, Model 202, in ethanol solution. Infrared spectra were measured on a Perkin-Elmer Infracord Model 137. Nuclear magnetic resonance spectra were measured on a Varian A-60 spectrometer in deuteriochloroform solution at the Simon Research Laboratory, Elgin, Ill., or at the National Institutes of Health, Bethesda, Md. Mass spectra were also run at the latter address. Elemental analyses were performed by either Midwest Microlab, Inc., Indianapolis, Ind., or Micro-Tech Laboratories, Skokie, Ill.

stirred suspension (5–7°) was added dropwise over 1 hr the diazonium solution prepared above. Stirring was continued for 1 hr more at room temperature. The suspension was extracted with 700 ml of ether; the extract was dried and concentrated to 100 ml. On cooling, a yellow solid crystallized. It was collected, washed with ether, and dried to yield 43.0 g (55.0%) of isomeric hydrazone esters, mp 50–65°.

A sample was recrystallized from hexane twice and dried at 27° under vacuum for 6 hr for analysis: ir ($CHCl_3$) 5.93 (ester C=O), 7.89 μ (ether); tlc (silica gel, benzene), two spots, R_f 0.29 and 0.80.

Anal. Calcd for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found: C, 69.49; H, 6.66; N, 8.70.

Fischer Cyclization of Ethyl Pyruvate 2-Benzyloxyphenylhydrazone.—A solution of 20.0 g (0.64 mol) of ethyl pyruvate 2-benzyloxyphenylhydrazone in 140 ml of saturated ethanolic hydrogen chloride was heated to reflux for 6 min. The suspension, which became quite dark, was cooled and poured into water. The products were extracted with ethyl acetate; the organic layer was dried and taken to dryness. The oil was dissolved in benzene–hexane (4:1) and poured over an alumina column 0.5 × 12 in. The first 20 ml from the column was taken to dryness and crystallized from hexane to give 0.50 g of solid, mp 76–79°. It was recrystallized from hexane to a constant melting point of 77–79°. It was dried then at room temperature 4 hr for analysis: ir ($CHCl_3$) 5.91 (ester C=O) and 7.92 μ (ether).

Anal. Calcd for $C_{18}N_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found: C, 69.32; H, 6.73; N, 8.87.

Fischer Cyclization of 19. A. Dilute Sulfuric Acid.—This reaction was run by the Pausacker procedure[13a] starting with 99 g (0.453 mol) of cyclohexanone 2-methoxyphenylhydrazone. The ether-soluble portion gave 59.5 g (65.3%) of an orange oil, which was distilled to give 34.3 (38%), bp 138–155° (0.4 mm). A second distillation gave an analytical sample of **20**, bp 140–143° (0.3 mm) [lit.[13a] bp 205–215° (15 mm)].

Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.48; H, 7.38; H, 6.68.

The ether-insoluble fraction was extracted with hot benzene which gave 8.0 g (9.6%) of solid, mp 148–152°. Several recrystallizations from benzene–hexane gave an off-white solid, mp 152–155°.

Anal. Calcd for $C_{25}H_{26}N_2O$: C, 81.04; H, 7.07; N, 7.56. Found: C, 80.69; H, 7.64; N, 7.55.

Recrystallization of a sample from ethanol to constant melting point gave a solid, mp 235–237°.

Anal. Found: C, 80.98; 80.79; H, 7.27, 7.07; N, 7.37, 7.50.

The solution ir spectra of the two compounds were superimposable: ir ($CHCl_3$) 2.8, 3.25, 3.32, 3.43, 6.13, 6.23, 6.28, 6.69, 7.8 μ; uv (EtOH) 240, 292 mμ (ϵ 49,300, 12,500); mass spectrum m/e 370; nmr δ 1.11–3.30 (m, with large peaks at 1.61, 1.86, and 2.68), 3.93 (s, OCH_3), 6.58–7.47 (m, 6–7), and 8.12 (broad s, NH); tlc [silica gel, benzene–hexane (9:1)], single spot, R_f 0.75.

On standing either as a solid or in solution, this compound began to show a second tlc spot at the origin; however, neither the melting point nor the infrared spectrum is affected.

B. Ethanolic Hydrogen Chloride.—A solution of 35.0 g (0.16 mol) of **19** in 600 ml of saturated ethanolic hydrogen chloride was heated and stirred at 55° for 50 min. The suspension was cooled and poured into water. The resulting semisolid was collected, dried, and triturated with ether. The ether was used to extract the filtrate from which the solid was obtained. The ether layer was dried (Na_2SO_4) and concentrated to dryness. The residual oil was taken up in benzene and poured over a dry packed column of alumina. There was obtained 2.9 g (9.2%) of oil, the ir and tlc of which were identical with those of authentic **20**. The compound was further identified as the picrate, mp 145–146° dec, undepressed on admixture with authentic picrate (lit.[15] mp 145–146° dec).

The ether-triturated solid (15.5 g) was crystallized from ethanol to yield in 4 crops 9.5 g (28.4%) of solid, mp 195–197° dec. A sample was recrystallized from ethyl acetate–ethanol to a constant melting point of 195–197° dec and dried at 27° under vacuum for 20 hr for analysis: ir ($CHCl_3$) 2.8, 3.01, 3.32, 3.45, 4.11 (broad), 5.02, 6.08, 6.16, 6.67, 7.71 μ; uv (EtOH) 240, 292 mμ (ϵ 35,400, 10,300); nmr (DMSO-*d*) δ 1.19–3.69 (m with large peaks at 1.81 and 2.66), 4.07 (s, OCH_3), 4.38 (large s, water from sample and/or DMSO), and 6.56–7.55 (m, aromatic); tlc [silica gel, benzene–hexane (9:1)], single spot, R_f 0.00.

Anal. Calcd for $C_{25}H_{29}ClN_2O_2$: C, 70.65; H, 6.89; N, 6.59; Cl, 8.34. Found: C, 70.74, 70.83; H, 7.10, 6.87; N, 6.47, 6.51; Cl, 8.31, 8.27.

This substance is insoluble in hot water, but dissolves readily in cold ethanol. It gives a positive silver nitrate test only on heating. After standing for a short time the solution begins to show a second spot at R_f 0.75 upon respotting.

Interconversion of B and A. A.—To a solution of 0.3 g of compound B in methanol was added methanolic potassium hydroxide. The yellow color disappeared. Removal of the solvent left 0.26 g of solid, mp 150–153°. Recrystallization from ethanol raised the melting point to 235–237°. This compound is identical with compound A with respect to melting point, mixture melting point, and ir.

B.—Compound A, 200 mg, mp 235–237°, was dissolved in 2 ml of ethanolic hydrogen chloride. The solution was concentrated at atmospheric pressure. Trituration of the residue with ethyl acetate–hexane gave a solid which was then recrystallized from ethanol–ethyl acetate to give a solid, mp 195–197° dec. This solid was identical with compound B with respect to melting point, mixture melting point, and ir.

Registry No.—**1** (*syn* isomer), 20538-15-2; **1** (*anti* isomer), 20538-16-3; **2**, 20538-12-9; ethyl pyruvate 2-benzyloxyphenylhydrazone (*syn* isomer), 20538-14-1; ethyl pyruvate 2-benzyloxyphenylhydrazone (*anti* isomer), 20538-13-0.

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