perature for 2 h and then heated at reflux for 48 h. After cooling to room temperature the mixture was filtered and washed with water to afford after drying 1790 mg of brown, crystalline powder.

A 400-mg sample of the brown powder and 650 mg of KCN in 10 mL of chloroform and 7 mL of methanol was stirred at room temperature for 48 h. TLC (silica gel, ethyl acetate) indicated at least three components. After the solvent was allowed to evaporate, the residue was washed thoroughly with water and dried to afford 306 mg of brown powder. The brown residue was extracted with hot benzene and the extract was chromatographed over silica gel. Elution with 10/1 benzene–CH_2Cl_2 and with 10/1 benzene–EtOAc eluted an orange band which upon concentration gave orange crystals of BAII **7**, mp 221.5–224 °C. The yield was 15% based on phthalonitrile. The infrared spectrum was consistent with the usual pattern for BAII and NMR data are included in Table VI. No other BAII products were observed, suggesting that either they were not formed or that if formed they had very unexpected solubility and chromatographic properties.

When phthalonitrile and 2,3-diaminopyridine were treated with $CaCl_2$ according to the procedure given earlier, a mixture of products was obtained. TLC analysis (SiO_2, ethyl acetate) of the mixture did not indicate the presence of **7**; however, we are unable to say with certainty if any other BAII products were present.

Acknowledgment. Unmitigated encouragement from and very helpful discussions with Dr. Lee Robert Mahoney are gratefully acknowledged.

Registry No.—**3**, 61702-18-9; phthalonitrile, 91-15-6; Mg BAII complex, 61846-66-0.

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Substituent Rearrangement and Elimination during Noncatalyzed Fischer Indole Synthesis

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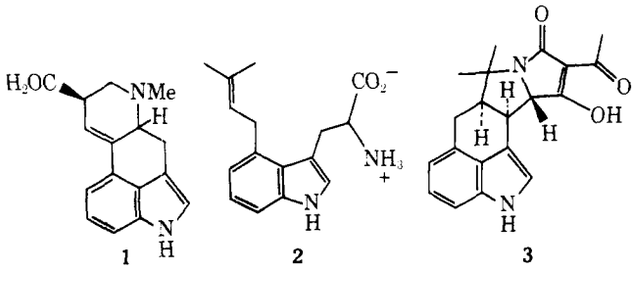
Received October 20, 1976

Treatment of 2,3,3-trimethyl-4-pentenal phenylhydrazone in refluxing ethylene glycol led to 1-(3-methylbut-2-en-1-yl)-3-methylindole, presumably through allylic rearrangement to the indolic nitrogen of the intermediate 3-(1,1-dimethylallyl)-3-methylindolenine; no rearrangement to a 4-allylindole derivative was observed. Treatment of 1,3-cyclohexanedione-2-chloro-6-(3-methylbut-2-en-1-yl) phenylhydrazone in refluxing *o*-dichlorobenzene led to 5-allyl-7-chloro indole derivatives, while in aqueous sulfuric acid a 4-alkyl-7-chloro indole derivative was obtained. These derivatives presumably arise via rearrangement of a C-3a isoprenylated intermediate. The formation of these products is discussed in relation to ergot alkaloid biosynthesis.

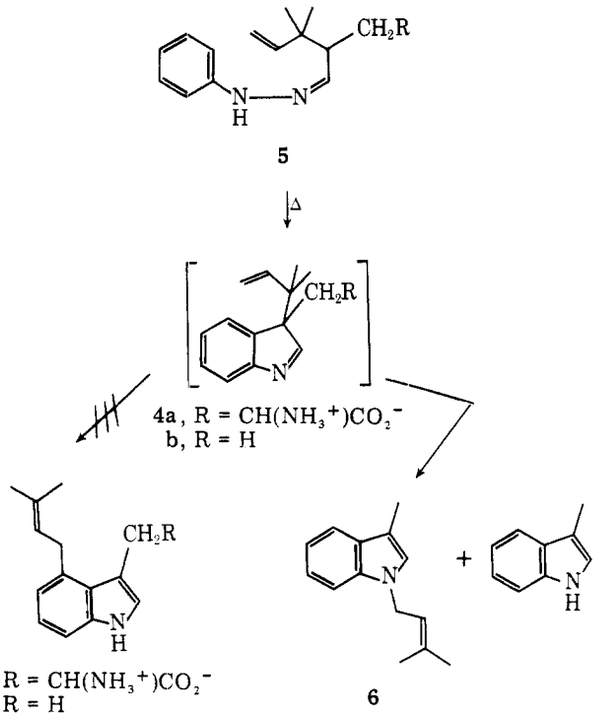
The biosynthesis of lysergic acid (**1**) proceeds from L-tryptophan[1] and mevalonic acid.[2] Recently, an enzyme, dimethylallyltryptophan synthetase,[3] has been isolated which directly forms **2** by coupling L-tryptophan with dimethylallyl pyrophosphate. A related alkaloid, cyclopiazonic acid (**3**), has been shown to derive from a C-4 isoprenylation of a tryptophan derivative.[4] Since such C-4 alkylations are without precedent in the chemistry of indoles, we undertook a study of some chemical model systems for this process.



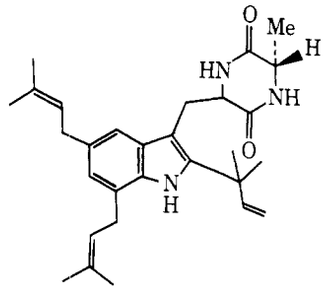
1 **2** **3**

Two hypotheses seemed to offer reasonable chemical explanations for an overall C-4 alkylation during the enzymic reaction. These involved a preliminary conversion of tryptophan to the C-3 substituted derivative, as **4a**, which could undergo subsequent [3,3]-sigmatropic rearrangement to **2** (Scheme I). An alternative is a sequential indoline formation, as **12**, from tryptophan and its direct isoprenylation at C-3a (Scheme III) to **13** followed by a [1,2] shift, thereby establishing the requisite 4-isoprenylated substitution. It is of interest that in this latter scheme isoprenylation of the indoline

Scheme I



12 at the two alternative activated positions, i.e., C-5 and C-7, gives the substitution pattern found in echinulin (14).

