Synthesis of Carbazomycin B

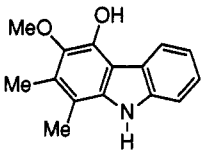
Derrick L. J. Clive,* Nola Etkin, Tomi Joseph, and J. William Lown

Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

Received January 28, 1992 (Revised Manuscript Received January 26, 1993)

Carbazomycin B (1) was synthesized by radical cyclization of the sulfonamide 14 (Scheme III), followed by deprotection and dehydrogenation.

Carbazomycin B (1),[1] a member of a small family of related substances,[2] is an inhibitor of 5-lipoxygenase[3] and possesses weak antibacterial and antiyeast activity.[1a] It also inhibits the growth of some phytopathogenic fungi.[1a]



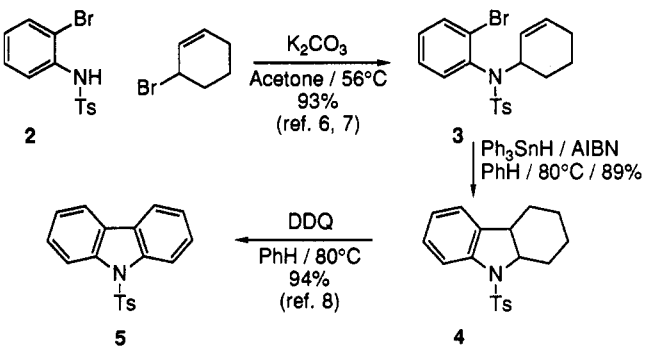
1

Several syntheses of 1 have been described.[4] We report here an alternative route based on radical cyclization.[5] Our approach is summarized in Scheme I, which shows a model study.

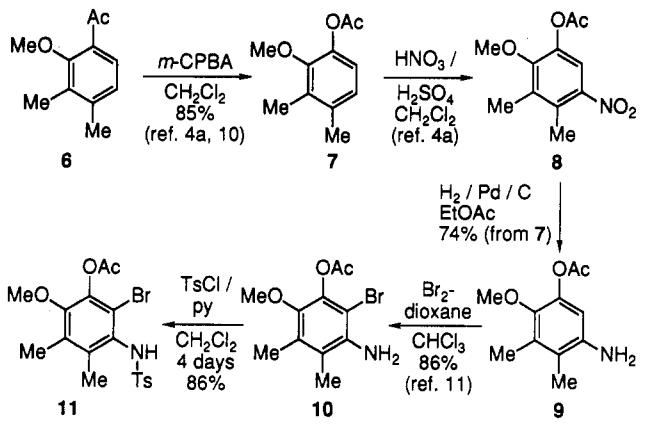
Alkylation of the sulfonamide 2 with 3-bromo-1-cyclohexene gave the expected product 3,[9] and this underwent efficient radical cyclization (3 → 4). Dehydrogenation with DDQ then generated the aromatic carbazole system (4 → 5).

We next prepared the substituted sulfonamide 11, by the route summarized in Scheme II. Alkylation of 11 (Scheme III) with 3-bromo-1-cyclohexene produced two conformational isomers (ca. 3:2) of gross structure 12.[12] Hydrolysis (KOH/EtOH) then afforded the corresponding phenols 13, and benzylation produced the *O*-benzyl derivatives 14. The isomers of 14 were not easily separable on a preparative scale, and so the mixture was treated with triphenyltin hydride in refluxing benzene. The required product (15) was formed, but only in 39% yield,

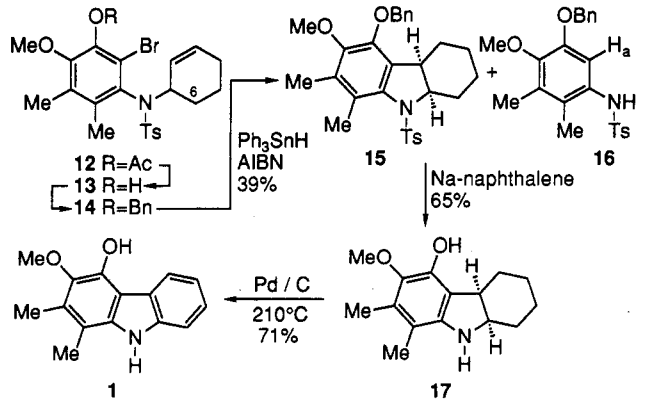
Scheme I



Scheme II



Scheme III



the major byproducts being 16 and the compound that results from replacement of the bromine atom in 14 by hydrogen. The fragmentation product 16 is not produced in a simple thermal process because the starting material 14 is stable in refluxing benzene.[13] Treatment of 15 with sodium–naphthalene served to remove the *N*-tolylsulfonyl

