# Synthesis of Cycloprop[*c*]indol-5-ones from 4-Diazo-3-[*N*-(2-propenyl)amido]cyclohexadien-1-ones. Exploration of Copper(I) and Copper(II) Complexes as Catalysts

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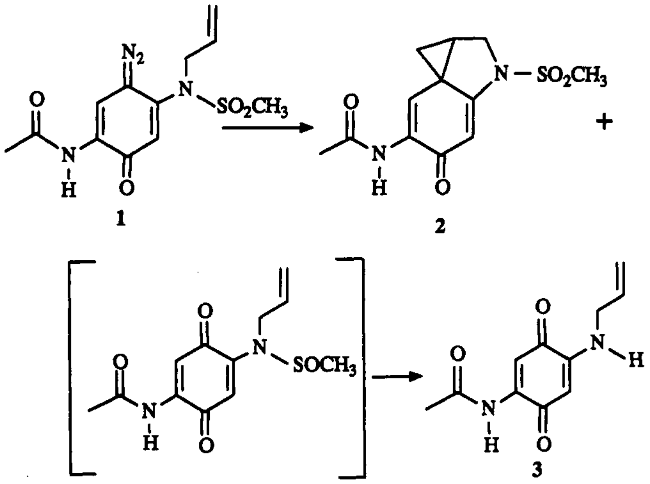
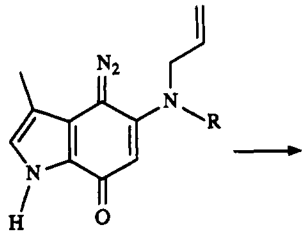
The cyclization of 4-diazo-3-[*N*-(2-propenyl)amido]cyclohexadienones to cycloprop[c]indol-5-ones under the influence of copper(I) and copper(II) compounds has been investigated. Catalysis is observed with copper(I) triflate, the carbon monoxide complex of copper(I) triflate, and the carbon monoxide complexes of trifluoropentanedionato- and hexafluoropentanedionatocopper(I). The best results, essentially quantitative conversion, are achieved with a catalyst solution containing trifluoropentanedionatocopper(I) carbonyl and 1 equiv of *n*-butylamine. No significant enantioselectivity is observed with a chiral salicyliminatocopper(II), [(trifluoroacetyl)camphorato]copper(I) carbonyl, or a trifluoropentanedionatocopper(I) carbonyl solution containing (*S*)-$\alpha$-naphthylethylamine. A mechanistic interpretation involving reductive dediazonization, *exo-trig* radical cyclization, and cyclopropane formation by the resulting intermediate is proposed.

In earlier work, we have demonstrated that 2-acetamido-5-[*N*-(2-propenyl)methanesulfonamido]-4-diazocyclohexadien-1-one (**1**) can be converted to the cycloprop[*c*]indolone ring system **2**, which is an analogue of the bioactive ring A of the antitumor antibiotic CC-1065, under either thermal or photolytic conditions. Under these conditions, **1** gives two principal products, the cycloprop[*c*]indolone **2** and the quinone **3**, presumably through a carbenoid mechanism. The latter compound is formed by hydrolysis of the unstable sulfinamide formed by an oxygen-transfer reaction of the carbenoid intermediate.[1]

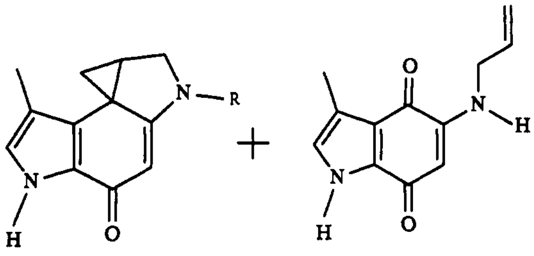


**1** **2** **3**

Similar studies on the 4-diazoindol-7-one **4a** gave the methanesulfonyl-protected ring A structure **5a**, with the quinone **6** being observed as a byproduct.



R
**4a** SO$_2$CH$_3$
**4b** COCH$_3$



**5** **6**

Some of the widely used transition-metal catalysts for carbenoid decomposition, such as rhodium(II) acetate, Cu(II)(acac)$_2$, and Cu(II)(sal)$_2$[2] were also included in the earlier study. These catalysts were beneficial in increasing the product ratio to favor **2** relative to **3**. However, the temperatures required for the Cu(II) catalysts were sufficiently high that it was difficult to determine the relative proportion of copper-catalyzed and thermal reaction that occurred. Several cases have been reported in which Cu(I) salts and complexes function as catalysts for carbenoid reactions of $\alpha$-diazo ketones and $\alpha$-diazo esters.[3–5] These reactions generally occur at relatively low temperature. We also wished to explore the possibility for observing enantioselectivity in the cyclopropanation reaction. For these reasons, we have examined a range of Cu(I) and Cu(II) compounds, some with chiral ligands, as catalysts for the intramolecular cyclopropanation reaction.

**Synthesis of Quinonediazides.**[6] 2-Acetamido-4-diazo-5-[*N*-(2-propenyl)methanesulfonamido]cyclohexadienone (**1**) was prepared as described previously.[1] An improved synthesis of 4-diazo-3-methyl-5-[*N*-(2-propenyl)methanesulfonamido]indol-7-one (**4a**) has been developed. The key intermediate 7-(benzyloxy)-3-

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[1] Sundberg, R. J.; Baxter, E. W.; Pitts, W. J.; Ahmed-Schofield, R.; Nishiguchi, T. *J. Org. Chem.* **1988**, *53*, 5097.

[2] Cu(sal)$_2$ = *bis*(*N-tert*-butylsalicylaldiminato)copper(II). Nozaki, H.; Takaya, S.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655. Corey, E. J.; Myers, A. G. *Tetrahedron Lett.* **1984**, *25*, 3559.

[3] Salomon, R. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 3300.

[4] Lewis, R. T.; Motherwell, W. B. *Tetrahedron Lett.* **1988**, *29*, 5033. Wiberg, K. B.; Kass, S. R.; Bishop, K. C., III. *J. Am. Chem. Soc.* **1985**, *107*, 996.

[5] Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssié, P. *J. Org. Chem.* **1980**, *45*, 695.

[6] The term "quinonediazides" is used in the literature as a generic name for 2-diazo- and 4-diazocyclohexadienones and ring-fused derivatives.