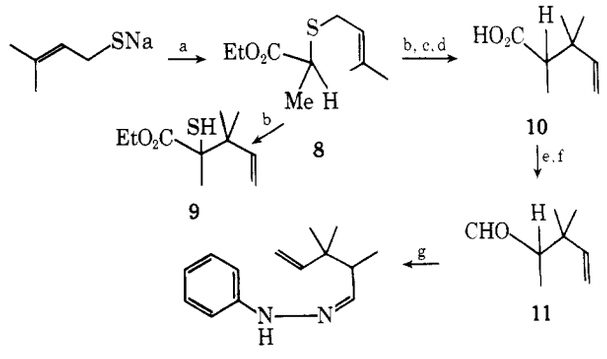


14

To test the first of these possibilities, we generated **4b,** in situ, by the Fischer cyclization of the hydrazone **5.** The well-documented[5] acid sensitivity of 3-allyl-3-alkylindolenines, rearranging to 2,3-disubstituted indoles, prompted our choice of nonacidic conditions. Such noncatalyzed Fischer indole cyclizations have been reported[6] and we found refluxing ethylene glycol to be satisfactory. However, at 198 °C the rearrangement took an unexpected course resulting in the isolation of the known[7] *N*-dimethylallyl-3-methylindole (**6,** 9%) as well as skatole (4%), as the only indolic products. None of the desired 4-substituted **7** was obtained upon chromatography of the crude reaction mixture. Since indole **7** would be expected to survive both the reaction conditions as well as chromatographic workup, the failure to observe **7** implies that indolenine **4b** rearranged preferentially outside the benzenoid system.[8] The formation of skatole probably occurs by thermal elimination of isoprene from **4b.**

The synthesis of hydrazone **5** was achieved in four steps from ethyl α-bromopropionate and is outlined in Scheme II. Sulfide **8** underwent [2,3]-sigmatropic rearrangement[9] when treated with lithium diisopropylamide; however, the resulting thiol **9** could not be cleanly desulfurized with Raney nickel. However, methylation of the thiolate anion followed by desulfurization of the resultant thioether with sodium ethanethiolate[10] proceeded with accompanying cleavage of

Scheme II

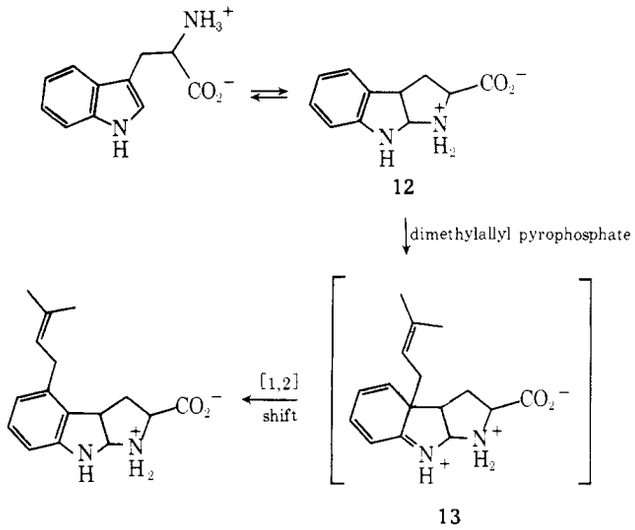


a, ethyl α-bromopropionate, EtOH; b, LDA, THF; c, MeI; d, EtSNa, HMPA; e, $LiAlH_4$; f, $CrO_3 \cdot 2Py$, CH_2Cl_2; g, phenylhydrazine, MeOH.

the ester, to yield acid **10** as a colorless liquid (80% from the thioether). Lithium aluminum hydride reduction and selective reoxidation gave the aldehyde **11** in 9% overall yield from ethyl α-bromopropionate.

The failure of this first possibility led us to explore routes for the in situ generation of C-3a substituted indoles to evaluate the possibility of their [1,2] rearrangement to 4-isoprenylated derivatives. As a reasonable path to an intermediate

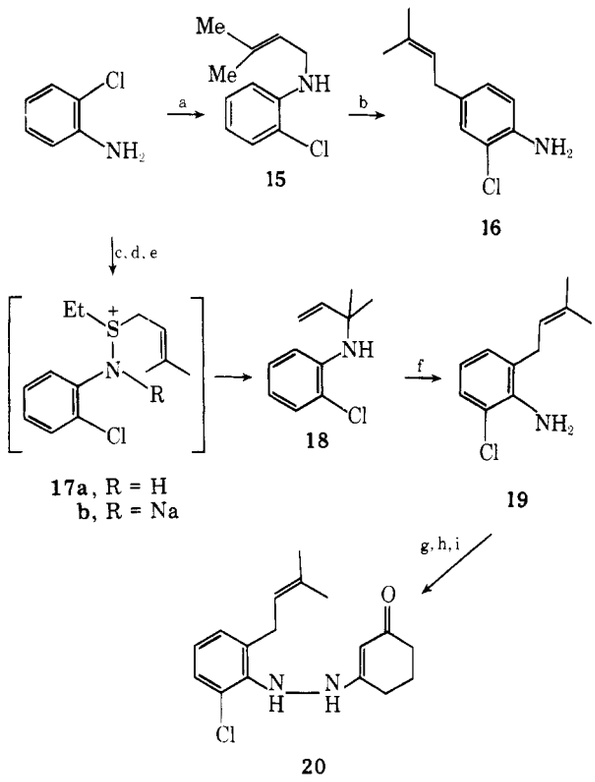
Scheme III



such as **13,** we considered a Fischer cyclization, on the stable enehydrazine **20,** Scheme V.

