Synthesis of Prenylated Indoles

Ernest Wenkert,* E. Charles Angell, Vitor F. Ferreira,[1] Enrique L. Michelotti, Serge R. Piettre, Jyh-Horng Sheu, and Charles S. Swindell

Departments of Chemistry, Rice University, Houston, Texas 77001, and University of California—San Diego, La Jolla, California 92093

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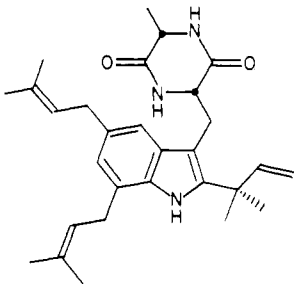
Interaction of magnesium indolates and allyl oxides in the presence of bis(triphenylphosphine)nickel dichloride results in indole β-allylation, except in cases involving highly substituted indoles and allyl alcohols. This method permits the β-prenylation of indole and α-prenylation of ketones (by way of their magnesium enaminates). Base-induced interaction of ethynyldimethylcarbinyl chloride and indole under a variety of conditions yields β-(β,β-dimethylvinyl)quinoline as well as variously dehydroprenylated indoles. α-Lithiation of *N*-(benzenesulfonyl)indole followed by treatment with prenyl bromide or β,β-dimethylacrylyl chloride produces α-prenyl- or α-oxoprenylindole derivatives, the sodium amalgam reduction of the former of which yields α-prenylindole. Interaction of β-cuprated *N*-(benzenesulfonyl)indole with the same halides followed by reduction affords β-prenylindole and β-oxoprenylindole, the latter also being the product of the reaction of magnesium indolate and the acid chloride. Lithium aluminum hydride reduction of 1-(benzenesulfonyl)-3-oxoprenylindole affords an alcohol, whose base hydrolysis produces β-dehydroprenylindole, a compound whose dimerization has led previously to naturally occurring yuehchukene.

The prenyl group, in the form of either a γ,γ-dimethylallyl or an α,α-dimethylallyl system, is a common structural feature of phenolic or indolic natural products. Thus, for example, among indolic materials the mould metabolite echinulin (**1**)[2] represents a variously triprenylated tryptophan-based compound and the plant product yuehchukene (**2**),[3] a structurally unusual dimer of β-dehydroprenylindole (**3**). In order to lay the groundwork for future natural product synthesis in this field, a broad study of the prenylation of indoles has been undertaken. For this purpose three distinctly different routes were investigated.



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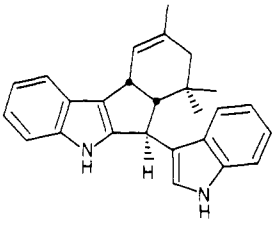

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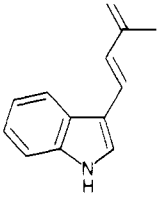
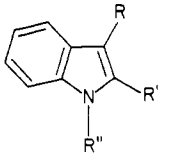


3

Organonickel Chemistry Approach.[4] The allylation of carbanionoid centers by the reaction of allyl alcohols with Grignard reagents in the presence of phosphine-ligated nickel species constitutes an important carbon–carbon bond-forming process,[5] which has found use in natural product synthesis.[6] In reactions with unsymmetrically alkylated allyl alcohols, e.g., either of the two forms of prenyl alcohol, the new bond has been shown to be created predominantly at the more substituted allyl carbon site.[4,5] This fact opened an easy route to the α-prenylated β-alkylindole moiety of echinulin (**1**) on the bases of three assumptions: (a) *N*-magnesioindole salts undergoing a nickel-catalyzed β-allylation, (b) the reaction between β-alkylindoles and prenyl alcohol not being too sterically repressed, and (c) the resultant β-alkyl-β-prenylindolenine undergoing facile Wagner–Meerwein rearrangement.[7] In view of there being few examples of the allylation process with Grignard reagents which are magnesium salts of delocalized, resonance-stabilized anions a short, general study of the allylation of indoles had to be instituted.

Treatment of indole (**4a**), a 0.1 equiv of bis(triphenylphosphine)nickel dichloride, and an excess of allyl alcohol with the stoichiometric quantity of methylmagnesium iodide required for indole and alcohol deprotonation and nickel complex reduction led to β-allylindole (**4b**)[9] in 59% yield. Thus the above assumption (a) appeared to have



4

a, R = R' = R'' = H
b, R = $CH_2CH{=}CH_2$, R' = R'' = H
c, R = R' = H, R'' = $CH_2CH{=}CH_2$
d, R = Me, R' = R'' = H
e, R = Me, R' = $CH_2CH{=}CH_2$, R'' = H
f, R = $CH_2CH{=}CH_2$, R' = Me, R'' = H
g, R = Me, R' = $CH_2CH{=}CMe_2$, R'' = H
h, R = $CMe_2CH{=}CH_2$, R' = R'' = H
i, R = $CH_2CH{=}CMe_2$, R' = R'' = H

(1) Conselho Nacional de Pesquisas (Brazil) fellowship holder, 1980–1984.
(2) Birch, A. J.; Blance, G. E.; David, S.; Smith, H. *J. Chem. Soc.* **1961**, 3128. Quilico, A. *Res. Prog. Org.-Biol. Med. Chem.* **1964**, *1*, 225.
(3) Kong, Y.-C.; Cheng, K.-F.; Cambie, R. C.; Waterman, P. G. *J. Chem. Soc., Chem. Commun.* **1985**, 47.
(4) Based on work presented in Swindell, C. S., Ph.D. Dissertation, Rice University, 1980. Wenkert, E. *Chimia* **1981**, *35*, 257.
(5) Felkin, H.; Swierczewski, G. *Tetrahedron* **1975**, *31*, 2735.
(6) Buckwalter, B. L.; Burfitt, I. R.; Felkin, H.; Joly-Goudket, M.; Naemura, K.; Salomon, M. F.; Wenkert, E.; Wovkulich, P. M. *J. Am. Chem. Soc.* **1978**, *100*, 6445.
(7) The β-prenylation of tryptophan or one of its derivatives and subsequent Wagner–Meerwein rearrangement has been postulated as the possible biosynthetic route to echinulin (**1**) by Wenkert and Sliwa (Wenkert, E.; Sliwa, H. *Bioorg. Chem.* **1977**, *6*, 443).[8]
(8) The echinulin structure in this publication is missing a 7-prenyl unit.
(9) Brown, J. B.; Henbest, H. B.; Jones, E. R. H. *J. Chem. Soc.* **1952**, 3172.

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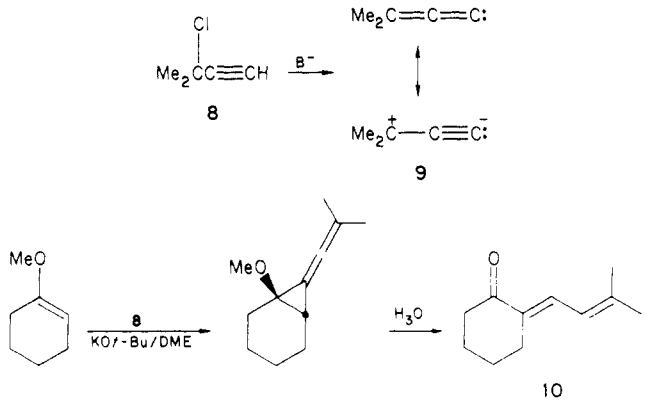
been justified. In order to determine whether C-allylation had been a primary process and the reaction had not yielded *N*-allylindole (**4c**) as an intermediate and been followed by a fast skeletal rearrangement, the N-alkyl derivative (**4c**)[10] was exposed to a 0.1 equiv of the nickel complex reduced by methylmagnesium iodide and shown to lead mostly to the recovery of starting material, accompanied by some indole (**4a**) (ca. 10%). The interaction of compound **4c** with an excess of methylmagnesium iodide in the presence of a catalytic quantity of the nickel species led to complete deallylation, indole being formed in 94% yield,[11] and the reaction with phenylmagnesium bromide gave indole along with allylbenzene.[12] These facts indicated that N-allylation was not involved in the above formation of β-allylindole (**4b**) and, further, that indole can act as an excellent leaving group in nickel-catalyzed Grignard reactions with *N*-allylindoles.

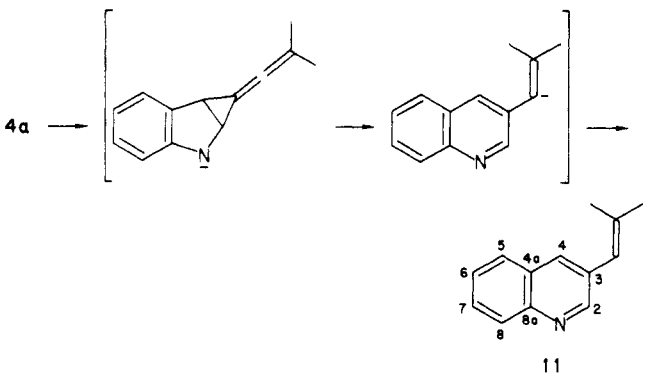
When the β-allylation under the conditions of the **4a** → **4b** transformation was carried out on skatole (**4d**), indole **4e**[13] was obtained in 16% yield.[14,15] Thus assumption (c) above had been vindicated, the putative intermediate indolenine **5** having undergone the expected rearrangement.[17] Treatment of indole (**4a**), dimethylvinylcarbinol, and the nickel complex with the proper amount of methylmagnesium iodide gave in 29% yield a ca. 3:1 mixture of the β-prenylindole isomers **4h**[18a] and **4i**.[17a,18] As in earlier observations,[4-6] the major product was the one containing a quaternary carbon center. The low product yields of the skatole–allyl alcohol and indole–prenyl alcohol reactions revealed strong steric interference by methyl substituents on either the indole or allyl alcohol moieties and constituted a bad omen for the success of the last, most desired reaction, that between skatole and dimethylvinylcarbinol. Indeed, the nickel-catalyzed interaction of these two substances under a variety of conditions failed completely, steric factors having suppressed completely the carbon–carbon bond-forming step.