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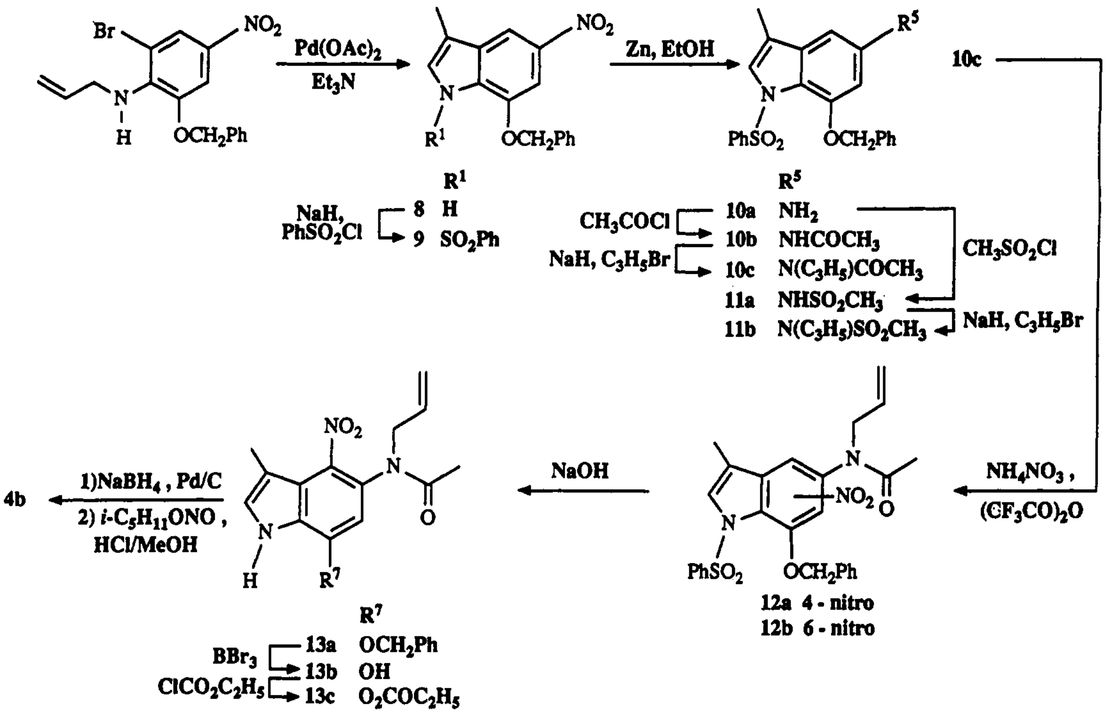
Scheme I

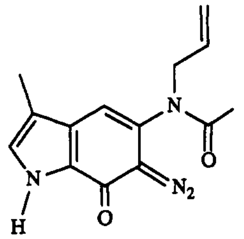


methyl-5-nitroindole (8) was prepared by palladium-catalyzed cyclization of 2-bromo-6-(benzyloxy)-4-nitro-*N*-(2-propenyl)aniline (7). A Hegedus cyclization[7a] using 5 mol % palladium acetate as catalyst and sodium carbonate as base gave a 45–55% yield of 8, but substantial competing N-deallylation of 7 was observed. Exploration of the effect of the base[7b] and the addition of silver carbonate[7c] showed triethylamine to be beneficial, whereas silver carbonate was deleterious. The cyclization reaction proceeded in 96% yield at room temperature after optimization. A similar synthesis has been developed independently by Martin.[8] The synthetic scheme was also adapted to the preparation of the acetyl-protected diazoindolone 4b (Scheme I).

Indole 8 was converted to the *N*-benzenesulfonyl derivative 9 by use of NaH in THF followed by benzenesulfonyl chloride (98%). For the preparation of 4a, the N-protected indole 9 was reduced with zinc in ethanol and then reacted with methanesulfonyl chloride to give 11a. Conversion to 4a then followed the previously published route.[1]

For the preparation of 4b, 10a was acetylated to give 10b (93%). The amide was then alkylated (allyl bromide, NaH in DMF; 75%). Nitration of 10c by ammonium nitrate in TFAA[9] gave a 6:1 mixture of two isomeric nitro derivatives 12a and 12b in 61% total yield. The major product was shown to be the 4-isomer by comparing NOE enhancements induced by irradiation of the 3-methyl protons. The major isomer 12a showed an enhancement of only the indole C-2 protons, while the minor isomer 12b showed enhancement for both aromatic protons and must therefore be the 6-nitro isomer.

The major isomer 12a was hydrolyzed to remove the benzenesulfonyl group and then debenzylated with boron tribromide. The phenol 13b was not purified but converted to the ethyl carbonate 13c. Reduction of the nitro group was accomplished with Pd/C–$NaBH_4$[10] without any reduction of the allyl group. Treatment of the amine with isoamyl nitrite followed by acid gave the quinonediazide 4b (30% yield for the final two steps). The 6-diazoindolone 14 was prepared as previously described.[1]



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**Copper(I)-Catalyzed Cyclopropanation.** Salomon and Kochi reported some time ago that copper(I) triflate was a very active catalyst for cyclopropanation of alkenes by diazomethane or ethyl diazoacetate.[3] Related studies with copper(II) triflate implicated Cu(I) as the catalytically active oxidation state. A distinctive structure–reactivity pattern for various alkenes was noted in comparison with copper(II) acetylacetonate. There have been subsequent synthetic applications of copper(I) triflate as a catalyst in cyclopropanation.[4] The alkene selectivity of copper(I) triflate has been compared with other carbene catalysts.[5] The special features of copper(I) triflate are attributed to its greater electrophilicity and stronger alkene coordination, as compared with Cu(I) in the presence of better donor ligands. Within the general mechanistic framework of metal ion catalyzed cyclopropanations,[11] the reaction would be formulated as an oxidative addition of the diazo compound to the Cu(I), with formation of a copper–carbene complex.

*p*-Quinonediazides are vinylogues of $\alpha$-diazo ketones, and cyclopropanation of alkenes has been observed under both

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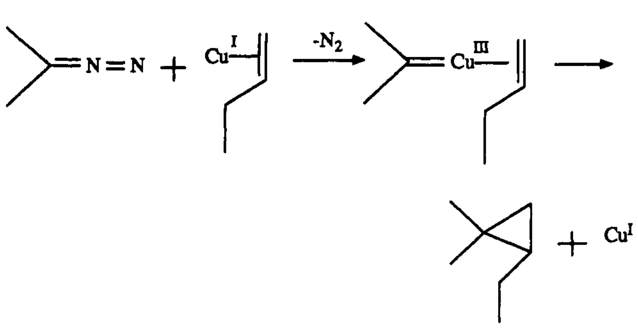
(7) (a) Odle, R.; Belvins, B.; Ratcliff, M.; Hegedus, L. S. *J. Org. Chem.* **1980**, *45*, 2709. (b) Larock, R. C.; Babu, S. *Tetrahedron Lett.* **1987**, *28*, 5291. (c) Abelman, M. M.; Oh, T.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 4130.

(8) Martin, P. *Helv. Chim. Acta* **1989**, *72*, 1554. The mp discrepancy has been resolved by private communication with Dr. Martin, who provided a corrected value of 182–183 °C for 8. The NMR spectra of the two samples are identical.

(9) Crivello, J. V. *J. Org. Chem.* **1981**, *46*, 3056.

(10) Smith, W. B. *J. Heterocycl. Chem.* **1987**, *24*, 745.

(11) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.



thermal and photochemical conditions.[12] There has been no extensive study of metal ion catalyzed reactions, and we are unaware of any previous study of Cu(I)-catalyzed reactions of quinonediazides.

Copper(I) triflate–benzene (10 mol %) had a significant catalytic effect on the conversion of **1** to **2** as reaction was observed at 40 °C. However, the extent of conversion did not exceed 40%. Under the best conditions found, the reaction gave a 35% yield of **2** at 40% conversion when carried out with 2,6-di-*tert*-butyl-4-methylpyridine present (10 mol %). The reactions failed to go to completion, presumably because of loss of catalytic activity. Among other copper(I) salts examined, CuBr–S$(CH_3)_2$, CuI, and CuCN–LiCl showed no catalytic activity, although the combination of CuBr and silver triflate gave ~15% of **2**.

Because of the very limited stability of the catalytic activity associated with copper(I) triflate, we sought more stable Cu(I) species that might retain catalytic activity. In the presence of carbon monoxide, copper(I) alkanesulfonates can form tetrahedral carbonylated species.[13] Work on the carbonylated complexes has demonstrated that they have somewhat improved stability as compared with copper(I) triflate but retain the ability to complex alkenes. When carbon monoxide was introduced into a THF solution of copper(I) triflate, a new carbonyl absorbance at 2127 $cm^{-1}$ was observed. On dilution, a sharp peak appeared at 2095 $cm^{-1}$. These solutions exhibited catalytic activity similar to the copper(I) triflate–benzene complex. An 18% yield of **2** was obtained, but the reaction failed to go to completion.