To this end, we examined possible routes to the aniline **19.** Previous reports by Hurd and Jenkins[11] established that zinc chloride in refluxing xylene caused clean [1,3]-sigmatropic rearrangement of *N*-allylanilines to the ortho-substituted derivatives. Following their method with *N*-allyl-2-chloroaniline only starting material was recovered after 3 h. Therefore, 2-chloro-*N*-(3,3-dimethylallyl)aniline (**15**) was prepared and refluxed in benzene with aluminum chloride to yield the unexpected para-substituted aniline **16.** The substitution pattern was assigned on the basis of the ^1H NMR spectrum by comparison with that of 2-chloro-4-methylaniline. As an alternative, Gassman[12] had reported specific ortho alkylations of aromatic amines via sulfonium salts such as **17a.** Following his procedure we generated **17a** by treating 2-chloroaniline with *tert*-butyl hypochlorite followed by 3,3-dimethylallyl ethyl sulfide. However, upon treatment with sodium methoxide in methanol the inverted *N*-allylaniline **18** was obtained. This result may be rationalized as proceeding

Scheme IV



a, dimethylallyl bromide
b, $AlCl_3$
c, *tert*-butyl hypochlorite
d, ethyl dimethylallyl sulfide
e, sodium methoxide
f, 1.0 N ethanolic HCl
g, NOCl, THF, −78 °C
h, $LiAlH_4$
i, 1,3-cyclohexanedione

through ylide formation (e.g., **17b**) followed by [2,3]-sigmatropic rearrangement with concomitant desulfurization of the sulfenamide. Similar rearrangements have been reported[13] upon treatment of allylic sulfides with Chloramine-T. Aniline **18** underwent an extremely mild amino-Claisen rearrangement to **19** upon prolonged treatment with ethanolic hydrochloric acid at 25 °C. Conversion to **19** appeared quantitative by NMR analysis after 85 h. Recently, other workers have reported a similar rearrangement at 80 °C.[14]

Since normal conditions for diazotization led to acid-catalyzed ring closure to a tetrahydroquinoline, nitrosyl chloride at −78 °C was found necessary. Reduction of the diazotized amine with lithium aluminum hydride gave a crude hydrazine which proved difficult to purify. A crystalline hydrazone was obtained (32% from aniline **19**) by direct coupling with 1,3-cyclohexanedione and appeared (NMR) to exist in solution exclusiely as the enehydrazine tautomer **20.**

Attempts at Fischer cyclization of enehydrazine **20** under a variety of acidic conditions gave complex mixtures which were difficult to separate. However, by refluxing in aqueous sulfuric acid 8-chloro-1,2,3,4-tetrahydro-4-oxocarbazole **23** (4%) and oxocarbazole **24** (2%) were obtained. Deallylated **23** could arise by thermal elimination of isoprene from intermediate **21** (Scheme V) while the rearranged **24** presumably results from hydration, followed by 1,2 shift of the resulting alkyl group. Such 1,2 shifts of a methyl group have been observed previously upon cyclization of cyclohexanone mesitylhydrazone[15] and more recently a similar shift of a phenyl group has been reported.[16] Attempts to provoke a thermal rearrangement of **20** by refluxing in xylene led to a substantial amount of unreacted starting material after 7 h. However, refluxing *o*-dichlorobenzene gave rapid decomposition and in 25 min three new crystalline carbazoles, **25, 26,** and **27** along with **23,** were isolated by chromatography.

The structural assignments were based on the ^1H NMR spectra (Table I). In these spectra the 4-oxo substituent causes a characteristic downfield shift of H-5, which is useful in determining the substitution pattern. Deallylated carbazole **23** was identical with an authentic sample, prepared using *o*-chloroaniline.

These products are best understood as arising from an initial Fischer cyclization of **20** to a pair of isomeric pyrollines **21** and **22.** Acid-catalyzed rearrangement and hydration gives **23** and **24,** while the thermal pathway from **21** leads by way of [3,3]- and [1,3]-sigmatropic shifts to **25** and **26.** Such competing [3,3] and [1,3] shifts have been observed previously[17] and have been associated with radical dissociation–recombination pathways. Such a pathway would also readily explain the presence of deallylated carbazole **23.** In contrast, dechlorination of **22** leads to carbazole **27.**

Scheme V

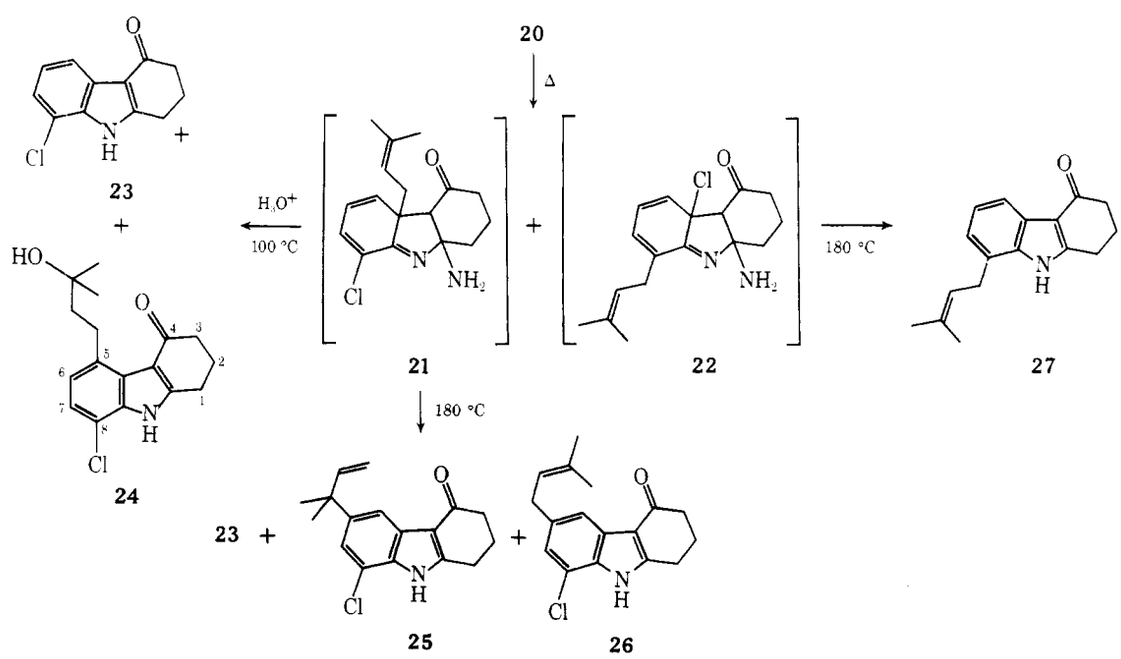


Table I[a]