(1) (a) Sakano, K.-I.; Ishimaru, K.; Nakamura, S. *J. Antibiot.* **1980**, *33*, 683. (b) Sakano, K.-I.; Nakamura, S. *J. Antibiot.* **1980**, *33*, 961. (c) Kaneda, M.; Sakano, K.-I.; Nakamura, S.; Kushi, Y.; Iitaka, Y. *Heterocycles* **1981**, *15*, 993.

(2) Naid, T.; Kitahara, T.; Kaneda, M.; Nakamura, S. *J. Antibiot.* **1987**, *40*, 157. Kaneda, M.; Naid, T.; Kitahara, T.; Nakamura, S.; Hirata, T.; Suga, T. *J. Antibiot.* **1988**, *41*, 602. Kondo, S.; Katayama, M.; Marumo, S. *J. Antibiot.* **1986**, *39*, 727.

(3) Hook, D. J.; Yacobucci, J. J.; O'Connor, S.; Lee, M.; Kerns, E.; Krishnan, B.; Matson, J.; Hesler, G. *J. Antibiot.* **1990**, *53*, 1347.

(4) (a) Knölker, H.-J.; Bauermeister, M.; Bläser, D.; Boese, R.; Pannek, J.-B. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 223. (b) Knölker, H.-J.; Bauermeister, M. *J. Chem. Soc., Chem. Commun.* **1989**, 1468. (c) Moody, C. J.; Shah, P. *J. Chem. Soc., Perkin Trans I* **1989**, 376. (d) Moody, C. J.; Shah, P. *J. Chem. Soc., Perkin Trans. I* **1989**, 2463.

(5) For recent uses of radical cyclization in synthesis, see: Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.

(6) Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620.

(7) Krolski, M. E.; Renaldo, A. F.; Rudisill, D. E.; Stille, J. K. *J. Org. Chem.* **1988**, *53*, 1170.

(8) Wassmundt, F. W.; Babic, G. T. *J. Org. Chem.* **1982**, *47*, 3585.

(9) Problems were encountered in the alkylation step during a cursory examination of other forms of *N*-protection.

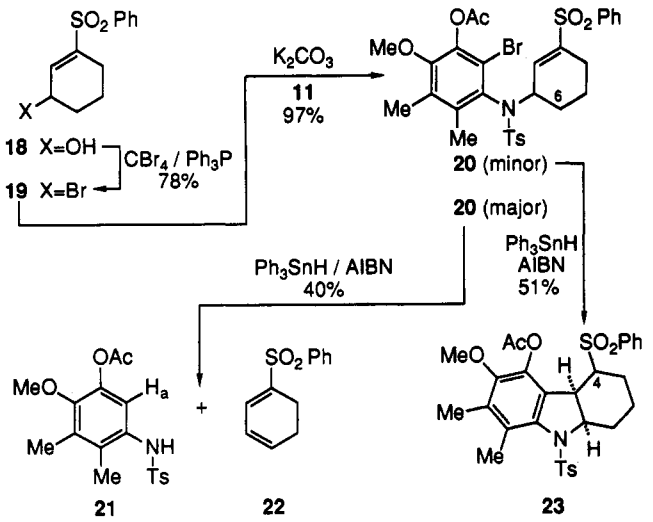
(10) Gardner, D.; Grove, J. F.; Ismay, D. *J. Chem. Soc.* **1954**, 1817.

(11) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 333.

(12) These isomers result from restricted rotation about at least one bond.