Fluorinated pentanedionatocopper(I) carbonyl complexes have also been characterized.[14] These compounds are quite labile but form alkene complexes. The fluorine substitution stabilizes these complexes relative to disproportionation to Cu(II) and Cu(0). We prepared solutions containing trifluoropentanedionatocopper(I) (tfpdCu) and hexafluoropentanedionatocopper(I) (hfpdCu) by reaction of the sodium dionate with copper(I) triflate in THF. On exposure to carbon monoxide, these solutions developed infrared absorptions indicative of carbonylation. These solutions were stable to extended storage in the presence of copper bronze in a carbon monoxide atmosphere. When used at 10–20 mol %, these solutions catalyzed conversion of **1** to **2** at 40 °C. Isolated yields were 60–75%, and no indication of formation of the quinone **3** was seen. A final improvement in the catalytic activity was noted when an amine was included. A catalyst solution containing 1 equiv of *n*-butylamine per tfpdCu gave complete conversion of **1** to **2**, with no trace of **3**. The product was isolated in 98% yield.

The indole quinonediazides **4a** and **4b** were also examined with the optimized catalyst system. With the tfpdCu(CO)-*n*-Bu$NH_2$ catalyst, a 63% yield of the CC-1065 A-ring structure **5a** was isolated. No quinone byproduct was observed. The *N*-acetyl-protected analogue **4b** reacted somewhat more slowly. After 4 h in refluxing $CH_2Cl_2$, a 36% yield of **5b** was obtained along with 31% of unreacted starting material. In contrast to the 4-diazoindol-7-ones **4a** and **4b**, the 6-diazo isomer **14** was reactive toward the tfpdCu(CO)-*n*-Bu$NH_2$ catalyst.

**Examination of Chiral Catalysts for Enantioselectivity.** There have been several investigations of copper(II) species as potential catalysts for enantioselective carbenoid cyclopropanation. The most successful of these catalysts are the salicylimines developed by Aratani.[15] Bis[3-(trifluoroacetyl)camphorato]copper(II) showed enantioselectivity in the cyclopropanation of styrene by 2-diazo-5,5-dimethylcyclohexanedione.[16]

We first tried a Cu(II) catalyst of the Aratani type.[17] Its behavior as a catalyst was similar to that of the achiral Cu(II)$(sal)_2$[2] we had studied earlier.[1] At 110 °C, there was a 2:1 preference for **2**/**3**. The salicyliminatocopper(II) complex derived from *R*-α-phenylethylamine as well as bis[3-(trifluoroacetyl)camphorato]copper(II) gave modest conversion of **1** to **2**, but no enantioselectivity was observed using Eu$(hfc)_3$ shift reagent.[18] The carbonylated Cu(I) complex of 3-(trifluoroacetyl)camphor was prepared, and at a mole ratio of 20% it effected formation of **2** in 71% yield. However, the product was racemic as far as could be determined by use of the shift reagent. In view of the beneficial effects of primary amines on catalytic activity of carbonylated Cu(I) species, we also examined the reactivity of solutions of tfpdCu containing (*S*)-α-naphthylethylamine. The solution was an effective catalyst with **2** being isolated in 77% yield, but the Eu$(hfc)_3$ shift reagent gave no indication of enantioselectivity.

**Mechanistic Considerations.** The mechanistic interpretation advanced for copper(I) triflate catalysis of cyclopropanation of simple alkenes by diazo compound indicates reaction of the diazo compound with the Cu(I)-complexed alkene.[3-5,11] The selectivity pattern of copper(I) triflate is attributed to the high alkene coordinating ability of copper(I) triflate.[5] The trends observed in our catalyst optimization studies are in the opposite sense, with the best results being achieved in the presence of dionates and amines that should decrease the extent of alkene coordination by Cu(I). We therefore investigated the possibility that the catalysis observed in these reactions occurs by a redox process rather than formation of a metal–carbene complex. Cyclization could occur at the aryl radical stage, as in Boger's synthetic route to the A-ring

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[12] Dewar, M. J. S.; Narayanaswami, K. *J. Am. Chem. Soc.* **1964**, *86*, 2422. Sriridov, B. D.; Nikiforov, G. A.; Stepanyants, A. U.; Lezina, V. P.; Ershov, V. V. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* (*Engl. Transl.*) **1973**, 1998. Nikiforov, G. A., Sriridov, B. D.; Ershov, V. V. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* (*Engl. Transl.*) **1968**, 542. Koser, G. F., Pirkle, W. H. *J. Org. Chem.* **1967**, *32*, 1992. Fleming, J. C.; Shechter, H. *J. Org. Chem.* **1969**, *34*, 3962. Cauquis, G., Reverdy, G. *Tetrahedron Lett.* **1972**, 3491; Dürr, H.; Kober, H. *Tetrahedron Lett.* **1972**, 1259. For other examples of carbenoid addition reactions of quinonediazides, see: Ershov, V. V.; Nikiforov, G. A.; de Jonge, C. B. H. I. *Quinone Diazides*; Elsevier: Amsterdam, 1981.

[13] Doyle, G.; Eriksen, K. A.; Van Engen, D. *Inorg. Chem.* **1983**, *22*, 2892.

[14] Doyle, G.; Eriksen, K. A.; Van Engen, D. *Organometallics* **1985**, *4*, 830.

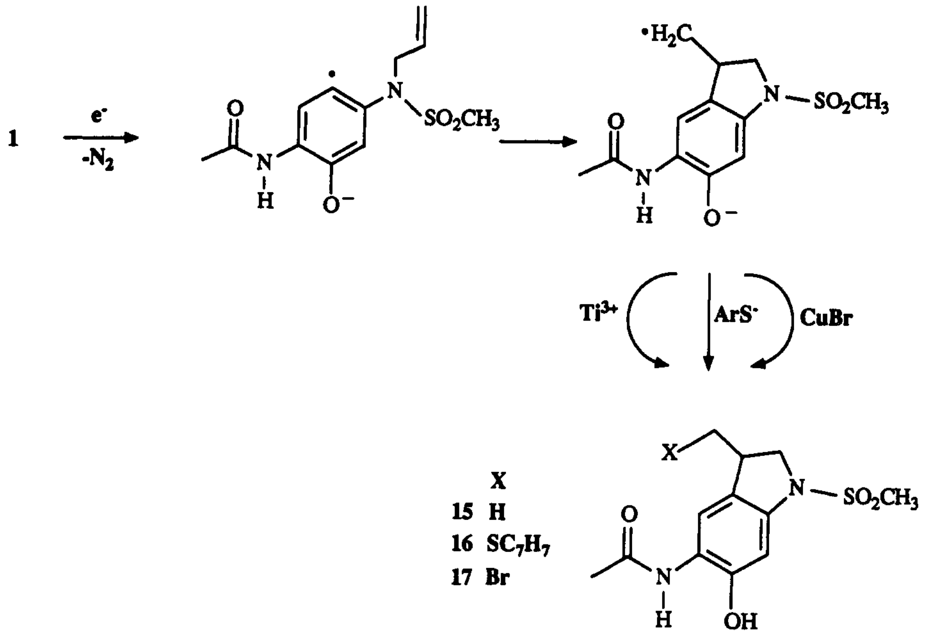
[15] Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, 1707; Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1982**, *23*, 685.

[16] Matlin, S. A.; Lough, W. J.; Chan, L.; Abram, D. M. H.; Zhou, Z. *J. Chem. Soc., Chem. Commun.* **1984**, 1038.