Carbazole	H_5	H_6	H_7	Mp, °C	Yield, %
24[b] 5-alkyl, 8-chloro		6.92 AB quartet	7.16 J = 8	180–181	2
25[c] 6-allyl, 8-chloro	8.00 d J = 1.5		7.13 d J = 1.5	278–279.5	4
23[c] 8-chloro	8.01 d of d J = 6.0, 2.0	7.29–7.11 complex multiplet		252–256	10[d]
26[c] 6-allyl, 8-chloro	8.03 d J = 1.5		6.98 d J = 1.5	244–246	2
27[c] 8-allyl	7.92 d of d J = 7.0, 1.75	7.09 d of d J = 7.0, 7.0	6.97 d of d J = 7.0, 1.75	194–196	5

[a] The chemical shifts are relative to internal Me_4Si (δ) and all coupling constants are in hertz. [b] Spectrum recorded in Me_2SO-d_6. [c] Spectrum recorded in acetone-d_6. [d] This yield was obtained in refluxing dichlorobenzene.

In summary, these studies show that 3a-dimethylallylated indoles such as **21** do undergo rearrangement to ring substituted derivatives. At high temperatures in neutral media they proceed to 5-substituted products by processes of the [3,3]- and [1,3]-sigmatropic type, which have ample precedent. In acid we have observed a 4-substituted product, **24**, presumably resulting from a [1,2] shift.

Whether such reactions may be useful in making 4-substituted indoles and whether such intermediates are involved in lysergic acid biosynthesis must await further studies.

Experimental Section

Melting points were determined on a Kofler hot stage microscope or Thomas-Hoover capillary melting point apparatus and are uncorrected. Microanalyses were performed by Midwest Microlabs Inc., Indianapolis, Ind., or Galbraith Laboratories, Inc., Knoxville, Tenn. IR spectra were recorded on a Perkin-Elmer Model 700 spectrophotometer. NMR spectra were recorded on a Hitachi Perkin-Elmer R-22B instrument or Varian Associated T-60 spectrometer. Silica gel for column chromatography was Merck silica gel 60, no. 7734, or Merck silica gel H type 60, no. 7736. NMR values are expressed in δ downfield from internal Me_4Si while UV maxima are expressed in nanometers.

1-(3-Methyl-2-butenyl)-3-methylindole (6).[7] Indole **6** was prepared by a modification of the literature procedure using HMPA instead of DMF as the solvent. **6** was obtained as a colorless liquid (47%), bp 86 °C (0.075 mm).

Indolization of Hydrazone 5. A solution of hydrazone **5** (1.0 g, 4.62 mmol) in dry ethylene glycol (10 mL) was refluxed under a nitrogen atmosphere for 5.5 h. The cooled reaction mixture was diluted with water (50 mL and extracted with ether. Normal workup and evaporation gave 660 mg of a brown oil.

Column chromatography on silica gel (50 g) eluting with benzene gave indole **6** as a colorless liquid, 78 mg (9%): mass spectrum (70 eV) M^+ m/e 199; the IR and NMR spectra were superimposable upon those obtained from an authentic sample prepared by a published procedure.[7]

Skatole eluted next and was obtained as a white solid, 25 mg (4%), mp 94–95 °C.

Continued elution with a benzene–ethyl acetate gradient led to intractable brown tars which proved difficult to characterize.

α-Carboethoxyethyl 3-Methyl-2-butenyl Sulfide (8). 3-Methyl-2-butenethiol (18.4 g, 180 mmol) in absolute ethanol (10 mL) was added dropwise, under N_2 and with stirring, to a precooled (0 °C) solution of sodium ethoxide (180 mmol) in ethanol (200 mL), and the resulting solution was stirred at 25 °C for 10 min. To the above solution was added dropwise ethyl α-bromopropionate (32.6 g, 180 mmol) as a solution in absolute ethanol (100 mL), and the resulting suspension was stirred at 25 °C for 3 h. The sodium bromide precipitate was filtered and the filtrate was evaporated to leave crude **8**, 35 g (96%), a colorless liquid. Bulb to bulb distillation at an oven temperature of 52 °C (0.15 mm) gave water-white **8**, 23 g (63%): IR (neat) 1732 cm^{-1}; NMR ($CDCl_3$) δ 1.3 (3, t, J = 7 Hz, ester Me), 1.45 (3, d, J = 7 Hz, secondary methyl), 1.75 (3, br s, vinyl methyl), 1.78 (3, br s, vinyl methyl), 3.3 (3, m, methylene and methine), 4.20 (2, q, J = 7 Hz), 5.24 (1, t, J = 8 Hz, vinyl H).

2-Carboethoxy-3,3-dimethyl-4-pentene-2-thiol (9). To a cold (0 °C) solution of lithium diisopropylamide (21.4 mmol) in dry THF (25 mL) was added under nitrogen sulfide **8** (2.88 g, 14.2 mmol), and the mixture was allowed to warm to 23 °C with stirring continued for 3 h. Evaporation of the solvent left an oil which was taken up in ether, washed with H_2O and brine, dried ($MgSO_4$), and evaporated to leave crude thiol **9** (2.75 g, 96%) in at least 95% purity as judged by ^1H NMR: bp 95 °C (3 mm) (bulb to bulb); IR (neat) 1725 cm^{-1}; NMR ($CDCl_3$) 1.20 (6, s, *gem*-dimethyl), 1.30 (3, t, J = 7 Hz, ester Me), 1.48 [3, d, J = 1 Hz, collapses to singlet with D_2O, (R)(R[1]) (SH) **Me**], 2.32 (1, br s, exchanges with D_2O, –SH), 4.2 (2, q, J = 7 Hz, CO_2CH_2–), 4.85–5.35 (2, m, vinyl methylene), 6.06 (1, d of d, J = 10, 19 Hz, vinyl H); mass spectrum (70 eV) M^+ m/e 202. Anal. Calcd for $C_{10}H_{18}O_2S$: C, 59.37; H, 8.96. Found C, 59.85; H, 9.01.