In essence the indole β-allylation is an alkylation of a secondary enamine magnesium salt and, in the case of the prenylation, mostly the introduction of a *tert*-alkyl group. This fact suggested a new, one-step procedure for α-*tert*-alkylation of aldehydes or ketones by way of their secondary enamine magnesium salt. Corroboration of this idea is shown by the α-prenylation of cyclopentanone. The interaction of the magnesium salts of cyclopentanone

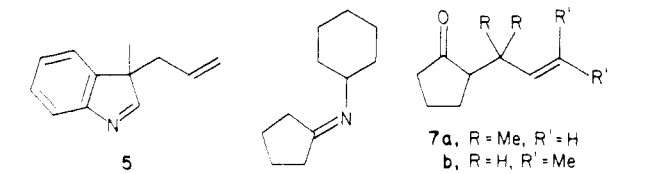
Scheme I



Scheme II



N-cyclohexylimine (**6**)[19] and dimethylvinylcarbinol with the reduced form of bis(triphenylphosphine)nickel dichloride (all produced by methylmagnesium bromide), followed by hydrolysis, produced in 42% yield a ca. 1:1 mixture of the α-prenylcyclopentanone isomers **7a**[20] and **7b**.[20,21]



Vinylidenecarbene Approach. The use of (dimethylvinylidene)carbene (**9**), generated by the treatment of ethynyldimethylcarbinyl chloride (**8**) or 1-bromo-3-methyl-1,2-butadiene with a strong base, in cyclopropane-forming reactions with nucleophilic olefins[22] represents an easy method of introduction of prenyl units, albeit in high oxidation state, into organic substrates. The facile formation of α-prenylidenecyclohexanone (**10**) in a two-step reaction sequence (Scheme I)[22b] constitutes a simple illustration of the application of this procedure.

(10) Bocchi, V.; Casnati, G.; Dossena, A.; Villani, F. *Synthesis* **1976**, 414.

(11) No reaction took place in the absence of the nickel complex.

(12) The hydrocarbon product of the reaction with methylmagnesium iodide must have been volatile 1-butene which, however, had not been trapped.

(13) (a) Jackson, A. H.; Smith, A. E. *Tetrahedron* **1965**, *21*, 989. (b) Hegedus, L. S.; Winton, P. M.; Varaprath, S. *J. Org. Chem.* **1981**, *46*, 2215.

(14) Since intermediate **5** could have undergone rearrangement leading to indole **4e** or **4f**, the structure of the product had to be ascertained unambiguously. Whereas, in principle, this task can be accomplished by ^{1}H NMR spectroscopy, the NMR data left the problem unresolved—the indole of the present work revealing methyl and saturated methylene signals at 2.13 and 3.24 ppm, respectively, those reported for indole **4e**[13b] at 2.12 and 3.07 ppm, respectively,[15] and those recorded for indole **4f**[16] at 2.13 and 3.32 ppm, respectively. However, the ^{13}C NMR spectral data (see Experimental Section) proved the structure unambiguously.

(15) The reaction of skatole (**4d**) with prenyl bromide under conditions of solvolysis has been shown to yield indole **4g**.[17a] The ^{1}H NMR signals of the indole-attached methyl and methylene groups of the product were shown to be at 2.19 and 3.29 ppm, respectively,[17a] making the assignment of a 3.07 ppm signal to the saturated methylene of indole **4e**[13b,14] suspect.

(16) Padwa, A.; Carlsen, P. H. *J. Tetrahedron Lett.* **1978**, 433. Padwa, A.; Carlsen, P. H. J. *J. Org. Chem.* **1978**, *43*, 2029.

(17) (a) Casnati, G.; Francioni, M.; Guareschi, A.; Pochini, A. *Tetrahedron Lett.* **1969**, 2485. (b) Casnati, G.; Dossena, A.; Pochini, A. *Ibid.* **1972**, 5277.

(18) (a) Araki, S.; Manabe, S.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1433. (b) Somei, M.; Natsume, M. *Tetrahedron Lett.* **1973**, 2451.

(19) Jewers, K.; McKenna, J. *J. Chem. Soc.* **1958**, 2209.

(20) Reetz, M. T.; Hüttenhain, S.; Walz, P.; Löwe, U. *Tetrahedron Lett.* **1979**, 4971.

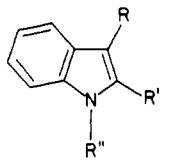
(21) Teisseire, P.; Bernard, P.; Corbier, B. *Recherches* **1956**, 30; *Chem. Abstr.* **1957**, *51*, 2565f. Grigoryan, E. A.; Kazaryan, A. Ts.; Lusararyan, K. S.; Martirosyan, G. T. *Arm. Khim. Zh.* **1974**, *27*, 304; *Chem. Abstr.* **1974**, *81*, 77388n. Andreev, V. M.; Bibicheva, A. I.; Zhuravleva, M. I. *Zh. Org. Khim.* **1974**, *10*, 1470. Streinz, L.; Romaňuk, M. *Collect. Czech. Chem. Commun.* **1978**, *43*, 647. Reetz, M. T.; Hüttenhain, S.; Hübner, F. *Synth. Commun.* **1981**, *11*, 217.

(22) (a) Sasaki, T.; Eguchi, S.; Ohno, M.; Nakata, F. *J. Org. Chem.* **1976**, *41*, 2408. (b) Wenkert, E.; Chou, K. J.; Hatch, R. P. *Synth. Commun.* **1977**, *7*, 375. (c) Landor, S. R.; Rogers, V.; Sood, H. R. *Tetrahedron* **1977**, *33*, 73.

Base-induced interaction of the reactive halides with α- and/or β-methylindoles has been shown to cause the latter to undergo mostly skeletal rearrangement into quinolines,[23] presumably by initial cyclopropanation followed by an electrocyclic ring opening (as portrayed for the reaction of indole (**4a**) in Scheme II). However, the formation of β-dehydroprenylindolenines in reactions of β-substituted indoles[23b] suggested that a reaction with indole (**4a**) itself, a process not studied heretofore, conceivably could be steered away from a cyclopropanation intermediate and toward a β-alkylation product, e.g., β-dehydroprenylindole (**3**). In view of this possibility a short investigation of base-initiated reactions of indole (**4a**) with ethynyldimethylcarbinyl chloride (**8**) was undertaken.

In order at first to guide the reaction toward the unwanted cyclopropanation process, excess chloride **8** and sodium hydride were allowed to react with *N*-carbomethoxyindole (**12a**) in ether solution.[24] Whereas the primary product proved to be elusive, it must have been the expected cyclopropane-containing substance in view of the isolation of quinoline **11** (in 37% yield). The latter was also the product (in 49% yield) of dehydrohalogenation of the chloride **8** with potassium hydroxide and a crown ether in the presence of indole (**4a**) in benzene solution.

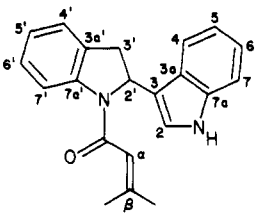
When indole (**4a**) was exposed to an excess of ethynyldimethylcarbinyl chloride (**8**) and sodium hydride in ether solution, there was obtained a mixture from which allene **12b** and indole **15** could be isolated (in 38 and 5%



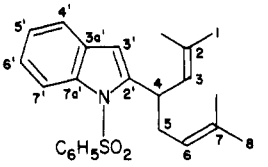
12a, R = R' = H, R" = CO_2Me
b, R = R' = H, R" = CH=C=CMe_2
c, R = $CMe_2C{\equiv}CH$, R' = R" = H
d, R = R' = H, R" = CH=CHC(Me)=CH_2 (*E*)
e, R = R' = H, R" = CH=CHC(Me)=CH_2 (*Z*)
f, R = R' = H, R" = COCH=CMe_2
g, R = COCH=CMe_2, R' = R" = H
h, R = $COCH_2C(Cl)Me_2$, R' = R" = H
i, R = $COCH_2CHMe_2$, R' = R" = H
j, R = $(CH_2)_2C(Cl)Me_2$, R' = R" = H
k, R = $(CH_2)_2C(Me)=CH_2$, R' = R" = H

yields, respectively). The third reaction product, indole **12c**, could be isolated (in 6% yield), when the crude reaction mixture was treated with a dimethylsulfoxide solution of potassium *tert*-butoxide thereby transforming the allene **12b** into more readily separable butadienes **12d** and **12e** (in 8 and 7% yields, respectively). The latter reaction executed on pure allene **12b** gave a 70% yield of a 3.3:1 mixture of the butadienes **12d** and **12e**. Exposure of indole (**4a**) to an excess of the reactive chloride **8** and potassium *tert*-butoxide in hexane solution afforded a simpler mixture of reaction products, indoles **12c** and **15** in 10 and 26% yields, respectively. Thus the reactions of indole (**4a**) under the last two sets of conditions had not involved cyclopropanations but, instead, had caused carbene **9** to behave as an electrophilic dehydroprenylating reagent, as portrayed in Scheme III.[25] The formation of indole **15** showed that the desired β-dehydroprenylation of indole (**4a**) had taken place, but the product had not been stable in the form of structure **3** or its anion and through its tautomer **14** had undergone Michael condensation with indole (**4a**).

Alkylation and Acylation Approach. Whereas, in principle, the β-prenylation of indole (**4a**), a substance with strong enamine behavior, should require merely the spontaneous interaction of the compound with an alkylating agent such as prenyl bromide, the reaction has been shown, in practice, to be highly complex due to problems of regiochemistry and polysubstitution tendency.[17,26] Similarly, the reaction between the magnesium salt of indole (**13**), prepared by exposure of indole (**4a**) to methylmagnesium bromide, and prenyl bromide now gave a mixture which in only 34% yield led to a 17:1 **4i-h** β-prenylindole combination. Early attempts of indole β-oxoprenylation fared not much better. The reaction between indole (**4a**) and β,β-dimethylacrylyl chloride in benzene solution produced *N*-acylindole **12f** and *N*-acylated indole dimer **16**[27] in 3 and 50% yields, respectively. The same reaction in ether solution led to products **12f** and **16** (in 2 and 30% yields, respectively) as well as



16



17

the desired indole **12g** (34%) and its hydrochlorination product **12h** (13%), a substance formed nearly quantitatively by exposure of β-oxoprenylindole (**12g**) to hydrogen chloride gas in methylene chloride solution. The gloomy picture, however, changed when the acylation was carried out on magnesium indolate (**13**). The products proved to be the *N*-acylindole **12f** (18%), the *N*,β-diacylated indole **18l** (9%), and, most importantly, the desired β-oxoprenylindole (**12g**) (60%).

The last product was considered to be a good precursor of β-prenylindole (**4i**) on the basis of the known propensity for β-acylindoles to undergo deoxygenation on lithium aluminum hydride reduction.[28] However, when this reaction was carried out on keto compound **12g**, there was obtained only a small amount of β-prenylindole (**4i**) (8%) accompanied by the major product, the dihydro ketone **12i** (40%). On the other hand, lithium aluminum hydride reduction of keto compound **12h** yielded β-alkylindole **12j** (80%). Unfortunately, base-induced dehydrohalogenation of the latter produced only mixtures of the desired indole (**4i**) and its isomer **12k**.[29]

The simplest procedure for the α- and β-prenylation of indole (**4a**) involved the use of sulfonamide intermediates for the introduction of the required side chains. Thus, for example, α-lithiation of *N*-(benzenesulfonyl)indole (**18a**),[30]

(23) (a) Bycroft, B. W.; Johnson, A. P.; Landon, W. *J. Chem. Soc., Chem. Commun.* **1969**, 463. (b) Landor, S. R.; Rogers, V.; Sood, H. R. *J. Chem. Soc., Perkin Trans 1* **1976**, 2103. (c) Eguchi, S.; Ikemoto, T.; Kobayakawa, Y.; Sasaki, T. *J. Chem. Soc., Chem. Commun.* **1985**, 958.