0022-3263/93/1958-2442$04.00/0

Scheme IV



and *O*-benzyl groups (**15** → **17**; 65% yield) and, finally, dehydrogenation with Pd/C gave carbazomycin B (**1**) in 71% yield. *O*-Methylation of **1** is known to form the related substance, carbazomycin A.[4c,d]

Because of the poor yield in the cyclization step with **14** we examined the sulfones **20** (Scheme IV) in the hope that the presence of an electron-deficient double bond would speed up cyclization (relative to other processes). The known alcohol **18**[14] was converted into the corresponding bromide **19**, and this was used to alkylate sulfonamide **11** (**19** → **20**). The conformational isomers corresponding to **20** were each obtained crystalline, and the structure of the major one was determined by X-ray analysis. On treatment with triphenyltin hydride, this material gave the two fragments **21** and **22**, and little, if any [^{1}H NMR (200 MHz)], of the desired cyclization product. Under the same conditions the minor isomer of **20** gave **23** in 51% yield, as a single substance whose stereochemistry at C-4 was not established; the cleavage products **21** and **22** could not be detected by TLC.

The unexpected fragmentation, **20** (major) to **21** and **22**, prompted us to do several labeling experiments. The isomer mixtures **14** and **20**, on treatment with triphenyltin deuteride in refluxing benzene (usual slow addition), gave **16** and **21** respectively, with no [^{1}H NMR (200 MHz)] incorporation of deuterium on the aromatic ring (see H_a in structures **16** and **21**). In the case of the experiment with **20**, the other product (**22**) also contained no deuterium [^{1}H NMR (200 MHz)]. These observations suggest that the fragmentation involves intramolecular hydrogen transfer from C(6) in **14** and **20**, but we did not think it worthwhile to support this possibility with further labeling experiments.[15]

In order to interpret the different behavior of the two isomers of **20**, it may have been helpful to define the structure of the minor isomer by X-ray analysis. Unfortunately, all the crystals we obtained were unsuitable for that purpose, and so we have been unable to make a comparison with the other X-ray structure. We did, however, carry out molecular modeling and force-field calculations[16] for the major and minor isomers of bromide **20**.

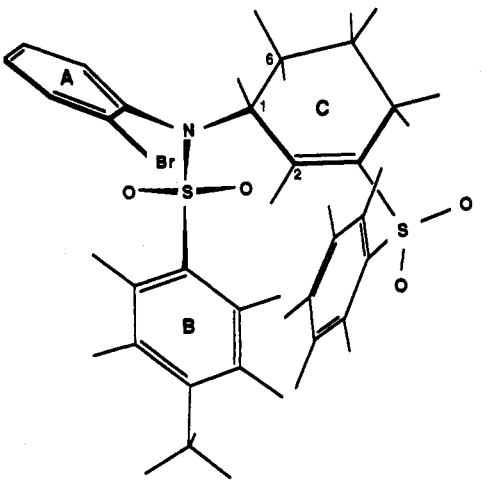


Figure 1.

The X-ray crystal data for the major isomer were taken as the starting point and subjected to energy minimization, the resulting structure (see Figure 1[17]) being very close to the X-ray structure, except for the orientation of the phenylsulfonyl group. Rings A and C were rotated 180° about their C–N bonds and the resulting structure was subjected to energy minimization to produce a second conformer (see Figure 2[17]) about 3 kcal/mol less stable

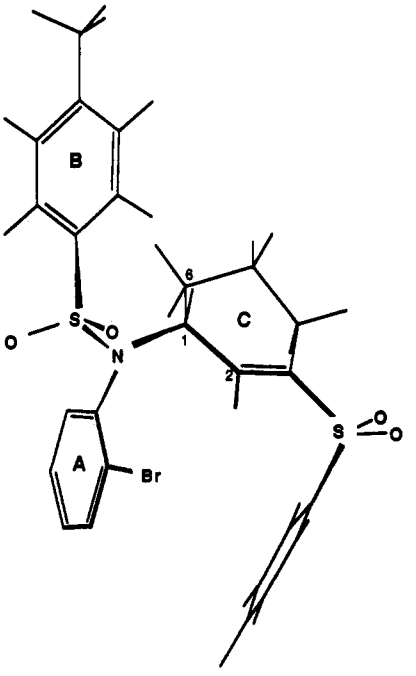


Figure 2.

than that of Figure 1. The latter was found to be the most stable of all the rotational isomers. Molecular dynamics calculations[16] showed no interconversion between the two isomers, and, in fact, they do not interconvert [^{1}H NMR (200 MHz)] when individual specimens [**20** (major) and

(13) Cyclization experiments with **12** or **13** gave less than 20% yield of the desired ring-closure product. Use of a higher boiling solvent (toluene or xylenes) with **12** did not raise the yield of cyclization product.