2,3,3,-Trimethyl-4-pentenoic Acid (10). To a cold (0 °C) solution of lithium diisopropylamide (260 mmol) in dry THF (150 mL) was added dropwise sulfide **8** (35 g, 173 mmol) as a solution in THF (300 mL) under nitrogen. After the addition was completed the red reaction mixture was first warmed to room temperature and stirre for an additional 30 min, then treated dropwise with methyl iodide (37 g, 260 mmol) and stirred for 3 h at 25 °C. Evaporation of the THF left a red oil which was dissolved in ether, washed with water and brine, dried ($MgSO_4$), and evaporated. Distillation afforded a pale yellow liquid, 14.8 g (39%), bp 84–86 °C (1.7–2.2 mm), identified as the rearranged thioether by its spectral properties: IR (neat) 1715 cm^{-1}; NMR ($CDCl_3$) δ 1.28 (6, s, *gem*-dimethyl), 1.33 (3, t, J = 7 Hz, CH_2CH_3), 1.50 (3, s, tertiary methyl), 2.02 (3, s, SCH_3), 4.17 (2, q, J = 7 Hz), 5.10 (2, m, vinyl CH_2), 6.07 (1, d of d, J = 18, 10 Hz, vinyl CH).

Ester hydrolysis was found to accompany desulfurization.[10] The thioether above (5.0 g, 23.1 mmol) was heated at 85 °C with an excess of sodium ethanethiolate (9.7 g, 120 mmol, 5 equiv) in dry HMPA under nitrogen for 2.5 h. The cooled reaction mixture was poured into 0.1 M aqueous HCl and extracted with ether. The ethereal extract was washed exhaustively with water and brine, dried ($MgSO_4$), and evaporated to leave acid **10** as a pale yellow liquid, 2.6 g (80%): IR (neat) 3450–2450 (br), 1710 cm^{-1}; NMR ($CDCl_3$) 1.13 (6, s, *gem*-dimethyl), 1.14 (3, d, J = 7 Hz, secondary CH_3), 2.52 (1, q, J = 7 Hz, methine), 5.15–4.75 (2, m, vinyl CH_2), 5.87 (1, d of d, J = 18, 9 Hz, vinyl H), 10.4 (1, br s, exchanges in D_2O, $-CO_2H$).

2,3,3-Trimethylpent-4-en-1-ol. To a suspension (0 °C) of lithium aluminum hydride (995 mg, 26.1 mmol) in dry ether (25 mL) was added dropwise under nitrogen 2,3,3-trimethylpent-4-enoic acid (3.5 g, 25 mmol) in dry ether. After the addition had been complete, the reaction was stirred at 25 °C for 10 h. Water (6 mL) was added and the resulting precipitate filtered and washed with ether. Normal workup and evaporation gave a yellow oil which was distilled to afford 2,3,3-trimethylpent-4-en-1-ol, 2.37 g (74%): bp 89–94 °C (25 mm); IR (neat) 3350 (br), 1040, 930 cm^{-1}; NMR ($CDCl_3$) δ 0.97 (3, d, J = 6 Hz, methyl), 1.03 (6, s, *gem*-dimethyl), 1.42 (1, m, methine), 1.73 (1, s, exchanges with D_2O, OH), 3.30 (1, d of d, J_{gem} = 9, J_{vic} = 7 Hz, CH_2OH), 3.75 (1, d of d, J_{gem} = 9, J_{vic} = 5 Hz, CH_2OH), 4.70–5.08 (2, m, vinyl CH_2), 5.82 (1, d of d, J = 18, 9 Hz, vinyl H).

2,3,3-Trimethyl-4-pentenal Phenylhydrazone (5). To a solution of CrO_3·2pyridine (160 mmol) in methylene chloride[18] (400 mL) was added 2,3,3-trimethyl-4-pentenol (3.42 g, 26.8 mmol) as a solution in methylene chloride (7 mL) and the resultant black suspension was stirred at 25 °C for 15 min. The methylene chloride solution was decanted from the black precipitate and washed with 10% NaOH, 1 N HCl, saturated $NaHCO_3$, and brine, then dried ($MgSO_4$) and evaporated to leave **11**, 2.28 g (68%), as a colorless liquid: IR (neat) 1720, 2750 cm^{-1}; NMR ($CDCl_3$) δ 1.06 (3, d, J = 7 Hz, secondary CH_3), 1.15 (6, s, *gem*-dimethyl), 2.24 (1, d of q, J = 7, 2 Hz, methine), 5.10–4.73

(2, m, vinyl methylene), 5.80 (1, m, vinyl H), 9.70 (1, d, J = 2 Hz, CHO).

Aldehyde 11 gave the phenylhydrazone **5** as a colorless oil (89%): bp 105 °C (0.35 mm) (Kugelrohr); IR (neat) 3310, 1601, 1510, 1270 cm^{-1}; NMR ($CDCl_3$) δ 1.03 (6, s, *gem*-dimethyl), 1.07 (3, d, J = 7 Hz, Me), 2.26 (1, q, J = 7 Hz, methine), 4.77–5.13 (2, complex m, vinyl CH_2), 5.60–6.13 (1, complex m, vinyl H), 6.63–7.42 (7, complex m, ArH, NH, N=CHR); mass spectrum (70 eV) M^+ m/e 216.

***N*-(3,3-Dimethylallyl)-2-chloroaniline (15).** To mechanically stirred ice-cold *o*-chloroaniline (71.9 g, 562 mmol) was added dropwise dimethylallyl bromide (41.85 g, 281 mmol) as a solution in dry ether (50 mL), under nitrogen. After the addition was complete, the mixture was allowed to warm to 25 °C and stirred for 16 h, the resulting suspension was diluted with ether and filtered, and the precipitate was washed with ether. The orange ethereal solution was washed with 10% NaOH and brine, dried (Na_2SO_4), and evaporated to leave 62 g of an oil. The oil was distilled through Vigreux and gave two fractions. The higher boiling was a colorless liquid, 30.8 g, bp 76–79 °C (0.15–0.25 mm), and this fraction was redistilled through Vigreux (10 cm) to give the *N*-allylaniline **15** as a colorless liquid, 24.5 (46%): bp 58–60 °C (0.04 mm); IR (neat) 3420, 1601, 1520, 765 cm^{-1}; NMR ($CDCl_3$) δ 7.36–6.52 (4, complex m, ArH), 5.36 (1, t, J = 6 Hz, vinyl H), 4.22 (1, br s, exchanges with D_2O), 3.72 (2, d, J = 6 Hz, methylene), 1.76 (3, d, J = 0.4 Hz, vinyl methyl, 1.73 (3, br s, vinyl methyl).