(24) This reaction was based on the observation of the copper-catalyzed reaction between ethyl diazoacetate and *N*-carbomethoxyindole (**12a**) leading to a cyclopropanecarboxylate, but the reaction with indole (**4a**) yielding ethyl β-indolylacetate (Wenkert, E.; Alonso, M. E.; Gottlieb, H. E.; Sanchez, E. L.; Pellicciari, R.; Cogolli, P. *J. Org. Chem.* **1977**, *42*, 3945).

(25) It is also possible that these reactions do not involve carbene **9**, but proceed by way of solvolysis of chloride **8** and the resultant α,α-dimethylpropargyl cation acting as the agent of alkylation of indole (**4a**).

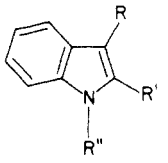
(26) Bocchi, V.; Casnati, G.; Marchelli, R. *Tetrahedron* **1978**, *34*, 929.

(27) For a reaction between indole (**4a**) and phosgene leading to a compound structurally related to **16**, see: Husain, M.; Husain, M.; Khan, N. H. *Indian J. Chem., Sect. B.* **1984**, *23*, 986.

(28) Leete, E.; Marion, L. *Can. J. Chem.* **1953**, *31*, 775. Speeter, M. E.; Anthony, W. C. *J. Am. Chem. Soc.* **1954**, *76*, 6208. Leete, E. *Ibid.* **1959**, *81*, 6023.

(29) Wenkert, E.; Ferreira, V. F., unpublished observations.

(30) Sundberg, R. J.; Russell, H. F. *J. Org. Chem.* **1973**, *38*, 3324. Illi, V. O. *Synthesis* **1979**, 136.



18a, R = R' = H, R'' = $SO_2C_6H_5$
b, R = H, R' = $COCH{=}CMe_2$, R'' = $SO_2C_6H_5$
c, R = H, R' = $COCH_2C(Cl)Me_2$, R'' = $SO_2C_6H_5$
d, R = H, R' = $CH_2CH{=}CMe_2$, R'' = $SO_2C_6H_5$
e, R = R'' = H, R' = $CH_2CH{=}CMe_2$
f, R = Br, R' = R'' = H
g, R = Br, R' = H, R'' = $SO_2C_6H_5$
h, R = $CH_2CH{=}CMe_2$, R' = H, R'' = $SO_2C_6H_5$
i, R = $COCH{=}CMe_2$, R' = H, R'' = $SO_2C_6H_5$
j, R = $CH(OH)CH{=}CMe_2$, R' = H, R'' = $SO_2C_6H_5$
k, R = $COCH_2CHMe_2$, R' = H, R'' = $SO_2C_6H_5$
l, R = R'' = $COCH{=}CMe_2$, R' = H

followed by treatment with β,β-dimethylacrylyl chloride, yielded the α-acylindole derivative **18b** (74%), whose exposure to hydrogen chloride gave the chloro compound **18c** (96%). Unfortunately neither α-acylindole could be desulfonylated, both solvolytic and reductive operations leading to intractable material. When *N*-(benzenesulfonyl)indole (**18a**) was metalated with lithium diisopropylamide and the resultant α-lithio compound treated with prenyl bromide, the α-prenylated derivative **18d** was obtained in 76% yield. It was accompanied by a diprenylation product (**17**) (13%), a compound which could be obtained in 83% yield from indole **18d** upon the latter's exposure to lithium diisopropylamide and prenyl bromide.[31] Sodium amalgam reduction[32] of sulfonamide **18d** liberated α-prenylindole (**18e**) in 96% yield.

For the indole β-prenylation process *N*-(benzenesulfonyl)-β-bromoindole (**18g**), the product of the base-promoted reaction of β-bromoindole (**18f**)[33] with benzenesulfonyl chloride, served as starting material. Metal–halogen exchange of the bromide with *tert*-butyllithium at −95 °C,[34] conversion of the resultant β-indolyllithium reagent into a cuprate by the addition of cuprous cyanide, and treatment of the organometallic reagent with prenyl bromide produced the β-alkylindole derivative **18h** (72%), whose reduction with sodium amalgam[32] led to β-prenylindole (**4i**) (95%). Treatment of the cuprate solution with β,β-dimethylacrylyl chloride afforded ketone **18i** (67%), identical with the product of the reaction (90%) of indole **12g** with benzenesulfonyl chloride and sodium hydroxide under phase-transfer conditions. Sodium amalgam reduction[32] or base-induced solvolysis[35] of sulfonamide **18i** gave β-oxoprenylindole (**12g**) (55 or 92%, respectively).

With numerous prenylated indoles now on hand, it was possible to start considering the use of these materials in natural products synthesis. The following short reaction sequence represents an example of such application. Lithium aluminum hydride reduction of ketone **18i** yielded alcohol **18j** (83%) and some saturated ketone **18k** (8%). Hydrolysis–dehydration of hydroxysulfonamide **18j** in alkaline, aqueous ethanol gave β-dehydroprenylindole (**3**),[36] which through an acid-induced dimerization has been transformed previously into yuehchukene (**2**).[36] This makes the present work a formal total synthesis of this natural product.

(31) The ease of benzylic metallation of indole **18d** may be due to favorable lithium cation association with the neighboring sulfonyl oxygens.
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Experimental Section

Melting points were determined on a Kofler micro hostage and are uncorrected. Infrared spectra were measured on Perkin-Elmer 137 and 1330 spectrophotometers and ultraviolet spectra of methanol solutions on Cary-17 and Perkin-Elmer 550 spectrophotometers. ^1H NMR spectra of $CDCl_3$ solutions with Me_4Si as internal standard were recorded on a Varian EM-390 spectrometer and a 360-MHz instrument with a highly modified Varian HR-220 console, an Oxford magnet, and a Nicolet 1180-E computer system. ^{13}C NMR spectra of $CDCl_3$ solutions were taken on Varian XL-100-15 and Nicolet NT-200 (wide-bore, broad-band, with Oxford magnet) spectrometers, operating at 25.2 and 50.3 MHz, respectively, in the Fourier transform mode. The carbon shifts are in parts per million downfield from Me_4Si; δ (Me_4Si) = δ ($CDCl_3$) + 76.9 ppm. Low-resolution mass spectra were obtained on Finnigan 3300 and 4021 GC–MS spectrometers and high-resolution mass spectra on a CEC 21-11013 instrument. All reactions were carried out under an atmosphere of nitrogen. At the end of the workup of the crude reaction products the organic extracts were washed with brine solution and dried over anhydrous sodium sulfate. Chromatographic separations were executed on silica gel.

β-Allylindole (4b). A 2.8 M ethereal methylmagnesium iodide solution, 3.57 mL (10 mmol), was added to a solution of 1.17 g (10 mmol) of indole (**4a**), and the mixture was refluxed for 2 h. In another flask a 2.8 M ethereal methylmagnesium iodide solution, 11.43 mL (32 mmol), was added to 654 mg (1.0 mmol) of bis(triphenylphosphine)nickel dichloride in 10 mL of dry benzene, the mixture was stirred for 15 min, and thereafter a solution of 2.04 mL (30 mmol) of allyl alcohol in 10 mL of dry ether was added. After 15 min of stirring, the latter mixture was poured by syringe into the former mixture. The combined solutions were concentrated by distillation, to remove the major amount of ether, the volume was reconstituted by the addition of dry benzene, and the mixture was refluxed for 22 h. It was acidified with saturated ammonium chloride solution and extracted with methylene chloride. The extract was dried, filtered through a short silica column, and evaporated. Chromatography of the residue and elution with carbon tetrachloride yielded 983 mg (59%) of indole **4b**:[9] UV (hexane) λ_{max} 265 nm (ϵ 5600); IR (neat) NH 3420 (m), C=C 1640 (m), 1620 (w), cm^{-1}; ^1H NMR δ 3.50 (d, 2, J = 6 Hz, CH_2), 4.9–5.3, 5.8–6.3 (m, 3, olefinic Hs), 6.8–7.0 (m, 1, indole α-H), 7.0–7.4, 7.5–8.1 (m, 4, Ar Hs); ^{13}C NMR δ 29.8 (CH_2), 111.1 (C-3, C-7), 115.1 (olefinic CH_2), 119.0 (C-4 or C-6), 119.2 (C-6 or C-4), 121.7 (C-2 or C-5), 121.9 (C-5 or C-2), 127.4 (C-3a), 136.4 (olefinic CH), 137.3 (C-7a); MS, *m/e* (rel intensity) 157 (M^+, 50), 156 (40), 130 (base), 129 (30), 77 (63), 76 (33).

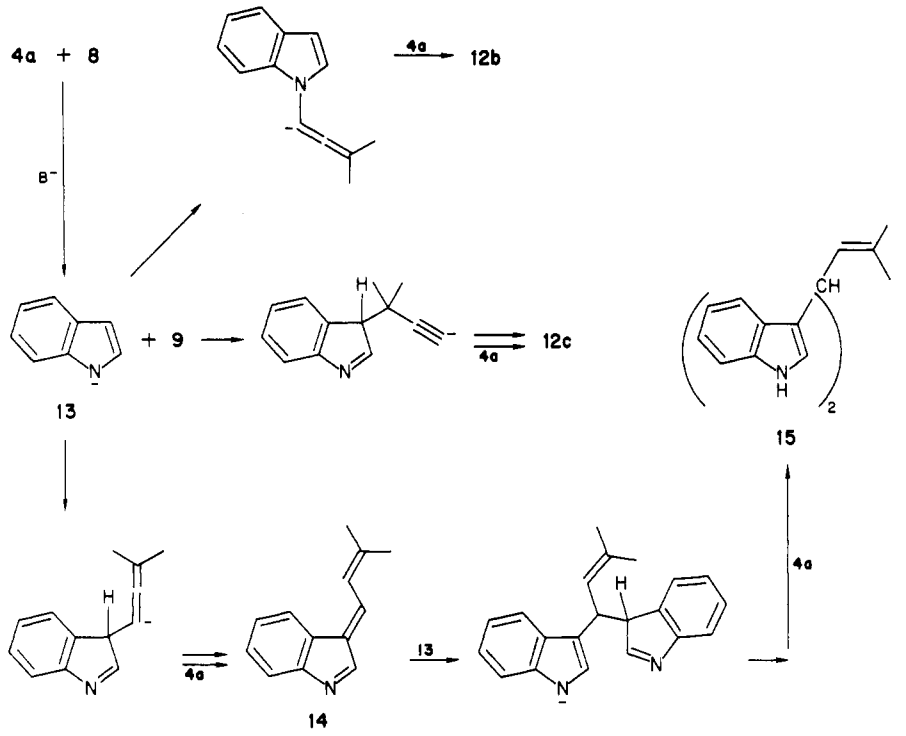
Dealkylation of *N*-Allylindole (4c). A solution of 1.48 g (9.4 mmol) of *N*-allylindole (**4c**)[10] in 10 mL of benzene was added to a catalyst solution prepared from 654 mg (1.0 mmol) of bis(triphenylphosphine)nickel dichloride and a 2.8 M ethereal methylmagnesium iodide solution, 0.7 mL (2.0 mmol), and the mixture was refluxed for 12 h. GC analysis (Varian 1200 flame ionization chromatograph, column of 5% OV 101 on 80–100 mesh Chromosorb W) showed the presence of starting indole and less than 10% indole (**4a**).