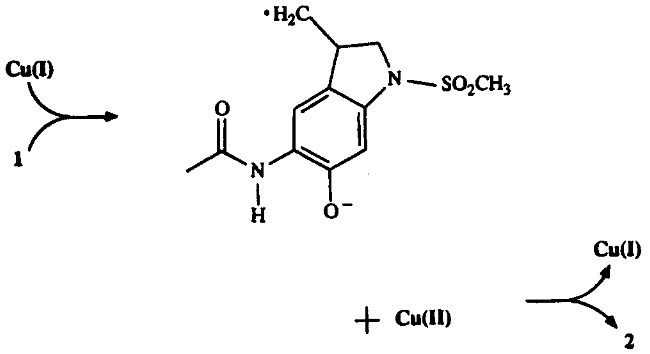
[17] We used the bis(salicyliminato)copper(II) complex derived from D-bis[1,1-(5-*tert*-butyl-2-(octyloxy)phenyl)phenylalinol]; Chemical Abstracts Registry Number [97335-38-1]: Aratani, T.; Yoshihara, H.; Susukamo, G. Eur. Pat. Appl. EP 128,012; *Chem. Abstr.* **1985**, *103*, 71551m. We thank Dr. Ichiro Shinkai for providing a sample of the catalyst.

[18] Eu$(hfc)_3$ is tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III). This reagent gave clear resolution of methylsulfonyl signal of racemic **2**.

Scheme II



Scheme III



structure.[19] To test this possibility, we subjected 1 to reagents that are known to cause reductive dediazonization of aryl diazonium ions.

Reaction with $TiCl_3$[20] led to reductive cyclization and formation of 15 in 20% yield. Reaction with 4-(methylthio)phenoxide[21] gave the cyclization product 16 in 30% yield. Reaction of 1 with $CuBr_2$ in DMSO[22] gave the bromide 17 (54%), which gave 2 on treatment with NaH. All of these reaction conditions correspond to known reactions of aryl diazonium ions that proceed through aryl radicals formed by reduction and loss of nitrogen, as illustrated in Scheme II.

Following this analogy, we suggest the stepwise mechanism in Scheme III for the formation of the cyclopropane 2 in the presence of Cu(I) catalysts. This mechanism is consistent with the beneficial effects of the donor ligands. This route would also be expected to be nonenantioselective, since the chiral center is formed from an achiral radical intermediate. The cyclopropanation could occur through a discrete alkylcopper intermediate or by oxidation of the radical and intramolecular alkylation.

## Experimental Section

**2-(Benzyloxy)-6-bromo-4-nitro-*N*-(2-propenyl)aniline (7).** 2-(Benzyloxy)-6-bromo-4-nitroaniline[8] (3.8 g, 11.8 mmol) was dissolved in 15 mL of DMF and cooled in an ice bath. Potassium *tert*-butoxide (1.38 g, 12.4 mmol) was added in several portions. The deep red-brown solution was stirred for 0.5 h. Allyl bromide (1.62 g, 12.4 mmol) was added dropwise, and the reaction mixture was stirred for 2 h at room temperature. The reaction mixture was poured into 20% $NaH_2PO_4$ and extracted with ethyl acetate. The product was purified by flash column chromatography (hexane/ethyl acetate 4:1) to yield 2.8 g (65%) of 7 as a thick yellow oil that solidified under vacuum. The product was recrystallized from methanol/ether to yield a yellow solid: mp 62–63 °C; IR (KBr) 3387, 3152 cm$^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.20 (dt, $J$ = 6, 1.5 Hz, 2 H), 4.87 (br s, 1 H), 5.08–5.18 (m, 4 H), 5.78–5.93 (m, 1 H), 7.35–7.45 (m, 5 H), 7.73 (d, $J$ = 2.5 Hz, 1 H), 8.12 (d, $J$ = 2.5 Hz, 1 H). Anal. Calcd for $C_{16}H_{15}BrN_2O_3$: C, 52.91; H, 4.16; Br, 22.00; N, 7.71. Found: C, 52.91; H, 4.17; Br, 21.94; N, 7.69.

**7-(Benzyloxy)-3-methyl-5-nitroindole (8).** Compound 7 (5.82 g, 16 mmol), tetra-*n*-butylammonium bromide (5.16 g, 16 mmol), and triethylamine (4.05 g, 40 mmol) were dissolved in 15 mL of DMF. Palladium acetate (72 mg, 0.32 mmol) was added, and the reaction mixture was stirred for 24 h. The reaction mixture was diluted with ethyl acetate, filtered through Celite, washed with $H_2O$, 5% HCl, and saturated aqueous NaCl, dried, and evaporated to give a brown-black solid. The crude product in $CH_2Cl_2$ was filtered through a silica gel column to remove colloidal palladium. Evaporation of the eluate yielded 4.32 g (96%) of 8 as a light orange solid that was pure by NMR and TLC. Recrystallization from ethyl acetate produced orange-brown needles: mp 191–192 °C (lit.[8] mp 109–110 °C); IR (KBr) 3324, 1518, 1233 cm$^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.35 (d, $J$ = 0.7 Hz, 3 H), 5.27 (s, 2 H), 7.06 (s, 1 H), 7.38–7.50 (m, 5 H), 7.65 (d, $J$ = 2 Hz, 1 H), 8.27 (d, $J$ = 2 Hz, 1 H), 8.46 (br s, 1 H); CIMS (*i*-Bu) $m/z$ 283 ($M^+$ + 1, 100). Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 68.11; H, 5.03; N, 9.88.

**7-(Benzyloxy)-3-methyl-5-nitro-1-(phenylsulfonyl)indole (9).** Sodium hydride (60% dispersion in mineral oil, 5.3 g, 133 mmol) was washed with hexane, suspended in 50 mL of THF, and cooled to 0 °C. A solution of nitroindole 8 (9.40 g, 33.3 mmol) in 50 mL of THF was cooled to 0 °C and added dropwise via syringe over 15 min. After the addition, the reaction mixture was stirred for 0.5 h (until bubbling had ceased) and benzenesulfonyl chloride (6.48 g, 36.6 mmol) was added dropwise. The reaction mixture was stirred for 0.5 h at 0 °C and for 2 h at room tem-

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[19] Boger, D. L.; Coleman, R. S. *J. Am. Chem. Soc.* **1988**, *110*, 4796.

[20] Citterio, A.; Cominelli, A.; Bonavoglia, F. *Synthesis* **1986**, 308.

[21] Abeywickrema, A. N.; Beckwith, A. L. J. *J. Am. Chem. Soc.* **1986**, *108*, 8227. Meijs, G. F.; Beckwith, A. L. J. *J. Am. Chem. Soc.* **1986**, *108*, 5890.

[22] Kobayashi, M.; Yamada, E.; Matsui, M.; Kobori, N. *Org. Prep. Proced.* **1969**, *1*, 221. Abeywickrema, A. N.; Beckwith, A. L. J. *J. Org. Chem.* **1987**, *52*, 2568.

perature, during which time the color became light orange. The reaction mixture was poured into a cold 5% HCl/20% $NaH_2PO_4$ solution and refrigerated for several hours. The precipitate was collected and dried to yield 13.8 g (98%) of **9**, which was recrystallized from ethyl acetate/hexane: mp 177–178 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 2.34 (d, 1.2 Hz, 3 H), 5.07 (s, 2 H), 7.24–7.52 (m, 10 H), 7.59 (d, $J$ = 2 Hz, 1 H), 7.77 (d, $J$ = 10 Hz, 1 H), 8.07 (d, $J$ = 2 Hz, 1 H); CIMS ($CH_4$) $m/z$ 423 ($M^+$ + 1, 100). Anal. Calcd for $C_{22}H_{18}N_2O_5S$: C, 62.55; H, 4.29; N, 6.63; S, 7.59. Found: C, 62.60; H, 4.33; N, 6.57; S, 7.67.