2-Chloro-4-(3,3-dimethylallyl)aniline (16). To a suspension of aluminum chloride (6.78 g, 51 mmol) in dry benzene (50 mL) was added a solution of **15** (10 g, 51 mmol) in dry benzene (100 mL) (a pale yellow solution developed) and then the solution was refluxed for 15 h. Upon cooling, the black precipitate was digested with 50% KOH (300 mL) and the aqueous phase extracted with ether. After normal workup and evaporation, the resultant oil was chromatographed on silica (80 g). Benzene (400 mL) elution gave a crude fraction (2.62 g) containing starting material and desired product. Distillation afforded **16** as a colorless liquid, 1.0 g (10%): bp 86–87 °C (0.04 mm); NMR ($CDCl_3$) δ 7.30–6.58 (3, complex m, ArH), 5.22 (1, t, J = 7 Hz, vinyl H), 3.83 (2, s, NH_2), 3.70 (2, d, J = 7 Hz, CH_2), 1.73 (3, br s, vinyl methyl), 1.70 (3, br s, vinyl methyl). The aromatic region was identical with that of an authentic sample of 2-chloro-4-methylaniline.

***N*-(1,1-Dimethylallyl)-2-chloroaniline (18).** To a solution of *o*-chloroaniline (59.1 g, 462 mmol) in dry methylene chloride (600 mL) at −78 °C was added, under $_2$, *tert*-butyl hypochlorite (55.3 mL, 462 mmol) as a solution in methylene chloride (500 mL). After stirring at −78 °C for 30 min a methylene chloride (300 mL) solution of 3,3-dimethylallyl ethyl sulfide (60 g, 462 mmol) was added dropwise under N_2. After stirring for an additional 30 min, the resulting black mixture was treated with sodium methoxide in methanol (462 mmol, 300 mL) and stirring was continued for an additional 15 min at −78 °C; then the mixture was allowed to warm to room temperature and stirred overnight. The resulting red-black mixture was washed with water and brine, then dried (Na_2SO_4) and evaporated to a black liquid. Distillation through Vigreux (10 cm) gave *N*-(1,1-dimethylallyl)-2-chloroaniline (**18**, 64.4 g, 77%) as a pale yellow liquid: bp 84–89 °C (1.9–2.0 mm); IR (film) 3400, 1598, 1510, 1470, 1330, 1200, 1045, 930, 755 cm^{-1}; NMR ($CDCl_3$) δ 7.38–6.45 (4, complex m, ArH), 6.04 (1, d of d, J = 18, 10 Hz, vinyl H), 5.15 (1, d of d, J = 18, 2 Hz, vinyl H), 5.10 (1, d of d, J = 10, 2 Hz, vinyl H), 4.6–4.35 (1, br, NH exchangeable in D_2O), 1.42 (6, s, *gem*-dimethyl).

6-Chloro-2-(3,3-dimethylallyl)aniline (19). *N*-(1,1-Dimethylallyl)-2-chloroaniline (10.2 g, 52 mmol) was stirred at 25 °C with 1.0 N ethanolic hydrochloric acid (77 mL, 77 mmol) for 85 h. The mixture was neutralized with bicarbonate and extracted with methylene chloride, and the organics were washed with brine, dried (Na_2SO_4), and evaporated to leave 10.1 g of a pale yellow liquid. An NMR spectrum of this crude material indicates that complete conversion had occurred. Distillation through Vigreux gave **19** as a colorless liquid, 6.5 g (64%): bp 84–96 °C (0.1 mm); IR (film) 3452, 3360, 1605, 1485 cm^{-1}; NMR ($CDCl_3$) δ 7.16 (1, d of d, J = 7, 2 Hz, ArH), 6.97 (1, d of d, J = 7, 2 Hz, ArH), 6.63 (1, d of d, J = 7, 7 Hz, ArH), 5.21 (1, t, J = 7 Hz, vinyl H), 4.40–3.55 (2, br s, exchanges with D_2O, NH_2), 3.23 (2, d, J = 7 Hz, CH_2), 1.74 (6, br s, vinyl methyls).

1,3-Cyclohexanedione 2-Chloro-6-dimethylallyl Phenylhydrazone (20). To a solution of 2-chloro-6-dimethylallylaniline (2.45 g, 12.5 mmol) and dry pyridine (1.01 mL, 12.5 mmol) in dry THF (150 mL) at −78 °C and under nitrogen was added nitrosyl chloride in methylene chloride (9.0 mL, 1.44 M, excess), slowly with care being taken to maintain the temperature below −65 °C during the addition. After stirring at −70 °C for 30 min, $LiAlH_4$ (950 mg, 25 mmol) was added slowly, maintaining the temperature below −60 °C during addition. The mixture was stirred at −70 °C for 30 min and allowed to warm to 25 °C with stirring continued for 1 h. The resulting mixture was cooled in an ice bath, treated sequentially with water (1 mL), 10% hydroxide (2 mL), and water (3 mL), and then stirred for 4 h. The white precipitate was filtered and washed with ether,and the combined organics were dried (Na_2SO_4) and evaporated to a yellow liquid (2.35 g).

A solution of cyclohexane-1,3-dione (1.40 g, 12.5 mmol) in methanol (20 mL) was added to the yellow liquid above (2.35 g) in methanol (10 mL), and the resulting solution was stirred overnight under N_2. Evaporation of the methanol left a red oil, which was taken up in methylene chloride and washed with brine, dried (Na_2SO_4), and evaporated to leave a red oil (3.6 g). The enehydrazine was obtained as an oily semisolid after chromatography on silica gel H (400 g) with ethyl acetate elution. The enehydrazine **20** was crystallized from ether–hexane as yellow crystals, 1.21 g (32%): mp 110–110.5 °C; IR ($CHCl_3$) 3350, 3400–3200, 1712, 1580 cm^{-1}; NMR ($CDCl_3$) δ 8.7–7.6 (1, br s, exchanges in D_2O, ArNH), 7.17–6.95 (2, complex m, ArH), 6.86 (1, d of d, J = 7, 7 Hz, *p*-ArH), 5.96 (1, br s, exchanges, NH), 5.57 (1, s enol H), 5.21 (1, br t, J = 7 Hz, vinyl H), 3.26 (2, d, J = 7 Hz, CH_2), 2.65–1.60 (6, m, ring protons), 1.72 (3, s, vinyl methyl), 1.63 (3, s, vinyl methyl); UV (EtOH) λ_{max} (log ϵ) 295 nm (4.38); MS (70 eV) m/e 304 (M^+), 306 ($M + 2^+$).