A solution of 1.57 g (10 mmol) of *N*-allylindole (**4c**)[10] in 10 mL of benzene was added to a catalyst solution prepared from 654 mg (1.0 mmol) of bis(triphenylphosphine)nickel dichloride and a 2.8 M ethereal methylmagnesium iodide solution, 4.3 mL (12 mmol), in 15 mL of benzene, and the mixture was refluxed for 15 h. Normal workup, chromatography of the crude product, and elution with pentane–benzene mixtures gave 1.10 g (94%) of indole (**4a**).

A mixture of 785 mg (5 mmol) of *N*-allylindole (**4c**)[10] and a 2.5 M ethereal methylmagnesium bromide solution, 2.4 mL (6 mmol), in 10 mL of benzene was refluxed for 40 h. GC analysis (vide supra) of the crude product revealed the absence of indole (**4a**) and normal workup led to the recovery of 571 mg (73%) of starting indole **4c**.

A solution of 3.14 g (20 mmol) of *N*-allylindole (**4c**)[10] in 10 mL of benzene was added to a catalyst solution prepared from 1.31

Scheme III



g (2.0 mmol) of bis(triphenylphosphine)nickel dichloride and a 2.5 M ethereal methylmagnesium bromide solution, 1.6 mL (4.0 mmol). After 15 min of stirring, the mixture was treated with 10 mL (22 mmol) of 2.2 M ethereal phenylmagnesium bromide solution and then refluxed for 41 h. Normal workup and distillation of the crude residue yielded allylbenzene, spectrally identical with an authentic sample, in the fraction boiling at 120–150 °C/151 torr. Chromatography of the nonvolatile residue of the distillation and elution with pentane–benzene mixtures yielded indole (**4a**).

2-Allyl-3-methylindole (4e). The procedure adopted for the above preparation of indole **4b** was used for the interaction of 654 mg (1.0 mmol) of bis(triphenylphosphine)nickel dichloride, 15 mL (42 mmol) of 2.8 M ethereal methylmagnesium iodide solution, 1.31 g (10 mmol) of skatole (**4d**), and 2.04 mL (30 mmol) of allyl alcohol in 10 mL of benzene. The mixture was refluxed for 96 h, then cooled at 0 °C, treated with 15 mL of 1 N hydrochloric acid solution and 10 mL of tetrahydrofuran (THF), and kept stirring for 30 min. Normal workup, chromatography of the crude product and elution with carbon tetrachloride yielded 121 mg (9%) of recovered skatole (**4d**) and then 224 mg (16%, based on consumed skatole) of liquid indole **4e**: IR (neat) NH 3410 (m), C=C 1637 (w), 1620 (w) cm^{-1}; ^1H NMR δ 2.13 (s, 3, Me), 3.24 (d, 2, J = 6 Hz, CH_2), 4.8–5.2, 5.5–6.0 (m, 3, olefinic Hs), 6.7–7.6 (m, 5, NH, Ar Hs); ^{13}C NMR δ 8.3 (Me), 30.6 (CH_2), 107.2 (C-3), 110.1 (C-7), 116.7 (olefinic CH_2), 118.1 (C-4 or C-6), 118.9 (C-6 or C-4), 121.0 (C-5), 129.2 (C-3a), 131.8 (C-2), 134.8 (olefinic CH), 135.1 (C-7a); [For comparison purpose: skatole (**4d**) δ (3-Me) = 9.4 ppm; 2,3-dimethylindole δ (2-Me) = 11.1 ppm and δ (3-Me) = 8.3 ppm] MS, m/e (rel intensity) 171 (M^+, base), 170 (47), 130 (47), 129 (47), 77 (67), 76 (23). Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.07; H, 7.81; N, 8.27.

β-Prenylindoles 4h and 4i.[17a,18] (This experiment proved to be reproducible only under conditions of the Felkin freezing technique[37] at the time of setting up of the reaction.) Catalyst preparation was carried out with 585 mg (0.9 mmol) of bis(triphenylphosphine)nickel dichloride and a 2.8 M ethereal methylmagnesium iodide solution, 6 mL (16.8 mmol), in 15 mL of benzene. After replacement of the ether by benzene and cooling of the solution to 0 °C, a solution of 574 mg (4.9 mmol) of indole (**4a**) in 3 mL of benzene was added, and the mixture stirred for 15 min. Thereafter, 1.05 mL (10 mmol) of dimethylvinylcarbinol was added, and the mixture was refluxed for 61 h. Normal workup and preparative thin-layer chromatography (TLC) on silica gel and elution with 1:1 pentane–benzene gave 333 mg (58%) of starting indole (**4a**) and 111 mg (29%, based on consumed indole) of a 3.1:1 mixture (by GC analysis, 2% OV 101 columns) of **4h** and **4i**. Chromatography of the mixture on silica gel impregnated with 15% of silver nitrate, and elution with benzene–ether mixtures gave crystalline β-prenylindole (**4i**):[17a,18] mp 48–49 °C (hexane at −20 °C) (lit. mp 43–45 °C,[17a] 49–50 °C[18b]); UV λ_{max} 220 nm (ϵ 25 140), 273 (4 860), 279 (5 150), 287 (4 440); IR (neat) NH 3415 (m), C=C 1640 (w) cm^{-1}; ^1H NMR δ 1.75, 1.78 (s, 3 each, 2 Me), 3.45 (d, 2, J = 7 Hz, CH_2), 5.43 (tm, 1, J = 7 Hz, olefinic H), 6.94 (br s, 1, indole α-H), 7.1–7.6 (m, 4, Ar Hs); MS, m/e (rel intensity) 185 (M^+, 80), 117 (base). Further elution gave liquid indole **4h**:[18a] UV (hexane) λ_{max} 265 nm (ϵ 4 800); IR (neat) NH 3420 (m), C=C 1640 (w), 1618 (w) cm^{-1}; ^1H NMR δ 1.45 (s, 6, 2 Me), 4.8–6.2 (m, 3, olefinic Hs); 6.70 (d, 1, J = 2 Hz, indole α-H), 6.7–7.7 (m, 5, NH, Ar Hs); MS, m/e (rel intensity) 185 (M^+, 75), 170 (88), 158 (70), 155 (67), 143 (60), 77 (base). Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.10; H, 8.28; N, 7.49.

A 3.1 M ethereal methylmagnesium bromide solution, 8.5 mL (26 mmol), was added dropwise to a stirring solution of 3.00 g (26 mmol) of indole (**4a**) in 50 mL of dry benzene under nitrogen at 0 °C. The stirring was continued for 30 min, then 3.84 g (26 mmol) of prenyl bromide was added, and the mixture was stirred for 2.5 h. It was poured into 100 mL of saturated sodium bicarbonate solution and extracted exhaustively with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated. Chromatography and elution with 20:1 hexane–ethyl acetate afforded 1.60 g (34%) of a 17:1 mixture of β-prenylindole isomers **4i** and **4h**, respectively. (Other chromatographic fractions contained N- and di-prenylated indoles in small quantities.)

α-Prenylcyclopentanones 7. A 2.8 M ethereal methylmagnesium bromide solution, 3.57 mL (10 mmol), was added to a solution of 1.65 g (10 mmol) of cyclopentanone *N*-cyclohexylimine (**6**)[19] in 10 mL of tetrahydrofuran (THF), and the mixture was heated at 60 °C for 2 h. In a separate flask, 4.29 mL (12 mmol) of the aforementioned solution of Grignard reagent was added to a solution of 654 mg (1.0 mmol) of bis(triphenylphosphine)-nickel dichloride in 10 mL of dry benzene, and after 15 min, 1.05 mL (10 mmol) of (dimethylvinyl)carbinol was added to the mixture. After 15 min, the latter was transferred by double-tipped needle into the magnesium enaminate solution, and 26 mL of

(37) Felkin, H.; Jampel-Costa, E.; Swierczewski, G. *J. Organomet. Chem.* **1977**, *134*, 265.

solvent was removed by distillation and replaced by dry benzene. After being refluxed for 38 h and then cooled, the mixture was acidified with saturated ammonium chloride solution and extracted with methylene chloride. The extract was dried and evaporated, and the residue was distilled through a Kugelrohr distillation (95–145 °C/0.1 torr). A mixture of the distillate, 571 μL (10 mmol) of acetic acid, and 2 mL of water in 10 mL of tetrahydrofuran was stirred for 15 h, then poured into 1 N hydrochloric acid solution, and extracted with methylene chloride. The extract was dried and evaporated. Flash-chromatography[38] of the residue on silica gel and elution with 30:1 hexane–ethyl acetate gave 350 mg (23%) of liquid ketone **7a**: IR (neat) vinyl CH 3090 (m), C=O 1735 (s), C=C 1635 (m), CMe_2 1380 (m), 1360 (m), vinyl CH 1000 (m), 910 (m) cm^{-1}; ^1H NMR δ 1.10, 1.13 (s, 3 each, 2 Me), 1.5–2.5 (m, 7, methylenes, CH), 4.8–5.1, 5.6–6.0 (m, 3, olefinic Hs); ^{13}C NMR δ 20.1 (C-4), 24.3 (Me), 25.4 (Me), 26.2 (C-3), 38.3 (quat C), 40.0 (C-5), 56.8 (C-2), 111.3 (olefinic CH_2), 145.3 (olefinic CH), 218.8 (C=O); *m/e* 152 (M^+, 4), 84 (50), 69 (60), 41 (base); exact mass 152.1199 (calcd for $C_{10}H_{16}O$ 152.1201.

Further elution yielded 287 mg (19%) of liquid ketone **7b**: IR (neat) C=O 1735 (s), C=C 1640 (m) cm^{-1}; ^1H NMR δ 1.60, 1.67 (s, 3 each, 2 Me), 1.4–3.0 (m, 9, methylenes, CH), 4.9–5.2 (m, 1, olefinic H); ^{13}C NMR δ 17.6 (*Z*-Me), 20.5 (C-4), 25.5 (*E*-Me), 27.7 (prenyl CH_2), 28.9 (C-3), 38.0 (C-5), 49.1 (C-2), 121.2 (olefinic CH), 132.7 (olefinic C), 220.0 (C=O); MS, *m/e* (rel intensity) 152 (M^+, 20), 84 (94), 69 (76), 41 (base); exact mass 152.1199 (calcd for $C_{10}H_{16}O$ 152.1201).