**5-Acetamido-7-(benzyloxy)-3-methyl-1-(phenylsulfonyl)indole (10b).** Nitroindole **9** (5 g, 11.8 mmol), $CaCl_2$ (1.20 g, 10.8 mmol) and acid-washed zinc (30 g, 0.46 g-atom) were suspended in 250 mL of 95% ethanol. The mixture was refluxed for 2 h, cooled to room temperature, filtered, and evaporated to yield the aminoindole **10a**: $^1H$ NMR ($CDCl_3$) $\delta$ 2.18 (d, $J$ = 1.2 Hz, 3 H), 4.93 (s, 2 H), 6.09 (d, $J$ = 2.5 Hz, 1 H), 6.34 (d, $J$ = 2.5 Hz, 1 H), 7.20–7.58 (m, 11 H); EIMS $m/z$ 392, 251, 91 (100), 77. The amine was suspended in 100 mL of $CH_2Cl_2$, pyridine (1.02 g, 13.0 mmol) was added, and the mixture was cooled to 0 °C. Acetyl chloride (1.03 g, 13.0 mmol) was added dropwise, and the mixture was stirred at 0 °C for 5 min and for 1 h at room temperature. The solution was washed with $H_2O$, 5% HCl, $NaHCO_3$, and NaCl, dried, and evaporated to yield **10b** (4.8 g, 93%) as an off-white powder that was pure by NMR and TLC. The product could be recrystallized from ethyl acetate/hexane to yield white crystals: mp 195–197 °C; IR (KBr) 3290, 1663 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.16 (s, 3 H), 2.24 (d, $J$ = 1.5 Hz, 1 H), 4.97 (s, 2 H), 6.94 (d, $J$ = 1.5 Hz, 1 H), 7.13 (br s, 1 H), 7.17 (d, $J$ = 1.5 Hz, 1 H), 7.20–7.68 (m, 11 H); MS ($CH_4$) $m/z$ 435 ($M^+$ + 1, 100), 295, 215, 143. Anal. Calcd for $C_{24}H_{22}N_2O_4S$: C, 66.34; H, 5.10; N, 6.45; S, 7.38. Found: C, 66.25; H, 5.14; N, 6.37; S, 7.47.

**7-(Benzyloxy)-3-methyl-1-(phenylsulfonyl)-5-[*N*-(2-propenyl)acetamido]indole (10c).** Sodium hydride 60% dispersion in mineral oil (1.33 g, 33.2 mmol) was washed with hexane, suspended in 10 mL of DMF, and cooled to 0 °C. Amide **10b** (4.80 g, 11.1 mmol) was dissolved in 5 mL of DMF, added dropwise to the sodium hydride suspension, and stirred for 15 min. Allyl bromide (1.47 g, 12.2 mmol) was added dropwise, and the mixture was stirred for 15 min at 0 °C and at room temperature for 1 h. The reaction mixture was poured into 200 mL of a 2% HCl/20% $NaH_2PO_4$/ice mixture and refrigerated. The product was filtered and dried to yield 5.0 g (95%) of **10c**. The crude product could be recrystallized from ethyl acetate to yield an off-white solid: mp 124–125 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 1.67 (s, 3 H), 2.25 (s, 3 H), 4.17 (d, $J$ = 7.5 Hz, 2 H), 4.90–5.05 (m, 4 H), 5.67–5.82 (m, 1 H), 6.37 (s, 1 H), 6.85 (s, 1 H), 7.15–7.38 (m, 7 H), 7.48 (t, $J$ = 7.5 Hz, 1 H), 7.68 (d, $J$ = 7.5 Hz, 3 H); CIMS (*i*-Bu) $m/z$ 475 ($M^+$ + 1, 100). Anal. Calcd for $C_{27}H_{26}N_2O_4S$: C, 68.33; H, 5.52; N, 5.90; S, 6.76. Found: C, 68.34; H, 5.57; N, 5.83; S, 6.70.

**7-(Benzyloxy)-5-(methanesulfonamido)-3-methyl-1-(phenylsulfonyl)indole (11a).** Amine **10a** (928 mg, 2.4 mmol) and pyridine (225 mg, 2.8 mmol) were suspended in 50 mL of chloroform and cooled to 0 °C. Methanesulfonyl chloride (298 mg, 2.6 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 0.5 h and at room temperature overnight. The solvent was evaporated, and the crude solid was recrystallized from ethyl acetate/hexane to yield 1.0 g (90%) of **11a**: mp 194–195 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 2.25 (s, 3 H), 2.80 (s, 3 H), 4.99 (s, 2 H), 6.40 (br s, 1 H), 6.61 (d, $J$ = 1.5 Hz, 1 H), 6.88 (d, $J$ = 1.5 Hz, 1 H), 7.25–7.34 (m, 7 H), 7.47 (t, $J$ = 7 Hz, 1 H), 7.57 (s, 1 H), 7.62 (d, $J$ = 7 Hz, 2 H).

**7-(Benzyloxy)-3-methyl-1-(phenylsulfonyl)-5-[*N*-(2-propenyl)methanesulfonamido]indole (11b).** Methanesulfonamide **11a** (500 mg, 1.1 mmol) was dissolved in 5 mL of DMF and cooled to 0 °C. Potassium *tert*-butoxide (143 mg, 1.3 mmol) was added, and the reaction mixture was stirred for 15 min until the base dissolved. Allyl bromide (154 mg, 1.3 mmol) was added dropwise, and the reaction mixture was stirred for 15 min at 0 °C and for 2 h at room temperature. The crude product was poured into 20% $NaH_2PO_4$, extracted with ethyl acetate, dried, and evaporated to yield a white foam. The product was pure by NMR and TLC. Recrystallization afforded 520 mg (96%) of product, mp 132–133 °C (lit.[1] mp 132 °C).

**7-(Benzyloxy)-3-methyl-4-nitro-1-(phenylsulfonyl)-5-[*N*-(2-propenyl)acetamido]indole (12a) and 7-(Benzyloxy)-3-methyl-6-nitro-1-(phenylsulfonyl)-5-[*N*-(2-propenyl)acetamido]indole (12b).** *N*-Allylamide **10c** (5.1 g, 10.8 mmol) and ammonium nitrate (861 mg, 10.8 mmol) were suspended in 20 mL of $CH_2Cl_2$. Trifluoroacetic anhydride (5 mL) was added, and the reaction mixture was stirred overnight during which time the ammonium nitate dissolved. The reaction mixture was carefully poured into 100 mL of an ice and saturated $NaHCO_3$ mixture, shaken until effervescence ceased, extracted with chloroform, washed, dried, and evaporated to yield a yellow glass. The crude product was purified by flash column chromatography to yield 3.4 g (combined total yield 61%) of a mixture of the 4- and 6-nitro regioisomers in a 6:1 ratio by NMR integration. Recrystallization from ethyl acetate/ether yielded 3.0 g (54%) of **12a**: mp 165–167 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 1.69 (s, 3 H), 2.17 (d, $J$ = 0.9 Hz, 3 H), 3.64 (dd, $J$ = 14.7, 7.5 Hz, 1 H), 4.52 (dd, $J$ = 14.6, 5.7 Hz, 1 H), 4.84–4.92 (m, 2 H), 5.05 (dd, $J$ = 17.9, 12.1 Hz, 2 H), 5.55–5.67 (m, 1 H), 6.30 (s, 1 H), 7.07–7.12 (m, 2 H), 7.30–7.44 (m, 5 H), 7.56 (t, $J$ = 7.4 Hz, 1 H), 7.71 (d, $J$ = 7.6 Hz, 2 H), 7.81 (s, 1 H). Homonuclear NOE irradiation of the C-3 methyl protons ($\delta$ 2.17) resulted in a 17% enhancement in the $H_{C-2}$ signal at $\delta$ 7.81. Anal. Calcd for $C_{27}H_{25}N_3O_6S$: C, 62.42; H, 4.85; N, 8.09; S, 6.17. Found: C, 62.48; H, 4.89; N, 8.06; S, 6.07.

