($CHCl_3$) 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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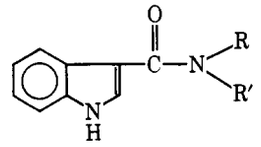
Amides of indole-3-carboxylic acid have been synthesized by a novel reaction employing the ultraviolet irradiation of 3-diazo-4-oxo-3,4-dihydroquinoline in the presence of amines. This diazide, when irradiated, is postulated to undergo an internal Wolff rearrangement to indole-3-ketene which can then 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

Table I



Product[a]	R	R[1]	% yield	Mp, °C	Mass spectrum, *m/e* (rel intensity)
2	Et	Et	39.4	150.5–151.5	216 (32.8), 144[b] (100), 116 (14.3), 72 (11.4)
3	H	*n*-Butyl	40.0	131–131.5	216 (29.9), 159 (14.9), 144 (100), 116 (14.2)
4	H	Ph	42.0	175[c]	236 (57.4), 144 (100), 93 (32.8), 54 (31.1)
5	H	CH_2Ph	56.4	178	250 (85.4), 144 (100), 106 (18.4)
6	H	CH_2CH_2Ph	58.9	157	264 (20.9), 160 (22.8), 144 (100)
7	H	*o*-ClPh	64.1	209	272 (M^{+2}, 5), 270 (16), 144 (100), 126.9 (18.4)
8	H	*o*-BrPh	49.6	197	315 (12.5), 144 (100)
9	CH_2Ph	CH_2Ph	60.2	187–188	340 (16.9), 249 (36.4), 144 (100)

[a] A satisfactory elemental analysis was obtained for all new compounds. [b] The 144 value corresponds to the acylium ion. [c] Literature value, 173–175 °C.[2]

knowledge, represents the only general synthesis of such compounds. Compounds synthesized by this method are listed in Table I.

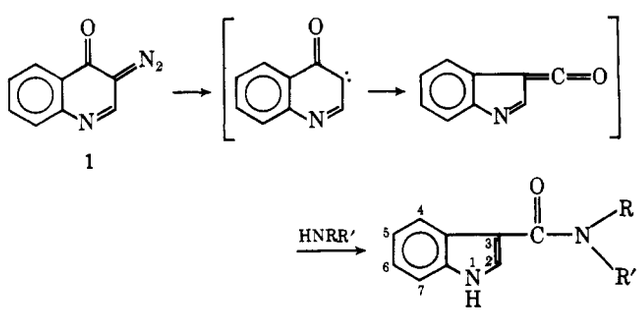
Discussion

All reactions were completed in approximately 6 h. During the course of the reaction, nitrogen, from the diazide photolysis, could be seen bubbling through the solution. The absence of bubbling served in itself as an indication of reaction completion.

Products were identified by their IR and NMR spectra. The classic indole N–H stretch occurred in the IR as a sharp peak from 3450 to 3250 cm^{-1}. The conjugated carbonyl stretch of the secondary amides was found to take place from 1650 to 1610 cm^{-1}, whereas in the tertiary amides it occurred at a lower frequency of 1600 cm^{-1}. In the NMR, an "indole fingerprint" was seen as the 2, 4 + 5 + 6, and 7 proton peak patterns appearing, respectively, as two doublets (J = 3 Hz) (δ 6.8–7.2) and a multiplet (δ 7.8). Mass spectral data show the indole acylium ion (*m/e* 144) as the base peak of all of our compounds.

Although mechanistic investigations are still underway, the reaction appears to proceed via an internal Wolff rearrangement[10] involving the formation of an intermediate carbenoid species which rearranges to the ketene (see Scheme I). This

Scheme I



1

2-9

then adds a molecule of amine to form the corresponding amide.

Experimental Section

The following instruments were used: IR (KBr), Hilger & Watts H-1200 Mark II; NMR, Varian EM390 (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad); mass spectra, HP-5982A GC/MS interfaced with an HP-5934A data system. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Melting points (uncorrected) were determined on a Thomas-Hoover capillary melting point apparatus. Silica gel GF_{254} plates (Merck, Germany) were used for thin and thick layer chromatography and were developed in methanol–chloroform (1:9). 3-Diazo-4-oxo-3,4-dihydroquinoline (1) was synthesized from 3-amino-4-hydroxyquinoline hydrochloride[11] which was diazotized according to Süss.[8]

In each reaction, 200 mg (8.55×10^{-1} mmol) of compound 1 was dissolved in 10 mL of methylene chloride (reagent grade) to which 0.5 mL of amine in 2 mL of methylene chloride was added. A little of this solution was set aside in a dark freezer compartment for use as a chromatographic reference standard. Methylene chloride was chosen as the solvent owing to its low boiling point, its availability, and its inert properties. The remaining mixture was transferred to a Pyrex test tube, lightly stoppered, and irradiated with a Hanovia high-pressure mercury vapor lamp until TLC showed the disappearance of starting material.