3-(β,β-Dimethylvinyl)quinoline (11). A solution of 1.54 g (15 mmol) of ethynyldimethylcarbinyl chloride (**8**) in 8 mL of dry ether was added dropwise over a 1.5-h period to a stirring mixture of 1.32 g (7.5 mmol) of *N*-carbomethoxyindole (**12a**)[24] and 360 mg (15 mmol) of sodium hydride in 20 mL of ether at 0 °C, and the stirring was continued at room temperature for 20 h. Ammonium chloride, 1.07 g (20 mmol), was added, and the mixture was stirred for 0.5 h. A saturated sodium bicarbonate solution was added dropwise until gas evolution ceased. The mixture was poured into 20 mL of water and extracted with ether. The extract was dried and evaporated. Chromatography of the residue and elution with 1:1 hexane–dichloromethane gave 672 mg (49%) of starting indole (**12a**). Elution with ethyl acetate afforded 249 mg (37%, based on consumed indole **12a**) of liquid quinoline **11**: UV λ_{max} 228 nm (ε 33 800), 285 (5 270), 323 (4 210); IR (CCl_4) C=C 1657 (w), 1620 (w), 1600 (w), 1568 (w) cm^{-1}; ^1H NMR δ 1.94, 1.99 (s, 3 each, 2 Me), 6.32 (br s, 1, olefinic H), 7.3–8.2 (m, 5, Ar Hs), 8.79 (d, 1, *J* = 2 Hz, H-2); ^{13}C NMR δ 19.3 (*Z*-Me), 26.8 (*E*-Me), 121.4 (olefinic CH), 126.3 (C-6), 127.4 (C-5), 127.6 (C-4a), 128.5 (C-7), 128.8 (C-8), 131.3 (olefinic C), 133.8 (C-4), 138.5 (C-3), 146.0 (C-8a), 151.7 (C-2); MS, *m/e* (rel intensity) 183 (M^+, base), 182 (43), 168 (78), 167 (64); exact mass 183.1047 (calcd for $C_{13}H_{13}N$ 183.1048).

The chloride **8**, 902 mg (8.8 mmol), was added dropwise over a 1-h period to a vigorously stirring mixture of 3.09 g (26.4 mmol) of indole (**4a**), 130 mg (0.36 mmol) of dibenzo-18-crown-6, and 40 mL of 50% aqueous potassium hydroxide solution in 25 mL of benzene at room temperature, and the stirring was continued for 20 h. The mixture was poured into 100 mL of water and extracted with ether. The extract was washed with ice-cold 10% hydrochloric acid. (Evaporation of the remaining ether solution and Kugelrohr distillation of the residue led to the recovery of 1.80 g of starting indole **4a**.) The aqueous solution was made basic with 10 N potassium hydroxide solution at 0 °C and extracted with ether. The extract was dried and evaporated. Chromatography of the residue on neutral alumina (activity III) and elution with 10:1 hexane–dichloromethane gave 800 mg (49%) of liquid quinoline **11**.

***N*-(γ,γ-Dimethylallenyl)indole (12b), β-(α,α-Dimethylpropargyl)indole (12c), (*E*)-1-(*N*-Indolyl)-3-methyl-1,3-butadiene (12d), (*Z*)-1-(*N*-Indolyl)-3-methyl-1,3-butadiene (12e), and 1,1-Di-β-indolyl-3-methyl-2-butene (15).** Indole (**4a**), 1.17 g (10 mmol), was added portionwise over a 0.5-h period to a stirring suspension of 480 mg (20 mmol) of sodium hydride in 20 mL of dry ether, and the mixture was stirred for 1.5 h. A solution of 1.55 g (15 mmol) of chloride **8** in 6 mL of dry ether was added over a 2.5-h period, and the stirring was continued for 20 h. The mixture was poured onto 20 g of ice and extracted with ether. The extract was washed with 100 mL of water, dried, and evaporated. Chromatography of the residue on 100 g of neutral alumina (activity III) and elution with 100:1 hexane–ethyl acetate led to 700 mg (38%) of unstable, liquid allenylindole **12b**: IR (CCl_4) vinyl CH 3059 (m), C=C=C 1969 (m), C=C 1646 (w), 1613 (m) cm^{-1}; ^1H NMR δ 1.87 (d, 6, *J* = 3 Hz, 2 Me), 6.48 (d, 1, *J* = 4 Hz, indole β-H), 6.88 (sept, 1, *J* = 3 Hz, olefinic H), 7.0–7.7 (m, 4, Ar Hs), 7.07 (d, 1, *J* = 4 Hz, indole α-H); MS, *m/e* (rel intensity) 183 (M^+, 23), 182 (43), 168 (34), 167 (32), 117 (base), 90 (47), 89 (34); exact mass 183.1045 (calcd for $C_{13}H_{13}N$ 183.1048).

Further elution gave a difficultly separable mixture of indole **12c** and other materials. Yet further elution afforded 75 mg (5%) of unstable, amorphous, solid indole **15**: IR (CCl_4) NH 3487 (m), 3421 (m), C=C 1617 (w) cm^{-1}; ^1H NMR δ 1.78, 1.86 (s, 3 each, 2 Me), 5.36 (d, 1, *J* = 10 Hz, allyl H), 5.72 (d, 1, *J* = 10 Hz, olefinic H), 6.88 (d, 1, *J* = 2 Hz, indole α-H), 7.0–7.7 (m, 4, Ar Hs); ^{13}C NMR δ 18.0 (Z-Me), 25.7 (E-Me), 33.1 (CH), 110.9 (C-7), 118.8 (C-5), 119.6 (C-3), 119.8 (C-4), 121.6 (C-2 or C-6), 121.7 (C-6 or C-2), 126.8 (C-3a), 127.6 (olefinic CH), 130.7 (olefinic quat C), 136.5 (C-7a); MS, *m/e* (rel intensity) 300 (M^+, 4), 183 (46), 182 (50), 168 (59), 167 (51), 117 (base), 90 (54), 89 (33); exact mass 300.1624 (calcd for $C_{21}H_{20}N_2$ 300.1626).

A solution of the crude product from another but identical experiment and 2.24 g (20 mmol) of potassium *tert*-butoxide in 20 mL of dimethyl sulfoxide was heated at 55 °C for 20 h. Upon workup as above, chromatography and elution with 120:1 hexane–ethyl acetate there was isolated 122 mg (7%) of liquid indole **12c**: UV λ_{max} 216 nm (ε 35 800), 261 (19 400), 298 (10 600); IR (CCl_4) vinyl CH 3084 (w), 3060 (w), 3035 (w), C=C 1644 (m), 1612 (w), 1578 (w), $R_2C=CH_2$ 896 (m), cis CH=CH 714 (m) cm^{-1}; ^1H NMR δ 1.61 (s, 3, Me), 4.99 (br s, 2, CH_2), 5.82 (d, 1, *J* = 9 Hz, H-2), 6.47 (d, 1, *J* = 3 Hz, indole β-H), 6.60 (d, 1, *J* = 9 Hz, H-1), 7.0–7.6 (m, 5, Ar Hs); ^{13}C NMR δ 21.2 (Me), 103.2 (C-3), 110.0 (C-7), 118.0 (CH_2), 120.3 (C-4), 120.7 (C-6), 122.1 (olefinic CH), 122.8 (C-5), 124.3 (C-2), 127.7 (olefinic NCH), 128.2 (C-3a), 136.4 (C-7a), 139.5 (olefinic quat C); MS, *m/e* (rel intensity) 183 (M^+, 23), 182 (base), 167 (31); exact mass 183.1049 (calcd for $C_{13}H_{13}N$ 183.1048).

Further elution yielded 150 mg (8%) of unstable, liquid indole **12d**: IR (CCl_4) vinyl CH 3082 (w), 3060 (w), 3039 (w), C=C 1644 (m), 1612 (w), 1574 (w), $R_2C=CH_2$ 882 (m) cm^{-1}; ^1H NMR δ 2.01 (s, 3, Me), 4.93, 5.00 (s, 1 each, CH_2), 6.41 (d, 1, *J* = 15 Hz, H-2), 6.57 (d, 1, *J* = 4 Hz, indole β-H), 7.0–7.7 (m, 6, Ar Hs, H-1); ^{13}C NMR δ 18.7 (Me), 105.0 (C-3), 109.4 (C-7), 115.1 (CH_2), 120.7 (C-6), 121.1 (C-5), 122.5 (olefinic NCH), 123.3 (olefinic CH), 123.5 (C-2), 129.0 (C-3a), 135.5 (C-7a), 139.8 (olefinic quat C); MS, *m/e* (rel intensity) 183 (M^+, 28), 117 (base); exact mass 183.1025 (calcd for $C_{13}H_{13}N$ 183.1048).

Further elution with 10:1 hexane–ethyl acetate gave 110 mg (6%) of liquid indole **12c**: IR (CCl_4) NH 3490 (m), 3422 (m), C≡CH 3311 (m), C≡C 2107 (w), C=C 1620 (w), 1580 (w) cm^{-1}; ^1H NMR δ 1.68 (s, 6, 2 Me), 2.22 (s, 1, C≡CH), 6.83 (d, 1, *J* = 3 Hz, indole α-H), 7.0–7.3, 7.8–8.1 (m, 4, Ar Hs); ^{13}C NMR δ 30.2, 30.2 (methyls), 30.4 (quat C), 67.9 (acetylenic CH), 91.2 (acetylenic C), 111.2 (C-7), 119.0 (C-5 or C-4), 119.8 (C-4 or C-5), 120.6 (C-2), 121.6 (C-3), 121.8 (C-6), 125.0 (C-3a), 136.9 (C-7a); MS, *m/e* (rel intensity) 183 (M^+, 27), 169 (base), 168 (84), 159 (63), 158 (47); exact mass 183.1048 (calcd for $C_{13}H_{13}N$ 183.1048).

Finally, the elution liberated 30 mg (2%) of indole **15**.

Potassium *tert*-butoxide, 515 mg (4.6 mmol), was added to a solution of 420 mg (2.3 mmol) of indole **12b** in 15 mL of dimethyl sulfoxide, and the mixture was heated at 55 °C for 20 h. Upon normal workup there was obtained 360 mg (70%) of a 3.3:1 **12d–12e** mixture (by ^1H NMR spectral analysis).