A pure sample of **12b** was isolated from a reaction in which **12a** and **12b** were treated with $BBr_3$. Compound **12a** was preferentially debenzylated. After recrystallization from ethyl acetate/hexane, pure **12b** was obtained as tan needles: mp 198–199 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 1.82 (s, 3 H), 2.27 (d, $J$ = 1 Hz, 3 H), 3.63 (dd, $J$ = 15.1, 7.6 Hz, 1 H), 4.66 (dd, $J$ = 14.8, 5.5 Hz, 1 H), 5.02–5.12 (m, 2 H), 5.23 (t, $J$ = 9 Hz, 2 H), 5.77–5.92 (m, 1 H), 7.05 (s, 1 H), 7.27–7.55 (m, 9 H), 7.63 (d, $J$ = 7.5 Hz, 2 H), 7.77 (d, $J$ = 0.7 Hz, 1 H) (homonuclear NOE irradiation of the C-3 methyl protons ($\delta$ 2.27) resulted in an 18% enhancement in the $H_{C-2}$ signal at $\delta$ 7.77 and an 18% enhancement in the $H_{C-4}$ signal at $\delta$ 7.05); CIMS (*i*-Bu) $m/z$ 520 ($M^+$ + 1, 100) 474, 380. Anal. Calcd for $C_{27}H_{25}N_3O_6S$: C, 62.42, H, 4.85; N, 8.09; S, 6.17. Found: C, 62.38; H, 4.90; N, 8.03; S, 6.11.

**7-(Benzyloxy)-3-methyl-4-nitro-5-[*N*-(2-propenyl)acetamido]indole (13a).** Nitroindole **12a** (1.90 g, 3.66 mmol) was suspended in a solution of 10 mL of 10% NaOH and 20 mL of 95% ethanol and refluxed for 45 min to produce a deep red solution. The reaction mixture was poured into a 5% HCl/ice mixture. The yellow precipitate was allowed to settle in the refrigerator. The product was filtered and dried to yield 1.31 g (94% yield) of yellow powder that was pure **13a** by NMR and TLC. The product could be recrystallized from ethyl acetate/hexane to give yellow cubes: mp 189–190 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 1.85 (s, 3 H), 2.19 (d, $J$ = 0.8 Hz, 3 H), 3.85 (dd, $J$ = 15, 7.5 Hz, 1 H), 4.59 (dd, $J$ = 14, 6.5 Hz, 1 H), 4.94–5.06 (m, 2 H), 5.22 (dd, $J$ = 20, 12 Hz, 2 H), 5.75–5.86 (m, 1 H), 6.37 (s, 1 H), 7.12 (s, 1 H), 7.37–7.45 (m, 5 H), 8.57 (br s, 1 H); CIMS (*i*-Bu) $m/z$ 362 ($M^+$ + 1, 100). Anal. Calcd for $C_{21}H_{21}N_3O_4S$: C, 66.48; H, 5.58; N, 11.07. Found: C, 66.54; H, 5.62; N, 10.98.

**7-Hydroxy-3-methyl-4-nitro-5-[*N*-(2-propenyl)acetamido]indole (13b).** Nitroindole **13a** (450 mg, 1.2 mmol) was dissolved in 10 mL of $CH_2Cl_2$ and cooled in an ice bath. In a separate flask, cyclohexene (487 mg, 5.9 mmol) was dissolved in 5 mL of $CH_2Cl_2$ and cooled. Boron tribromide (1 M) solution in $CH_2Cl_2$ (2.6 mL, 2.6 mmol) was added to the cyclohexene solution, stirred for 10 min, and then added dropwise to the indole solution. The reaction mixture was stirred for 15 min, during which time a precipitate formed. The reaction mixture was quenched with a few drops of absolute ethanol followed by the addition of 20% $NaH_2PO_4$. The organic layer was separated, dried, and evaporated to yield a yellow glass that was purified by flash column chromatography, (hexane/ethyl acetate (3:1 → 1:1)) to yield 241 mg (70%) of the phenol **13b**. NMR showed the product to be contaminated by an unidentified product, and the mixture was used without further purification in the next step: $^1H$ NMR ($CDCl_3$) $\delta$ 1.96 (s, 3 H), 2.18 (s, 3 H), 4.04 (dd, $J$ = 15, 7 Hz, 1 H), 4.56 (dd, $J$ = 15, 7 Hz, 1 H), 5.08–5.15 (m, 2 H), 5.80–5.95 (m, 1 H), 6.38 (s, 1 H), 7.10 (s, 1 H), 9.15 (br s, 1 H), 10.05 (br s, 1 H).

**7-[(Ethoxycarbonyl)oxy]-3-methyl-4-nitro-5-[*N*-(2-propenyl)acetamido]indole (13c).** Phenol **13b** (275 mg, 0.95 mmol) was dissolved in 15 mL of $CH_2Cl_2$ and cooled in an ice bath. Pyridine (90 mg, 1.1 mmol) was added followed by ethyl chloroformate (123 mg, 1.1 mmol). The reaction mixture was stirred for 15 min at 0 °C and for 0.5 h at room temperature. The reaction mixture was diluted with $CH_2Cl_2$, washed, dried, and evaporated to yield a yellow solid. The crude product was purified by recrystallization from ethyl acetate to yield 240 mg (70%) of **13c** as yellow cubes: mp 181–182 °C; $^1$H NMR ($CDCl_3$) $\delta$ 1.43 (t, $J$ = 7.5 Hz, 3 H), 1.92 (s, 3 H), 2.20 (s, 3 H), 3.83 (dd, $J$ = 15, 7 Hz, 1 H), 4.39 (q, $J$ = 7.5 Hz, 2 H), 4.67 (dd, $J$ = 15, 6 Hz, 1 H), 8.60 (br s, 1 H). Anal. Calcd for $C_{17}H_{19}N_3O_6S$: C, 56.51; H, 5.30; N, 11.63. Found: C, 56.58; H, 5.33; N, 11.54.

The mother liquor contained some *N,O*-diethoxycarbonylated indole as a byproduct: $^1$H NMR ($CDCl_3$) $\delta$ 1.43 (2t, $J$ = 7 Hz, 6 H), 1.90 (s, 3 H), 2.12 (s, 3 H), 3.74 (dd, $J$ = 15, 6 Hz, 1 H), 4.35 (q, $J$ = 6 Hz, 2 H), 4.40 (q, $J$ = 7 Hz, 2 H), 4.68 (dd, $J$ = 15, 7 Hz, 1 H), 5.05–5.15 (m, 2 H), 5.77–5.92 (m, 1 H), 6.94 (s, 1 H), 7.55 (s, 1 H).