After irradiation, the reaction mixture was allowed to sit for 0.5 h. Crystals separated from solutions for products **5, 7–9,** by the end of this period. The crystals were filtered, dissolved in 20 mL of ethanol, and boiled with 0.25 g of Norite. The resulting solution was filtered and 4 mL of water was added to the filtrate. This volume was then reduced under vacuum until crystals were seen to precipitate from solution. For reactions 2–4 and 6, crystals did not appear upon standing. In those cases, the volume of the reaction mixture was reduced under vacuum to 2 mL and the resulting mixture chromatographed on a preparative plate which was developed, dried, and then redeveloped. The UV-quenching band (R_f determined on TLC) was then scraped off and eluted with 100 mL of methanol–chloroform (1:9). All of the elutant was collected in one flask. The solvent was evaporated and the partially purified product was repurified as mentioned above.

The products are listed in Table I together with the physical properties. the IR and NMR spectra of all compounds were consistent with the assigned structure.

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Registry No.—1, 13240-40-9; 2, 61788-23-6; 3, 61788-24-7; 4, 17954-06-2; 5, 61788-25-8; 6, 61788-26-9; 7, 61788-27-0; 8, 61788-28-1; 9, 61788-29-2; diethylamine, 109-89-7; butylamine, 109-73-9; aniline, 62-53-3; benzylamine, 100-46-9; phenethylamine, 64-04-0; *o*-chlorophenylamine, 95-51-2; *o*-bromophenylamine, 615-36-1; dibenzylamine, 103-49-1.

Supplementary Material Available. Infrared, NMR, and analytical data for compounds 2–9 (2 pages). Ordering information is given on any current masthead page.

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Remote Oxidation in the Fe(II)-Induced Decomposition of a Rigid Epidioxide[1a]

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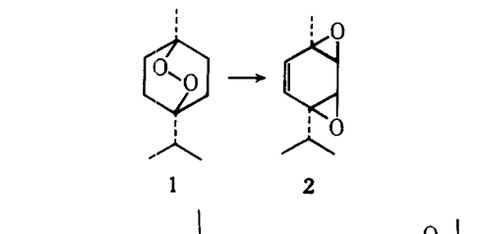
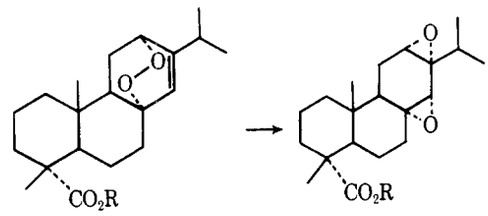
Reaction of the diterpenoid epidioxide **5** with ferrous sulfate gave by remote oxidation the tetrahydrofuran **14a** and the olefin **18a** and by reduction the diol **6**. Structures of **14a** and **18a** were established by a combination of chemical and physical methods and were confirmed by x-ray diffraction of a derivative of **14a**. The mechanism of the Fe(II)-induced remote oxidation of epidioxides which actually involves the Fe(II)–Fe(III) redox system is discussed. The $FeSO_4$–$Cu(OAc)_2$ system also caused remote oxidation in the decomposition of **5**. Highest yields of remote oxidation products were produced by $VO(AcAc)_2$. An unusual isomerization of a 12-chloro derivative of **5** was discovered.

The thermal rearrangement of unsaturated epidioxides to diepoxides, exemplified by the conversion of ascaridole (**1**) to **2**[2,3] and of the epidioxide **3a** of levopimaric acid to **4**,[4] has



1 **2**



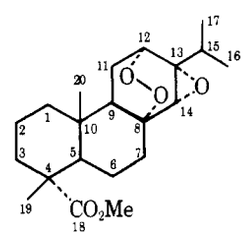
3a, R = H
b, R = Me

4a, R = H
b, R = Me

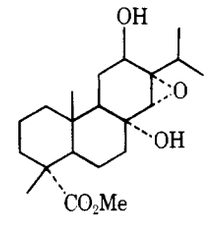
assumed importance not only because of its use in the preparation of the long-elusive arene dioxides and trioxides,[5,6] but also because of the discovery of naturally occurring diepoxides[7–9] and the tumor-inhibitory activity of this functionality.[9] The rearrangement can also be induced photolytically;[10] it is less well known that it can also be effected by ferrous ion at much lower temperatures[11] and that, at least in the case of **3**, this procedure leads to greatly improved yields.

The mechanism proposed for the thermal and photolytic reaction involves homolytic fission of the O–O bond followed by attack of the oxygen atoms on the double bond and cyclization. No mechanism has been proposed for the Fe(II)-induced reaction, but in light of the usual one-electron reduction of the O–O bond by Fe(II),[12] one may conclude that the radical anion chemistry displayed by hydroperoxides and dialkyl peroxides without proximate double bonds is altered to *apparent* diradical chemistry in the unsaturated endoperoxide by oxidation of the initially formed anion radical.

Earlier[13] we had prepared the epoxidic epidioxide **5** from **3b** and were now interested in the behavior of this saturated endoperoxide under the influence of Fe(II). This resulted in approximately equal amounts of diol **6**[13] and two new isomeric



5



6

compounds of formula $C_{21}H_{32}O_5$. Structure elucidation of these substances revealed that they had been formed by a new type of remote oxidation reaction. The details of this discovery constitute the subject of this communication.

Results

Preparation of Starting Material. Reaction of sodium levopimarate with singlet oxygen by the original procedure[14] gave variable yields (30–50%) of **3a**; other products which have