A solution of 1.54 g (15 mmol) of chloride **8** in 8 mL of hexane was added dropwise over a 6.5-h period to a vigorously stirring slurry of 1.17 g (10 mmol) of indole (**4a**) and 2.80 g (25 mmol) of potassium *tert*-butoxide in 20 mL of hexane at room temperature, and the stirring continued for 7 h. The mixture was

(38) Still, W. C.; Khan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(39) Skatole (**4d**) and *N*-(β,β-dimethylacrylyl)indoline [IR (CH_2Cl_2) C=O 1645 (s), 1622 (s), C=C 1590 (s) cm^{-1}; ^1H NMR δ 1.91, 2.08 (s, 3 each, Me), 3.08 (t, 2, *J* = 9 Hz, CH_2), 4.00 (t, 2, NCH_2), 5.88 (s, 1, α-keto H), 6.8–8.5 (m, 4, Ar Hs); ^{13}C NMR δ 20.2 (*cis*-Me), 27.0 (*trans*-Me), 27.9 (C-3), 48.2 (C-2), 116.8 (C-7), 118.1 (α-C), 123.1 (C-4), 124.3 (C-5), 127.1 (C-6), 131.4 (C-3a), 151.2 (β-C), 165.4 (C=O)] served as models for the ^{13}C NMR spectral analysis.

poured into 50 mL of water and extracted with ether. The extract was dried and evaporated. Chromatography of the residue and elution with 10:1 hexane–ethyl acetate led to the recovery of 125 mg (10%) of indole (**4a**) and the isolation of 160 mg (10%, based on consumed indole **4a**) of indole **12c**. Elution with 3:1 hexane–ethyl acetate yielded 356 mg (26%, based on consumed indole **4a**) of indole **15**.

Acylation of Indole (4a) with β,β-Dimethylacrylyl Chloride. β,β-Dimethylacrylyl chloride, 509 mg (4.3 mmol), was added dropwise to a solution of 500 mg (4.3 mmol) of indole (**4a**) in 10 mL of dry ether. The mixture was stirred at room temperature for 2 h, then poured into 50 mL of saturated sodium bicarbonate solution, and extracted with ether. The extract was washed, dried ($MgSO_4$), and evaporated. Chromatography and elution with 2:1 hexane–ethyl acetate led to 20 mg (2%) of liquid *N*-(β,β-dimethylacrylyl)indole (**12f**):[18b] UV λ_{max} 248 nm (ε 24 600), 300 (8100); IR (CH_2Cl_2) C=O 1680 (s), C=C 1630 (s) cm^{-1}; ^1H NMR δ 1.97, 2.17 (s, 3 each, Me), 6.31 (m, 1, α-keto H), 6.56 (d, 1, J = 4 Hz, β-indole H), 7.23, 7.32 (t, 1 each, J = 8 Hz, H-5, H-6), 7.46 (d, 1, J = 4 Hz, α-indole H), 7.53 (d, 1, J = 8 Hz, H-4), 8.45 (d, 1, J = 8 Hz, H-7); MS, m/e (rel intensity) 199 (M^+, 34), 117 (base), 83 (84), 55 (33); exact mass 199.0996 (calcd for $C_{13}H_{13}ON$ 199.0997).

It gave next 292 mg (34%) of crystalline β-(β,β-dimethylacrylyl)indole (**12g**):[18b] mp 136–137 °C (CH_2Cl_2, −20 °C) (lit.[18b] mp 136.5–138 °C); UV λ_{max} 246 nm (ε 11 600), 262 (9100), 312 (10 800); IR (CH_2Cl_2) NH 3445 (s), 3255 (br m), C=O 1640 (s), C=C 1600 (s), 1580 (m) cm^{-1}; ^1H NMR δ 1.97, 2.24 (s, 3 each, Me), 6.61 (br s, α-keto H), 7.1–8.6 (m, 4, Ar Hs), 7.81 (d, 1, J = 3 Hz, α-indole H); MS, m/e (rel intensity) 199 (M^+, base), 198 (66), 182 (60), 144 (79), 117 (37), 116 (34), 89 (38). Anal. Calcd for $C_{13}H_{13}ON$: C, 78.36; H, 6.57; N, 7.03. Found: C, 78.23; H, 6.63; N, 6.95.

There appeared next 132 mg (13%) of crystalline β-indolyl β-chloroisobutyl ketone (**12h**): mp 121–122 °C (hexane–dichloromethane, 0 °C); UV λ_{max} 238 nm (ε11 800), 255 (8800), 296 (11 300); IR (CH_2Cl_2) NH 3440 (s), 3280 (br m), C=O 1635 (s), C=C 1580 (w) cm^{-1}; ^1H NMR δ 1.81 (s, 6, 2 Me), 3.31 (s, 2, CH_2), 7.1–8.5 (m, 4, Ar Hs), 7.82 (d, 1, J = 3 Hz, α-indole H); MS, m/e (rel intensity) M^+ missing, 199 (73), 198 (36), 182 (36), 144 (base), 117 (34), 116 (25); exact mass (M^+ − HCl) 199.0997 (calcd for $C_{13}H_{13}ON$ 199.0997).

Lastly there was obtained 408 mg (30%) of crystalline amide **16**: mp 182–183 °C (4:1 acetone–hexane, 0 °C); UV λ_{max} 220 nm (ε 47 300), 268 (11 200), 273 (10 900), 285 (8700); IR (KBr) NH 3400 (s), 3350 (s), C=O 1660 (s), 1630 (s), C=C 1580 (m) cm^{-1}; ^1H NMR δ (MeCN-d_3) 1.73, 2.03 (s, 3 each, Me), 3.50 (t, 2, J = 8 Hz, CH_2), 4.64 (t, 1, J = 8 Hz, H-2′), 4.79 (br s, 1, α-H), 6.8–7.5 (m, 9, α-indole H, Ar Hs); ^{13}C NMR δ 19.4 (*cis*-Me), 26.9 (*trans*-Me), 34.0 (C-2′), 36.9 (C-3′), 111.2 (C-7), 117.8 (C-7′), 117.9 (C-3), 118.8 (α-C), 119.0 (C-4), 120.6 (C-6), 122.1 (C-2), 122.2 (C-5), 124.6 (C-4′), 125.6 (C-5′), 126.4 (C-3a), 129.9 (C-6′), 135.2 (C-7a′), 136.2 (C-3a′), 136.3 (C-7a), 150.4 (β-C), 164.6 (C=O);[39] MS, m/e (rel intensity) 316 (M^+, 10), 245 (base), 233 (22), 117 (21); exact mass 316.1573 (calcd for $C_{21}H_{20}ON_2$ 316.1575).

β,β-Dimethylacrylyl chloride, 1.02 g (8.6 mmol), was added dropwise to a solution of 1.00 g (8.6 mmol) of indole (**4a**) in 30 mL of dry benzene. The mixture was stirred at room temperature for 12 h and then poured into 50 mL of saturated bicarbonate solution. The mixture was extracted with ether, and the extract was washed, dried, and evaporated. Crystallization of the residue from methylene chloride gave 679 mg (50%) of amide **16**. Chromatography of the mother liquor led to 50 mg (3%) of amide **12f**.

A 3 M ethereal solution of methylmagnesium bromide, 16.7 mL (50 mmol), was added to a solution of 5.85 g (50 mmol) of indole (**4a**) in 250 mL of dry benzene at 0 °C, and the mixture was stirred for 1 h. Thereafter, 6.52 g (55 mmol) of β,β-dimethylacrylyl chloride was added dropwise, and the stirring was continued for 45 min. The mixture was poured into 300 mL of saturated sodium bicarbonate solution. The gummy material adhering to the reaction flask was dissolved in 200 mL of acetone, and the resultant solution was added to the aqueous solution. The latter was extracted with ether, and the extract was dried and evaporated. Chromatography of the residue and elution with 2:1 hexane–ethyl acetate led to 1.79 g (18%) of liquid amide **12f** and 1.25 g (9%) of colorless crystalline amide **18l**: mp 146–147 °C (ether); UV λ_{max} 236 nm (ε 29 200), 247 (28 300), 313 (16 200); IR (CH_2Cl_2) C=O 1685 (s), 1648 (s), 1630 (s), 1610 (s), C=C 1535 (s) cm^{-1}; ^1H NMR δ 2.00, 2.08, 2.23, 2.26 (s, 3 each, methyls), 6.40, 6.60 (s, 1 each, olefinic Hs), 7.3–7.4 (m, 2, Ar Hs), 8.09 (s, 1, indole α-H), 8.3–8.4 (m, 2, Ar Hs); MS, m/e (rel intensity) 281 (M^+, 9), 199 (30), 198 (20), 197 (12), 83 (base), 55 (19). Anal. Calcd for $C_{18}H_{19}O_2N$: C, 76.84; H, 6.80; N, 4.98. Found: C, 76.64; H, 6.54; N, 4.72.

Further elution gave 6.02 g (60%) of crystalline ketone **12g**.

Dry hydrogen chloride gas was bubbled through a solution of 900 mg (4.5 mmol) of ketone **12g** in dry methylene chloride at room temperature for 0.5 h. The solution was stirred for 15 h and then poured into 100 mL of saturated sodium bicarbonate solution. The mixture was agitated for 15 min, and the organic layer was separated, dried, and evaporated. Crystallization of the residue from a hexane–dichloromethane mixture gave 1.01 g (95%) of colorless, crystalline chloride **12h**: mp 121–122 °C; UV λ_{max} 238 nm (ε 11 800), 255 (8800), 296 (11 300); IR (CH_2Cl_2) NH 3440 (s), 3280 (br m), C=O 1635 (s), C=C 1580 (w), 1520 (s) cm^{-1}; ^1H NMR δ 1.81 (s, 6, methyls), 3.31 (s, 2, CH_2), 7.1–7.4 (m, 3, Ar Hs), 7.82 (d, 1, J = 3 Hz, indole α-H), 8.43 (m, 1, Ar H); MS, m/e (rel intensity) 199 (M^+, 73), 198 (36), 182 (36), 144 (base), 117 (34), 116 (25), 89 (22); exact mass (M^+ − HCl) 199.0997 (calcd for $C_{13}H_{13}ON$ 199.0997).

Reductions of Ketones 12g and 12h. A mixture of 199 mg (1.0 mmol) of ketone **12g** and 35 mg (0.65 mmol) of lithium aluminum hydride in 25 mL of dry tetrahydrofuran was stirred at 0 °C for 0.5 h and then at room temperature for 1 h. It was poured into 30 mL of 4% sodium hydroxide solution and extracted 3 times with 30 mL of ether. The extract was washed, dried, and evaporated. Chromatography of the residue and elution with 4:1 hexane–ethyl acetate yielded 15 mg (8%) of crystalline β-prenylindole (**4i**) and 80 mg (40%) of colorless, crystalline ketone **12i**: mp 127–128 °C (4:1 dichloromethane–hexane); UV λ_{max} 237 nm (ε 11 200), 252 (8300), 292 (11 200); IR (CH_2Cl_2) NH 3445 (s), 3260 (br m), C=O 1635 (s), C=C 1580 (w), 1520 (s) cm^{-1}; ^1H NMR δ 1.01 (d, 6, J = 7 Hz, methyls), 2.18 (m, 1, CH), 2.73 (d, 2, J = 7 Hz, CH_2), 7.2–7.5 (m, 3, Ar Hs), 7.84 (d, 1, J = 3 Hz, indole α-H), 8.4–8.5 (m, 1, Ar H); MS, m/e (rel intensity) 201 (M^+, 27), 159 (27), 144 (base), 117 (39), 83 (32); exact mass 201.1154 (calcd for $C_{13}H_{15}ON$ 201.1153).