**4-Diazo-3-methyl-5-[*N*-(2-propenyl)acetamido]-4,7-dihydroindol-7-one (4b).** Indole carbamate **13c** (154 mg, 0.43 mmol) was dissolved in 2 mL of methanol. In a separate flask, palladium on carbon 5% (31 mg) was suspended in 1 mL of methanol. Sodium borohydride (97 mg, 2.25 mmol) was dissolved in 1 mL of $H_2O$ and added to the Pd/C suspension. The solution was cooled to 0 °C, and $N_2$ was bubbled through the solution for 5 min. The solution of **13c** was added and the resulting mixture stirred for 10 min, diluted with ethyl acetate, filtered through Celite, washed with cold $H_2O$, aqueous NaCl, dried, and evaporated at room temperature. The residue was dried under vacuum. The crude aniline was cooled in a dry ice–$CCl_4$ bath and dissolved in 2 mL of methanol and 2 mL of $CH_2Cl_2$. Isoamyl nitrite (191 mg, 1.64 mmol) was added, followed by 2 drops of 8 N methanolic HCl. The reaction mixture was stirred for 1 h, diluted with $NaHCO_3$, extracted with $CH_2Cl_2$, dried ($Na_2CO_3$), and evaporated. The crude product was purified by flash column chromatography to yield 30 mg (26%) of **4b**: IR (KBr) 3150, 2062, 1680 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.07 (s, 3 H), 2.27 (s, 3 H), 4.32 (d, $J$ = 7 Hz, 2 H), 5.15–5.32 (m, 2 H), 5.78–5.92 (m, 1 H), 6.27 (s, 1 H), 7.12 (s, 1 H), 11.62 (br s, 1 H).

**Stock Solution of Copper(I) Triflate Carbonyl Complex.** Cuprous oxide (358 mg, 2.5 mmol) was suspended in 8 mL of THF, trifluoromethanesulfonic acid (751 mg, 5 mmol) was added, and a slow stream of carbon monoxide was passed through the solution. After 0.5 h, the cuprous oxide had dissolved to give a colorless solution. Carbon monoxide was passed through the solution for an additional 0.5 h, and sufficient THF was added to bring the final volume of the solution to 10 mL (0.5 M). The colorless solution was filtered and stored under a carbon monoxide atmosphere in a sealed flask: IR (THF) 2127 cm$^{-1}$.

**Hexafluoropentanedionatocopper(I) Carbonyl Complex.** Copper(I) triflate–benzene complex (450 mg, 0.90 mmol) was transferred to a tared flask fitted with a rubber septum and dissolved in 10 mL of THF. In a separate flask, sodium hydride (60% dispersion in mineral oil; 78 mg, 1.95 mmol) was washed with hexane and suspended in 10 mL of THF. Hexafluoropentanedione (372 mg, 1.79 mmol) was added dropwise (foaming was noted). When the bubbling had ceased, a stream of carbon monoxide was passed through the solution and the cuprous triflate solution was added dropwise with rapid stirring. After the addition was complete, the light yellow solution was treated with carbon monoxide for an additional 0.5 h and brought to a final volume of 25 mL, filtered under a positive pressure of carbon monoxide, and stored in a sealed flask: IR (THF) 2105 cm$^{-1}$.

**Trifluoropentanedionatocopper(I) Carbonyl Complex.** Sodium hydride (60% dispersion in mineral oil; 21 mg, 0.525 mmol) was washed with several portions of hexane and suspended in 3 mL of THF. Trifluoropentanedione (77 mg, 0.5 mmol) was added dropwise. After the bubbling had ceased, carbon monoxide was passed through the solution and copper(I) triflate–carbonyl complex (0.5 M solution; 1 mL 0.5 mmol) was added dropwise. THF was added to bring the volume to 5 mL (0.1 M). The colorless solution was filtered under a positive pressure of carbon monoxide and stored in a sealed flask: IR (THF) 2092 cm$^{-1}$.

**Trifluoropentanedionatocopper(I) Carbonyl–*n*-Butylamine Complex.** Sodium hydride (60% dispersion in mineral oil; 21 mg, 0.525 mmol) was washed with several portions of hexane and suspended in 3 mL of THF. Trifluoropentanedione (77 mg, 0.5 mmol) was added dropwise. After the bubbling had ceased, carbon monoxide was passed through the solution, copper(I) triflate–carbonyl complex solution (1 mL, 0.5 mmol) was added dropwise, and the solution was stirred for 5 min. *n*-Butylamine (37 mg, 0.525 mmol) was added dropwise, during which time the solution became faintly blue. THF was added to bring the volume to 5 mL (0.1 M), and the solution was filtered under a positive pressure of carbon monoxide into a sealed flask that contained copper powder (copper bronze, 100 mg): IR (THF) 2060 cm$^{-1}$. [3-(Trifluoroacetyl)camphorato]copper(I) carbonyl– and trifluoropentadionatocopper(I) carbonyl–(*S*)-$\alpha$-naphthylethylamine complex were prepared similarly.

**Decomposition of Diazocyclohexadienone 1 in the Presence of Trifluoropentanedionatocopper(I) Carbonyl–*n*-Butylamine Complex.** Compound **1** (10 mg, 0.032 mmol) was dissolved in 10 mL of $CH_2Cl_2$, and a slow stream of carbon monoxide was passed through the solution. TfpdCuCO–*n*-BuNH$_2$ complex (0.1 M solution, 32 $\mu$L, 0.003 mmol) was added and the reaction mixture refluxed for 2 h. An additional 32 $\mu$L of catalyst solution was added and the reaction mixture refluxed for an additional 2 h. The solvent was evaporated and the residue purified by flash column chromatography to yield 8.9 mg (98%) of **2**.

**Decomposition of Diazoindolone 4a in the Presence of Trifluoropentanedionatocopper(I) Carbonyl–*n*-Butylamine Complex.** Compound **4a** (10 mg, 0.033 mmol) was dissolved in 10 mL of $CH_2Cl_2$ and a slow stream of carbon monoxide passed through the solution. TfpdCuCO–*n*-BuNH$_2$ complex (0.1 M solution, 32 $\mu$L, 0.003 mmol) was added and the reaction mixture refluxed for 2 h. An additional 32 $\mu$L of catalyst solution was added and the reaction mixture refluxed for an additional 2 h. The solvent was evaporated and the residue purified by flash column chromatography to yield 5.7 mg (63%) of compound **5a** and 1.1 mg (11%) of starting material.

**Decomposition of Diazoindolone 4b in the Presence of Trifluoropentanedionatocopper(I) Carbonyl–*n*-Butylamine Complex.** Compound **4b** (15 mg, 0.055 mmol) was dissolved in 5 mL of $CH_2Cl_2$, and a stream of carbon monoxide was passed through the solution. TfpdCuCO–*n*-BuNH$_2$ (55 $\mu$L, 0.1 M solution, 0.005 mmol) was added, and the mixture was refluxed for 2 h. An additional 55 $\mu$L of catalyst solution was added and the reaction mixture refluxed for an additional 2 h. The solution was evaporated and the crude product purified by flash column chromatography (hexane/ethyl acetate (2:1) → 100% ethyl acetate) to yield 4.8 mg (36%) of the product **5b** and 4.0 mg (31%) of starting material.