Anal. Calcd for $C_{17}H_{21}Cl_1N_2O$: C, 66.98; H, 6.95; N, 9.12. Found: C, 67.04; H, 6.98; N, 9.04.

1,3-Cyclohexanedione Mono-2-chlorophenylhydrazone. To a refluxing solution of 2-chlorophenylhydrazine hydrochloride (3.38 g, 18.9 mmol) in absolute ethanol (25 mL) was added 1,3-cyclohexanedione (2.18 g, 18.9 mmol) as a solution in absolute ethanol (50 mL). The mixture was refluxed for 10 min, diluted with water, and cooled to give a red solid. Recrystallization from aqueous ethanol gave an orange hydrazone, 2.35 g (53%): mp 185–187 °C; NMR (Me_2SO-d_6) δ 1.75–2.80 (6, m, ring methylene), 4.4–5.6 (1, v br s, exchanges in D_2O, NH), 5.50 (1, s, enol H), 6.58–7.40 (4, m, Ar H), 7.95–8.42 (1, br s, exchanges in D_2O, NH).

8-Chloro-1,2,3,4-tetrahydro-4-oxocarbazole (23). A suspension of 1,3-cyclohexanedione 2-chlorophenylhydrazone (1.50 g, 6.36 mmol) in 20% aqueous H_2SO_4 (150 mL) was heated at reflux (125 °C bath) for 5 h. The cooled reaction mixture was diluted with water and extracted with ethyl acetate. Washing of the organic solution with bicarbonate and brine and drying over Na_2SO_4 gave a brown solid after evaporation. Trituration with carbon tetrachloride left a green solid which was recrystallized from acetonitrile five times to give analytically pure **23**, 79 mg (6%): mp 252–256 °C; IR ($CHCl_3$) 3425, 1650, 1470 cm^{-1}; NMR (acetone-d_6) 2.36–2.11 (2, m, ring methylene), 2.49 (2, t, J = 6 Hz, ring methylene), 3.08 (2, t, J = 6 Hz, ring methylene), 7.29–7.11 (2, complex m, Ar H_6 + H_7), 8.01 (1, d of d, J = 6, 2 Hz, Ar H_5); UV (EtOH) λ_{max} (log ϵ) 243 nm (4.16), 265 (4.09), 297 (4.01) shifted to267 (4.40), 327 (4.30) upon addition of hydroxide.

Anal. Calcd for $C_{12}H_{10}NOCl$: C, 65.61; H, 4.59. Found C, 65.46; H, 4.62.

8-Chloro-5-(3-hydroxy-3-methylbutyl)-4-keto-1,2,3,4-tetrahydrocarbazole (24). A degassed solution of the enehydrazine **20** (200 mg, 656 mmol) in aqueous H_2SO_4 (11 mL, 1.64 M, 18 mmol) was heated gently at 102 °C for 15 min. Upon cooling the mixture was diluted with water (100 mL) and extracted with ethyl acetate. The organic phase was washed with brine, dried (Na_2SO_4), and evaporated to leave 44 mg. Preparative TLC elution with ether gave a fraction at R_f 0.32–0.27, 6 mg (4%), identified as the deallylated carbazole **23** by its chromatographic and spectral properties.

A second fraction at R_f 0.16–0.19 provided 5 mg which upon crystallization gave **24** as white needles, 4 mg (2%): mp 180–181 °C; IR ($CHCl_3$) 3550–3325, 3420, 1645, 1460 cm^{-1}; NMR (Me_2SO-d_6) 7.16, 6.92 (2, AB q, J = 8 Hz, ArH), 3.02 (2, t, J = 7 Hz, CH_2), 1.19 (6, s, *gem*-dimethyl), the remaining methylene resonances were obscured by D_5 acetone; mol wt ($C_{17}H_{20}NO_2Cl$) calcd 305.11826, found 305.11851.

Thermal Indolization of the Enehydrazine 20. A solution of the enehydrazine **20** (3.37 g, 11.1 mmol) in dry, degassed *o*-dichlorobenzene (25 mL) was refluxed under nitrogen for 25 min. (The initial suspension dissolves upon warming.) The cooled reaction mixture was concentrated to ca. 12 mL at 25 °C (0.1 mm) to leave a black, viscous liquid. Filtration through a column of silica gel H (75 g) eluting with 50–75% ethyl acetate in hexane gave a mixture of carbazoles as a brown solid (1.5 g). The solid was carefully chromatographed on silica gel H (100 g) using a positive nitrogen pressure.

Elution with ethyl acetate/hexane (1/4) gave carbazole **25**, 132 mg (4%), as white microplates after recrystallization from acetonitrile: mp 278–279.5 °C; NMR (acetone-d_6) 1.47 (6, s, *gem*-dimethyl), 2.58–2.07 (4, m, ring methylene), 3.04 (2, t, J = 6 Hz, ring methylene), 5.14–4.90 (2, m, vinyl methylene), 6.06 (1, d of d, J = 18, 10 Hz, vinyl H), 7.13 (1, d, J = 1.5 Hz, ArH-7), 8.00 (1, d, J = 1.5 Hz, ArH-5); IR

($CHCl_3$) 3430, 1650, 1475 cm^{-1}; UV (EtOH) λ_{max} (log ϵ) 247 nm (4.43) 265 (4.24), 293 (4.10), shifted upon addition of 50% NaOH to 327 (4.32), 2.69 (4.41); mol wt calcd for $C_{17}H_{18}ClNO$ 287.10769, found 287.10854. The analytical sample was prepared upon repeated recrystallization from acetonitrile.