A mixture of 300 mg (1.3 mmol) of ketone **12h** and 50 mg (1.3 mmol) of lithium aluminum hydride in 25 mL of dry ether was stirred at 0 °C for 3 h and then worked up as above. Crystallization of the crude product from hexane yielded 225 mg (80%) of colorless, crystalline chloride **12j**: mp 64–65 °C; UV λ_{max} 220 nm (ε 26 900), 271 (5900), 279 (6400), 286 (5500); IR (CH_2Cl_2) NH 3460 (s), C=C 1615 (w), 1600 (w) cm^{-1}; ^1H NMR δ 1.68 (s, 6, methyls), 2.0–2.3 (m, 2, CH_2), 2.8–3.1 (m, 2, benzyl Hs), 6.93 (m, 1, indole α-H), 7.0–7.7 (m, 4, Ar Hs); MS, m/e (rel intensity) 221 (M^+, 18), 130 (base); exact mass 221.0971 (calcd for $C_{13}H_{16}NCl$ 221.0970).

1-(Benzenesulfonyl)-2-prenylindole (18d) and Derivatives. A solution of 1.03 g (4.0 mmol) of *N*-(benzylsulfonyl)indole (**18a**)[40] in 11 mL of dry tetrahydrofuran was added dropwise over a 5-min period to a solution of 450 mg (4.2 mmol) of lithium diisopropylamide (prepared from 424 mg of diisopropylamine and a 1.6 N hexane solution of *n*-butyllithium) in 10 mL of dry tetrahydrofuran at a temperature below −60 °C (the external temperature being −78 °C), and the resultant yellow mixture was stirred at −70 °C for 1.5 h. It then was permitted to warm to 5 °C, whereupon 758 mg (6.4 mmol) of β,β-dimethylacrylyl chloride was added rapidly at −65 °C. The mixture was allowed to warm to room temperature for 15 h, then was poured into 175 mL of a 1% hydrochloric acid solution, and extracted with methylene chloride. The extract was washed with water as well as brine, dried, and evaporated. Chromatography of the residue and elution with 20:1 hexane–ethyl acetate gave 245 mg (24%) of starting sulfonamide and 733 mg (72%, based on consumed **18a**) of ketone **18b**: mp 120–121 °C (CH_2Cl_2–hexane); UV λ_{max} 247 nm (ε 17 700), 259 (15 600), 269 (14 500), 295 (16 800); IR (CH_2Cl_2) C=O 1660 (s), C=C 1615 (s), SO_2 1368 (s), 1172 (s) cm^{-1}; ^1H NMR δ 2.00,

(40) Illi, V. O. *Synthesis* **1979**, 136.

2.25 (s, 3 each, methyls), 6.59 (s, 1, olefinic H), 7.00 (s, 1, indole β-H), 7.2–8.2 (m, 9, Ar Hs); MS, *m/e* (rel intensity) 339 (M^+, base), 324 (37), 260 (24), 170 (92), 141 (42), 77 (67). Anal. Calcd for $C_{19}H_{17}O_3NS$: C, 67.23; H, 5.05; N, 4.17. Found: C, 67.14; H, 4.93; N, 3.86.

A solution of 1-(benzenesulfonyl)-2-lithioindole was prepared as above, and 1.78 g (12 mmol) of prenyl bromide was added rapidly at −65 °C. Workup as above and chromatographic elution with 50:1 hexane–ethyl acetate afforded 160 mg (13%, based on consumed **18a**) of viscous, oily 4-[2-(1-(benzenesulfonyl)-indolyl)]-2,7-dimethyl-2,6-octadiene (**17**): UV λ_{max} 250 nm (ε 20 000); IR C=C 1585 (w), 1555 (w), SO_2 1362 (s), 1182 (s), 1165 (s) cm^{-1}; ^1H NMR δ 1.58, 1.58, 1.64, 1.69 (s, 3 each, methyls), 2.25, 2.56 (m, 1 each, C-5 Hs), 4.35 (m, 1, H-4), 5.07 (t, 1, *J* = 7 Hz, H-6), 5.16 (d, 1, *J* = 9 Hz, H-3), 6.46 (s, 1, indole β-H), 7.1–8.2 (m, 9, Ar Hs); ^{13}C NMR δ 17.8 (2-Me), 18.2 (7-Me), 25.7 (C-1, C-8), 35.7 (C-5), 37.5 (C-4), 108.8 (C-7′), 115.2 (C-3′), 120.1 (C-4′), 121.6 (C-6′), 123.5 (C-6 or C-5′), 123.7 (C-5′ or C-6), 126.1 (*o*-C), 126.5 (C-3), 128.8 (*m*-C), 129.8 (C-3a′), 132.8 (C-2 or C-7), 133.0 (C-7 or C-2), 133.2 (*p*-C), 137.3 (C-7a′), 139.1 (*ipso*-C), 146.3 (C-2′); MS, *m/e* (rel intensity) 393 (M^+, 16), 324 (96), 184 (58), 183 (base), 168 (50); exact mass 393.1760 (calcd for $C_{24}H_{27}O_2NS$ 393.1763).

Further elution gave 780 mg (76%, based on consumed **18a**) of colorless crystals of sulfonamide **18d**: mp 91–92 °C (ether–hexane); UV λ_{max} 248 nm (ε 14 000); IR (CH_2Cl_2) C=C 1585 (w), 1562 (w), SO_2 1363 (s), 1168 (s), cm^{-1}; ^1H NMR δ 1.60, 1.77 (s, 3 each, methyls), 3.66 (d, 2, *J* = 7 Hz, CH_2 Hs), 5.37 (m, 1, olefinic H), 6.36 (s, 1, indole β-H), 7.1–8.3 (m, 9, Ar Hs); ^{13}C NMR δ 17.6 (*Z*-Me), 25.6 (*E*-Me), 27.8 (CH_2), 108.9 (C-7), 114.5 (C-3), 119.4 (C-4), 120.0 (C-6), 123.3 (CH or C-5), 123.7 (C-5 or CH), 126.0 (*o*-C), 129.0 (*m*-C), 129.5 (C-3a), 133.4 (*p*-C), 134.8 (C), 137.2 (C-7a), 139.1 (*ipso*-C), 141.0 (C-2); MS, *m/e* (rel intensity) 325 (M^+, 64), 183 (base), 168 (77), 154 (25), 77 (25). Anal. Calcd for $C_{19}H_{19}O_2NS$: C, 70.12; H, 5.88; N, 4.30. Found: C, 70.00; H, 5.80; N, 4.16.

Finally, elution gave 220 mg (21%) of starting sulfonamide.

A 1.56 N hexane solution of *n*-butyllithium, 0.23 mL (0.36 mmol), was added to a solution of 36 mg (0.36 mmol) of diisopropylamine in 10 mL of dry tetrahydrofuran at 0 °C. Thereafter, 98 mg (0.30 mmol) of sulfonamide **18d** was added rapidly at −78 °C, and the resultant black solution was stirred at this temperature for 0.5 h. Prenyl bromide, 67 mg (0.45 mmol), was added dropwise, and the resultant colorless solution was permitted to come back to room temperature. The mixture was poured into 40 mL of water and extracted with methylene chloride. The extract was dried and evaporated. Chromatography of the residue and elution with 25:1 hexane–ethyl acetate gave 98 mg (83%) of sulfonamide **17**.

The above hydrochlorination procedure for ketone **12g** and its workup was applied to 170 mg (0.50 mmol) of ketone **18b**, leading to 180 mg (96%) of colorless, crystalline chloro ketone **18c**: mp 105–106 °C (ether–hexane); UV λ_{max} 236 nm (ε 9600), 287 (13 800); IR (CH_2Cl_2) C=O 1675 (s), C=C 1600 (m), 1580 (w), 1530 (m), SO_2 1365 (s), 1170 (s) cm^{-1}; ^1H NMR δ 1.83 (s, 6, methyls), 3.48 (s, 2, CH_2 Hs), 7.05 (s, 1, indole β-H), 7.1–8.2 (m, 9, Ar Hs); MS, *m/e* (rel intensity) 375 (M^+, 45), 284 (base), 199 (49), 198 (85), 184 (42), 143 (63). Anal. Calcd for $C_{19}H_{18}O_3NSCl$: C, 60.71; H, 4.83; N, 3.73. Found: C, 60.70; H, 4.92; N, 3.63.

1-(Benzenesulfonyl)-3-bromoindole (18g). A mixture of 9.80 g (50 mmol) of β-bromoindole (**18f**)[33] and 1.65 g (4.8 mmol) of tetra-*n*-butylammonium bisulfate in 250 mL of benzene and 50 mL of 50% potassium hydroxide solution was stirred vigorously for 5 min. A solution of 15.0 (84 mmol) of benzenesulfonyl chloride in 250 mL of benzene was added, the mixture stirred for 1 h, 5.00 g more of the chloride was added, and the stirring continued for another hour. The organic solution was separated, washed exhaustively, dried, and evaporated. Crystallization of the solid residue from hexane–dichloromethane gave 15.2 g (91%) of colorless, crystalline sulfonamide **18g**: mp 122–124 °C; UV λ_{max} 252 nm (ε 11 900), 280 (4900), 287 (4800); IR (CH_2Cl_2) C=C 1595 (w), 1580 (m), SO_2 1365 (s), 1170 (s) cm^{-1}; ^1H NMR δ 7.2–8.1 (m, 9, Ar Hs), 7 62 (s, 1, indole α-H); MS, *m/e* (rel intensity) 337 (M^+, 33), 335 (M^+, 31), 196 (94), 194 (95), 141 (48), 115 (74), 88 (51), 77 (base). Anal. Calcd for $C_{14}H_{10}O_2NSBr$: C, 50.01; H, 2.98; N, 4.17. Found: C, 50.23; H, 2.96; N, 4.29.

1-(Benzenesulfonyl)-3-prenylindole (18h) and 1-(Benzenesulfonyl)-3-(β,β-dimethylacrylyl)indole (18i). A 2.0 M pentane solution of *tert*-butyllithium, 1 mL, was added rapidly to a solution of 336 mg (1.0 mmol) of bromide **18g** in 32 mL of a 3:1 tetrahydrofuran–ether mixture at −95 °C, and the resultant yellow solution was stirred for 6 min. (In order to avoid the unwanted isomerization of the β-lithiated indole derivative into ita α-lithio counterpart, the temperature must not be allowed to rise above −90 °C.) Cuprous cyanide, 100 mg (1.1 mmol), was added, and the stirring was continued for 3 min.