**5-Acetamido-6-hydroxy-1-(methanesulfonyl)-3-methyl-2,3-dihydroindole (15).** A 0.65 M stock solution was prepared by dissolving $TiCl_3$ (1.0 g, 6.5 mmol) in 10 mL of degassed water to which sodium acetate trihydrate (0.9 g, 6.6 mmol) had been added. Diazocyclohexadienone **1** was dissolved in 3 mL of a 1:1 mixture of acetone and water. Then, 50 $\mu$L of the 0.65 M $TiCl_3$ solution was added dropwise, during which time the purple color of the titanium solution and the yellow color of the diazo compound were rapidly dispelled. The reaction mixture was stirred for 15 min, diluted with aqueous NaCl, and extracted with ether. The extract was dried and evaporated. The crude product was purified by flash column chromatography to yield 1.8 mg (20%) of **15**: $^1$H NMR ($CDCl_3$) $\delta$ 1.30 (d, $J$ = 6.6 Hz, 3 H), 2.25 (s, 3 H), 2.87 (s, 3 H), 3.39 (m, $J$ = 7.5 Hz, 1 H), 3.46 (m, 1 H), 4.12 (t, $J$ = 9 Hz, 1 H), 7.00 (s, 1 H), 7.05 (s, 1 H); 7.44 (br s, 1 H), 8.16 (br s, 1 H); CIMS (*i*-Bu) $m/z$ 285 ($M^+$ + 1, 100).

**5-Acetamido-6-hydroxy-1-(methanesulfonyl)-3-[[(4-methylphenyl)thio]methyl]-2,3-dihydroindole (16).** Diazocyclohexadienone **1** (40 mg, 0.13 mmol) was dissolved in 4 mL of DMSO and cooled in an ice bath. In a separate flask, sodium hydride (60% dispersion in mineral oil; 54 mg, 1.3 mmol) was washed with hexane. 4-(Methylthio)phenol (160 mg, 1.3 mmol) was dissolved in 1 mL of DMSO and added to the sodium hydride, and the mixture was cooled in an ice bath. After the bubbling had stopped (0.5 h), this solution was added dropwise to the solution of **1** and the reaction mixture stirred for 0.5 h. The solution was cautiously poured into 20% $NaH_2PO_4$ and extracted with ethyl acetate. Purification of the product by flash column chromatography (hexane/ethyl acetate) yielded 20 mg (38%) of **16**, which was recrystallized from ethyl acetate/hexane to yield an off-white solid: mp 143–145 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.21 (s, 3 H), 2.31 (s, 3 H), 2.86 (s, 3 H), 2.91 (m, 1 H), 3.18 (dd, $J$ = 13, 5 Hz, 1 H), 3.42 (m, 1 H), 3.85 (dd, $J = 11, 6$ Hz, 1 H), 4.05 (dd, $J = 10, 9$ Hz, 1 H), 7.00 (s, 1 H), 7.10 (d, $J = 8$ Hz, 2 H), 7.24 (d, $J = 8$ Hz, 2 H), 7.29 (s, 1 H), 7.75 (br s, 1 H), 8.51 (br s, 1 H); CIMS (*i*-Bu) *m/z* 407 ($M^+ + 1$), 391 (90), 371 (40), 285 (100), 269 (75), 221 (90).

**5-Acetamido-3-(bromomethyl)-6-hydroxy-1-(methanesulfonyl)-2,3-dihydroindole (17).** Diazocyclohexadienone 1 (10 mg, 0.032 mmol) and $CuBr_2$ were suspended in 1 mL of DMSO, and the mixture was stirred overnight. The reaction mixture was diluted with 20% $NaH_2PO_4$ and extracted with ethyl acetate. The combined organic layers were dried ($MgSO_4$) and evaporated and the residue purified by flash column chromatography to yield 6.3 mg (54%) of 17. A spot that comigrated with a TLC standard of 2 was observed but could not be isolated on this small scale: $^1H$ NMR (DMSO) $\delta$ 2.14 (s, 3 H), 2.84 (s, 3 H), 3.38 (dd, $J = 8, 10$ Hz, 1 H), 3.58 (dd, $J = 11, 4$ Hz, 1 H), 3.68 (m, 1 H), 3.85 (dd, $J = 11, 5$ Hz, 1 H), 4.02 (dd, $J = 10, 8$ Hz, 1 H), 7.02 (s, 1 H), 7.73 (s, 1 H), 8.06 (s, 1 H). When 17 was treated with sodium hydride (2 equiv) in THF at 0 °C, it was cyclized to 2 in 90% yield.

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**Supplementary Material Available:** Proton NMR spectra for compounds **4b**, **5a**, **5b**, **7–9**, **10b**, **10c**, **12a**, **12b**, and **15–17**. Infrared spectra for compounds **4b**, **8**, and **10b** and mass spectra for compounds **4b**, **15**, and **16** (34 pages). Ordering information is given on any current masthead page.

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# Action of Alkali on *O*-Benzylated Aldoses: A Simple Rationalization of Some Reactions Occurring in Alkaline Media

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Treatment of some *O*-benzyl-protected aldopyranoses and aldofuranoses with sodium 2-propoxide or $K_2CO_3$ brought about their equilibration and the loss of the elements of benzyl alcohol, with concomitant formation of a *Z* aldehyde. The latter rearranged rapidly in solution to the corresponding *E* lactol.

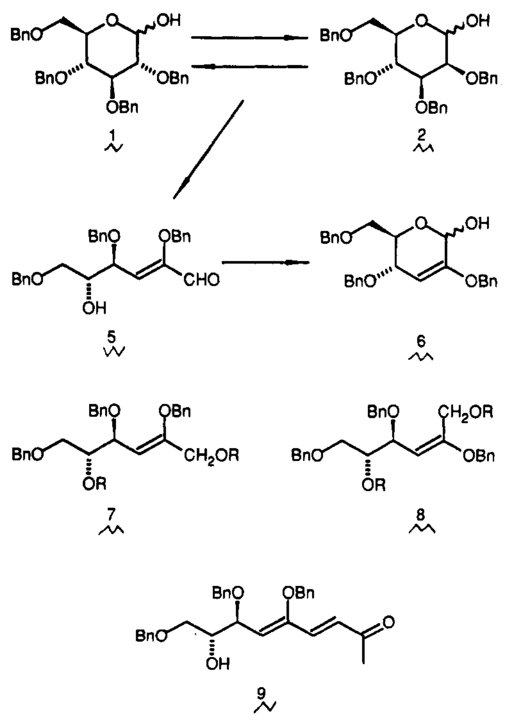
## Introduction

The chemical transformations of glucose and mannose in alkaline media have been extensively studied.[1-3] In contrast, no systematic studies of the effect of alkalis or alkaline reaction conditions on their 2,3,4,6-tetra-*O*-benzyl derivatives have been made, despite the wide use of these derivatives as intermediates in a variety of reactions.[4]

A few reports[5,6] have, however, described the stereospecific elimination of benzyl alcohol from *O*-perbenzylated sugars during $NaBH_4$ reduction and the unsuccessful attempts to isolate any intermediate aldehydes produced.

In earlier works,[7] we found that the weakly basic Wittig–Horner reagent derived from diethyl (cyanomethyl)phosphonate caused the undesired equilibration of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (1) and 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose (2), which was followed, in some cases,[7,8] by the elimination of benzyl alcohol. So we decided to investigate the action of both mild and strong bases on those two sugars (Scheme I) and their analogues, 2,3,5-tri-*O*-benzyl-D-arabinofuranose (3) and 2,3,5-tri-*O*-benzyl-D-ribofuranose (4) (Scheme II). Our aims were to rationalize the behavior of the *O*-benzyl-protected aldoses in these and other known reactions in alkaline media[5-10] and to obtain data that would be useful for predicting the behavior of these compounds in other possible reactions that occur in alkaline media.

Scheme I[a]



[a] a, R = H; b, R = Ac.

## Results and Discussion

The results (summarized in Scheme I) showed that simple bases ($K_2CO_3$ and sodium 2-propoxide) brought

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