Anal. Calcd for $C_{17}H_{18}ClNO$: C, 70.99; H, 6.31; N, 4.87. Found: C, 71.07; H, 6.34; N, 4.85.

Continued elution with the same solvent gave carbazole **23,** 230 mg (10%), as colorless needles after recrystallization from acetonitrile, mp 253 -255 °C. The spectral properties were identical with those obtained by the unambiguous route. Continued elution with this same solvent mixture gave carbazole **27,** 135 mg (5%), as colorless needles after recrystallization from acetonitrile: mp 194–196 °C; NMR (acetone-d_6) 1.73 (3, br s, vinyl methyl), 1.76 (3, br s, vinyl methyl), 2.07–2.54 (4, complex m, ring methylene), 3.02 (2, t, J = 6 Hz, ring methylene), 3.57 (2, d, J = 7 Hz, allylic methylene), 5.41 (1, t, J = 7 Hz, vinyl H), 6.97 (1, d of d, J = 7, 1.75 Hz, Ar H_7), 7.09 (1, d of d, J = 7, 7 Hz, Ar H_6), 7.92 (1, d of d, J = 7, 1.75 Hz, Ar H_5), 10.29–10.87 (1, br s, exchanges with D_2O, NH); IR ($CHCl_3$) 3430, 1650, 1470 cm^{-1}; UV (EtOH) λ_{max} (log ϵ) 300 nm (4.27), 265 (4.34), 245 (4.43), shifted upon addition of 50% NaOH to 329 (4.43), 268 (4.50); mol wt calcd for $C_{17}H_{19}NO$ 253.14666, found 253.14559. The analytical sample was prepared upon repeated recrystallization from acetonitrile.

Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.06, H, 7.61; N, 5.50.

Elution with 50% ethyl acetate–hexane gave carbazole **26,** 64 mg (2%), as colorless needles after recrystallization from acetonitrile: mp 244–246 °C, ^1H FT NMR (acetone-d_6) 1.80 (6, br s, vinyl methyl), 2.67–2.13 (4, m, ring methylene), 3.02 (2, t, J = 6 Hz), 3.61 (2, d, J = 7 Hz, allylic methylene), 5.49 (1, br t, vinyl H), 6.98 (1, d, J = 1.5 Hz, Ar H_7), 8.03 (1, d, J = 1.5 Hz, Ar H_5), 10.76–11.36 (1, br s, exchanges with D_2O, NH); IR ($CHCl_3$) 3430, 1650, 1601, 1470 cm^{-1}; UV (EtOH) λ_{max} (log ϵ) 295 nm (4.12), 268 (4.25), 248 (4.34), shifted to 328 (4.32), 282 (4.41) upon addition of 50% OH; mol wt calcd for $C_{17}H_{18}ClNO$ 287.10769, found 287.10938.

Continued elution with 50% EtOAc–hexane gave unreacted starting enehydrazine **20** (200 mg) by NMR.

Acknowledgment. We wish to thank the National Science Foundation, the National Institutes of Health, and Merck Sharp and Dohme for financial support.

Registry No.—**5,** 61740-71-4; **6,** 31463-81-7; **8,** 61740-72-5; **9,** 61740-73-6; **9** Me ether, 61740-74-7; **10,** 61740-75-8; **11,** 61740-76-9; **15,** 61740-77-0; **16,** 61740-78-1; **18,** 61740-79-2; **19,** 61740-80-5; **20,** 61740-81-6; **23,** 61740-82-7; **24,** 61740-83-8; **25,** 61740-84-9; **26,** 61740-85-0; **27;** 61740-86-1; skatole, 83-34-1; 3-methyl-2-butenethiol, 5287-45-6; sodium ethoxide, 141-52-6; ethyl α-bromopropionate, 535-11-5; methyl iodide, 74-88-4; sodium ethanethiolate, 811-51-8; 2,3,3-trimethylpent-4-en-1-ol, 30458-03-8; *o*-chloroaniline, 95-51-2; dimethylallyl bromide, 870-63-3; phenylhydrazine, 100-63-0; 3,3-dimethylallyl ethyl sulfide, 10276-06-9; cyclohexane-1,3-dione, 504-02-9; 2-chlorophenylhydrazine HCl, 41052-75-9; 1,3-cyclohexanedione mono-2-chlorophenylhydrazone, 61740-87-2.

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3-Diazo-4-oxo-3,4-dihydroquinoline. A Novel Synthon for Indole-3-carboxamides

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Received December 7, 1976

Amides of indole-3-carboxylic acid have been synthesized by a novel reaction employing the ultraviolet irradiation of 3-diazo-4-oxo-3,4-dihydroquinoline in the presence of amines. This diazide, when irradiated, is postulated to undergo an internal Wolff rearrangement to indole-3-ketene which can then add any primary or secondary amine to form the corresponding amide in modest to good yield.

In the past, indole-3-carboxamides have been prepared by the reaction between indole-3-magnesium iodide and *N,N*-dialkylchloroformamides,[1,2] by the dicyclohexylcarbodiimide condensation of aniline with indole-3-carboxylic acid,[3] by the reaction of phenyl isothiocyanate with indole,[4] by the treatment of amines with indole-3-carbonyl chloride,[5] by the reaction of indole with chlorothioformamidinium salts followed by treatment with hydroxides,[6] and by the reductive cyclization of *N,N*-dialkyl-2-(2-nitrophenyl)-2-cyanoacetamides[7] using Pd/C. Most of these syntheses are cumbersome and do not represent a generally applicable synthetic route. On the other hand, it is known that indole derivatives can be obtained from diazoquinolines by photochemical rearrangement. In this manner, 3-diazo-4-oxo-3,4-dihydroquinoline (I) when irradiated in aqueous acetic acid is transformed into indole-3-carboxylic acid.[8]

We have previously shown that when 3-diazo-4-oxo-3,4-dihydroquinoline (I) is irradiated in the presence of an alcohol the corresponding 3-indolecarboxylate ester is formed.[9] We now wish to report that this pathway can also be used as a general route for the synthesis of indole-3-carboxamides. This reported procedure appears to be the simplest one and, to our