Prenyl bromide, 240 mg (1.6 mmol), was added to the solution of the organocopper reagent at −95 °C, and the stirring was continued for 0.5 h. Then the mixture was stirred at −78 °C for 1 h, and, finally, it was permitted to reach room temperature and kept for 14 h. It was poured into 200 mL of water and extracted with 120 mL of methylene chloride. The aqueous solution was saturated with sodium chloride and reextracted with methylene chloride. The combined extracts were washed with water and brine, dried, and evaporated. Chromatography of the residue and elution with 20:1 hexane–ethyl acetate gave 235 mg (72%) of colorless, crystalline sulfonamide **18h**: mp 85–86 °C (ether); UV λ_{max} 249 nm (ε 10 400), 279 (3400), 286 (3200); IR (CH_2Cl_2) C=C 1600 (w), 1580 (w), SO_2 1360 (s), 1170 (s) cm^{-1}; ^1H NMR δ 1.71, 1.76 (s, 3 each, methyls), 3.33 (d, 2, *J* = 7 Hz, CH_2 Hs), 5.34 (br t, 1, *J* = 7 Hz, olefinic H), 7.2–8.0 (m, 10, Ar Hs); MS, *m/e* (rel intensity) 325 (M^+, base), 310 (38), 257 (33), 184 (95), 168 (96), 77 (49). Anal. Calcd for $C_{19}H_{19}O_2NS$: C, 70.12; H, 5.88; N, 4.30. Found: C, 70.31; H, 5.86; N, 4.19.

Further elution gave 13 mg (5%) of sulfonamide **18a**.

β,β-Dimethylacrylyl chloride, 190 mg (1.6 mmol), was added to the organocopper reagent at −95 °C, and the reaction and workup continued as above. Chromatography of the crude product and elution with 20:1 hexane–ethyl acetate gave first 26 mg (10%) of sulfonamide **18a**, then 24 mg (7%) of ketone **18b**, and, finally, 228 mg (67%) of colorless, crystalline ketone **18i**: mp 140–141 °C (ether); UV λ_{max} 224 nm (ε 15 900), 242 (16 200), 296 (12 100); IR (CH_2Cl_2) C=O 1645 (s), C=C 1605 (s), 1530 (s), SO_2 1370 (s), 1160 (s) cm^{-1}; ^1H NMR δ 2.03, 2.06 (s, 3 each, methyls), 6.63 (s, 1, olefinic H), 7.3–8.5 (m, 9, Ar Hs), 8.21 (s, 1, indole α-H); MS, *m/e* (rel intensity) 339 (M^+, base), 324 (29), 199 (90), 183 (68), 170 (90), 154 (84), 143 (50), 83 (65), 77 (55). Anal. Calcd for $C_{19}H_{17}O_3NS$: C, 67.23; H, 5.05; N, 4.17. Found: C, 67.37; H, 5.23; N, 4.18.

A mixture of 398 mg (2.0 mmol) of ketone **12g**, 68 mg (0.2 mmol) of tetra-*n*-butylammonium bisulfate and 2 mL of 50% aqueous sodium hydroxide solution in 6 mL of benzene was stirred vigorously at room temperature for 5 min. A solution of 530 mg (3.0 mmol) of benzenesulfonyl chloride in 2 mL of benzene was added dropwise, and stirring was continued for 0.5 h. The mixture was poured into 10 mL of water and extracted with ether. The extract was washed with sodium bicarbonate solution and brine, dried over K_2CO_3, and evaporated. Washing of the residue with dry ether yielded 612 mg (90%) of colorless, crystalline ketone **18i**.

Removal of the Benzenesulfonyl Group from Sulfonamides 18d, 18h, and 18i. Sodium amalgam, 750 mg of 6%, was added to a solution of 0.50 mmol of sulfonamide and 284 mg (2.0 mmol) of disodium hydrogenphosphate in 5 mL of dry methanol, and the mixture was stirred at room temperature for 1 h. After the solution was removed from the insoluble solid and mercury, it was poured into 50 mL of water, and the mixture was extracted with ether. The extract was dried and evaporated.

By this method sulfonamide **18d** was converted into 89 mg (96%) of solid, whose crystallization from hexane gave α-prenylindole (**18e**): mp 63–64 °C; UV λ_{max} 218 nm (ε 25 400), 268 (9700), 284 (7200); IR (CH_2Cl_2) NH 3455 (m), C=C 1580 (w), 1545 (w) cm^{-1}; ^1H NMR δ 1.73, 1.78 (s, 3 each, methyls), 3.47 (d, 2, *J* = 7 Hz, CH_2 Hs), 5.38 (t, 1, *J* = 7 Hz, olefinic H), 6.22 (s, 1, indole β-H), 7.0–7.6 (m, 4, Ar Hs); MS, *m/e* (rel intensity) 185 (M^+, base), 184 (21), 170 (70), 130 (63), 117 (67). Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.22; H, 8.20; N, 7.43.

Sulfonamide **18h** was transformed into 88 mg (95%) of solid, whose crystallization from hexane afforded β-prenylindole (**4i**).

Sulfonamide **18i** was converted into a crude product, whose chromatography and elution with 2:1 hexane–ethyl acetate led to 55 mg (55%) of crystalline ketone **12g**.

A solution of 170 mg (0.50 mmol) of sulfonamide **18i** and 113 mg (1.0 mmol) of potassium *tert*-butoxide in 10 mL of moist

tetrahydrofuran was stirred at room temperature for 1 h and then poured into 50 mL of 1% hydrochloric acid solution. The mixture was extracted with 30 mL of methylene chloride, and the aqueous solution was saturated with sodium chloride and reextracted with methylene chloride. The combined extracts were dried and evaporated. Purification of the residue as above yielded 92 mg (92%) of crystalline ketone **12g**.

1-(Benzenesulfonyl)-3-(α-hydroxyprenyl)indole (18j). A mixture of 380 mg (10.0 mmol) of lithium aluminum hydride and 1.36 g (4.0 mmol) of ketone **18i** in 30 mL of dry tetrahydrofuran was stirred at 0 °C for 1 h. Ethyl acetate, 5 mL, was added dropwise, and the mixture was allowed to warm to room temperature. It then was poured into 30 mL of water and extracted with methylene chloride. The extract was dried (K_2CO_3) and evaporated. Crystallization of the residual, yellow oil from 4:1 ethanol–hexane gave 1.13 g (83%) of colorless, crystalline alcohol **18j**: mp 111–112 °C; UV λ_{max} 249 nm (ε 12900), 276 (5500), 283 (5100); IR (CH_2Cl_2) OH 3580 (m), 3430 (br w), C=C 1605 (w), 1580 (w), SO_2 1365 (s), 1170 (s) cm^{-1}; ^1H NMR δ 1.77, 1.80 (s, 3 each, methyls), 5.51 (dm, 1, J = 9 Hz, olefinic H), 5.64 (d, 1, J = 9 Hz, OCH), 7.1–8.0 (m, 9, Ar Hs), 7.51 (s, 1, indole α-H); MS, m/e (rel intensity) 341 (M^+, 2), 182 (base), 167 (79). Anal. Calcd for $C_{19}H_{19}O_3NS$: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.56; H, 5.55; N, 4.11.

Evaporation of the mother liquor from the above crystallization, chromatography of the residue, and elution with 4:1 hexane–ethyl acetate gave 82 mg (6%) of colorless crystalline ketone **18k**: mp 99–100 °C (hexane–ether); UV λ_{max} 217 nm (ε 24200), 265 (9100), 273 (10200), 285 (11000); IR (CH_2Cl_2) C=O 1655 (s), C=C 1600 (m), 1580 (w), 1530 (s), SO_2 1370 (s), 1165 (s) cm^{-1}; ^1H NMR δ 1.02 (d, 6, J = 7 Hz, methyls), 2.32 (m, 1, CH), 2.76 (d, 2, J = 7 Hz, CH_2 Hs), 7.3–8.4 (m, 9, Ar Hs), 8.21 (s, 1, indole α-H); MS, m/e (rel intensity) 341 (M^+, 57), 299 (56), 284 (base), 200 (76), 141 (54), 77 (41). Anal. Calcd for $C_{19}H_{19}O_3NS$: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.56; H, 5.51; N, 3.90.

β-Dehydroprenylindole (3). A solution of 1.37 g (4.0 mmol) of alcohol **18j** and 8.40 g (150 mmol) of potassium hydroxide in 50 mL of a 4:1 ethanol–water mixture was heated at 50–54 °C for 2 h. It then was poured into 100 mL of water and extracted with ether. The extract was washed with brine, dried (K_2CO_3), and evaporated. Rapid chromatography of the solid residue, 710 mg, on neutral alumina (activity III) and elution with 2:1 hexane–ethyl acetate afforded 600 mg (82%) of pale yellow, powdery β-dehydroprenylindole (**3**): mp 129–130 °C (lit.[36] mp 130–132 °C); UV, IR, and ^1H NMR spectrally identical with an authentic sample.[41]

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Michael Adducts of a Half-Blocked Enedione as Sources of 3-Substituted 2,5-Diketones and 2,5-Dialkylfurans

Donald Mackay,* Edward G. Neeland, and Nicholas J. Taylor

The Guelph Waterloo Centre for Graduate Work in Chemistry, Chemistry Department, University of Waterloo, Waterloo, Ontario, N2L 3G1 Canada

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The dioxazolylbutenones **2a**, formed by isomerization of the Diels–Alder adducts of 2,5-dimethylfuran with (nitrosocarbonyl)benzene [2 + 4], are efficient Michael acceptors of a wide variety of carbon and heteroatom nucleophiles. The resulting adducts **5** function as half-blocked 1,4-diones. They can be converted into the corresponding diketones **10** by hot aqueous EtOH or Pd–H_2 or into the 3-substituted 2,5-dimethylfurans **19** by BF_3, either directly or by way of **10**. Hydroperoxide anion adds conjugatively to **2a** to give the epoxide **23**, but 1,2-addition is competitive and is followed by dioxazole ring opening to give a peroxy compound regarded as **21**. The [2 + 4] cycloaddition of 2,5-dialkylfurans and nitrosocarbonyl compounds is general, but 2-methylfuran appears to add (although in poor yield) in the opposite [4 + 2] mode, the adduct spontaneously isomerizing to the mono-*O*-benzoyloximino enedione **32**.

The nitrosocarbonyl group was first established as the oxidation intermediate from a hydroxamic acid in 1973.[1] Its dienophilic behavior at its nitroso end has been successfully exploited by a number of workers,[1-5] but its ability to act as an enophile in Diels–Alder reactions has also been recognized.[6-8]

We have shown that both (nitrosocarbonyl)alkanes and -arenes react as hetero dienes with 2,5-dimethylfuran to

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