(14) Trost, B. M.; Seoane, P.; Mignani, S.; Acemoglu, M. *J. Am. Chem. Soc.* **1989**, *111*, 7487.

(15) For recent examples of intramolecular hydrogen abstraction, see: Denenmark, D.; Hoffmann, P.; Winkler, T.; Waldner, A.; De Mesmaeker, A. *Synlett* **1991**, 621.

(16) The Insight-II program of Biosym Inc. was used. The supplementary material gives details of the calculations and the original diagrams on which Figures 1 and 2 (see later) are based.

(17) The figure gives the essential features only.

20 (minor)] are heated overnight in benzene—thermal conditions that resemble those used for the radical cyclization. The compounds also do not fragment under these conditions.

We built CPK models of the derived radicals based on the conformations identified for the bromides, and the following observations were easily made:

In the case of the radical derived from the major isomer of **20** there is no serious impediment to rotation about N–C(1) (Figure 1) but rotation about the other bonds to N is strongly hindered; rotation about one N–C bond alone does not convert the major into the minor isomer. In no accessible conformation is the radical suitably oriented[18] to attack the carbon–carbon double bond of ring C; however, it can approach the C(6) (Figure 1) hydrogens, one of which, we suggest, is abstracted in the formation of **21** and **22**.

In the case of the radical derived from the minor isomer of **20** rotation about N–C(1) (Figure 2) appears to be much more restricted (than for the corresponding major isomer) and approach to the C(6) hydrogens is strongly hindered. However, the radical, without significant change in conformation from that of its parent bromide, is suitably placed to attack the carbon–carbon double bond of ring C.

The above analysis supports the view that the difference in behavior of the isomeric bromides **20** is due to three factors: (a) energy barriers are too high for interconversion; (b) in one isomer the radical cannot easily approach the ring C double bond but can approach the C(6) hydrogens; (c) in the other isomer the radical cannot approach the C(6) hydrogens but, evidently, can attack the double bond.

In summary, the use of radical cyclization for synthesis of carbazomycin B has illustrated some limitations of the methodology in a conformationally restricted system.

Experimental Section

General. We used the same general procedures as described previously.[19]

1,2,3,4,4a,9a-Hexahydro-9-[(4-methylphenyl)sulfonyl]carbazole (4). Triphenyltin hydride (0.25 mL, 0.979 mmol) in anhydrous benzene (10 mL) and AIBN (19.6 mg, 0.120 mmol) in benzene (10 mL) were added over 10 h (double syringe pump) to a refluxing solution of **3** (265.1 mg, 0.653 mmol) in the same solvent (40 mL). The solution was refluxed a further 6 h, cooled, and then stirred for several hours at room temperature with a saturated solution of aqueous KF. The aqueous phase was extracted with ether, and the combined organic extracts were washed with water and brine, dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel using 10:1 hexanes–EtOAc gave **4** (189.7 mg, 89%) as a white, homogeneous (TLC, silica, 10:1 hexanes–EtOAc) solid: mp 116 °C; FT-IR ($CHCl_3$ cast) 1166, 1352 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.0–2.25 (m, 3 H), 2.3–2.7 (m, 4 H), 2.95–3.10 (m, 2 H), 3.33 (s, 3 H), 3.84 (m, 1 H), 4.25 (dt, 1 H, J = 10, 6 Hz), 6.98–7.26 (m, 5 H), 7.54–7.64 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.67, 21.53, 22.44, 24.50, 29.16, 39.93, 13.61, 117.94, 123.07, 124.69, 126.73, 127.61, 129.60, 135.92, 136.80, 141.52, 143.57; exact mass, m/z calcd for $C_{19}H_{21}NO_2S$ 327.1293, found 327.1295. Anal. Calcd for $C_{19}H_{21}NO_2S$: C, 69.69; H, 6.46; N, 4.28; O, 9.77; S, 9.79. Found: C, 69.78; H, 6.48; N, 4.48; O, 9.40; S, 9.97.

***N*-[2-Bromo-4-methoxy-5,6-dimethyl-3-(phenylmethoxy)phenyl]-*N*-(2-cyclohexenyl)-4-methylbenzenesulfonamide (14).** A mixture of **13** (1.5408 g, 3.21 mmol) in CH_2Cl_2 (30 mL), aqueous NaOH (1.25 N, 30 mL), benzyl bromide (1.20 mL, 10.1 mmol), and tetrabutylammonium bromide (0.12 g, 0.37 mmol) was stirred vigorously for 16 h. The phases were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel using 10:1 hexanes–EtOAc gave **14** (1.7285 g, 94%) as a white solid composed of two isomers (TLC, silica, 10:1 hexanes–EtOAc): mp 143–144 °C; FT-IR ($CHCl_3$ cast) 1459, 1398, 1343, 1157, 1092, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.40–1.70 (m, 3 H), 1.80–2.05 (m, 3 H), 2.18, 2.21 (two s, 3 H), 2.25 (s, 1.14 H), 2.34 (s, 1.86 H), 2.42 (two s, 3 H), 3.87 (s, 3 H), 4.46 (m, 0.38 H), 4.81 (m, 0.62 H), 4.97 (two s, 2 H), 5.57 (m, 0.38 H), 5.83 (m, 1.62 H), 7.20–7.30 (m, 2 H), 7.30–7.40 (m, 3 H), 7.45–7.55 (m, 2 H), 7.67–7.80 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.13, 18.93, 19.01, 21.51, 21.60, 21.66, 24.40, 24.48, 28.28, 28.74, 58.89, 60.71, 74.75, 74.86, 120.23, 121.25, 127.82, 128.11, 128.16, 128.36, 128.45, 128.61, 128.64, 128.98, 129.11, 129.24, 130.24, 130.87, 131.10, 134.16, 136.93, 136.97, 138.36, 138.45, 139.56, 139.96, 142.91, 143.04, 147.57, 152.08, 152.18; exact mass, m/z calcd for $C_{29}H_{32}BrNO_4S$ 571.1215, found 571.1205. Anal. Calcd for $C_{29}H_{32}BrNO_4S$: C, 61.05; H, 5.65; N, 2.46; O, 11.22; S, 5.62. Found: C, 60.90; H, 5.85; N, 2.44; O, 10.91; S, 5.53.

1,2,3,4,4a,9a-Hexahydro-6-methoxy-7,8-dimethyl-9-[(4-methylphenyl)sulfonyl]-5-(phenylmethoxy)carbazole (15). Triphenyltin hydride (0.70 mL, 2.74 mmol) in anhydrous benzene (5 mL) and AIBN (157.3 mg, 0.960 mmol) in benzene (5 mL) were added over 10 h (double syringe pump) to a refluxing solution of **14** (985.9 mg, 1.730 mmol) in the same solvent (40 mL). The solution was refluxed a further 6 h, cooled, and evaporated. Flash chromatography of the residue over silica gel using 10:1 hexanes–EtOAc gave **15** (333.2 mg, 39%) as a white, homogeneous (TLC, silica, 10:1 hexanes–EtOAc) solid: mp 186 °C; FT-IR ($CHCl_3$ cast) 1452, 1352, 1137 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.94–1.44 (m, 5 H), 1.55 (m, 1 H), 1.99 (m, 1 H), 2.26 (s, 3 H), 2.30–2.50 (m, 1 H), 2.26 (s, 3 H), 2.40 (s, 3 H), 2.60 (m, 1 H), 3.82 (s, 3 H), 4.18 (dt, 1 H, J = 10, 6 Hz), 4.73 (s, 2 H), 7.15 (d, 2 H, J = 8 Hz), 7.34 (s, 5 H), 7.43 (d, 2 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.69, 17.38, 21.21, 21.54, 23.31, 24.54, 28.63, 40.01, 60.66, 64.64, 74.80, 127.49, 128.04, 128.09, 128.49, 128.68, 128.78, 129.34, 130.92, 136.10, 137.32, 137.68, 143.66, 147.17, 150.19; exact mass, m/z calcd for $C_{29}H_{33}NO_4S$ 491.2130, found 491.2135. Anal. Calcd for $C_{29}H_{33}NO_4S$: C, 70.85; H, 6.77; N, 2.85; S, 6.52. Found: C, 71.12; H, 6.76; N, 2.83; S, 6.30.

1,2,3,4,4a,9a-Hexahydro-5-hydroxy-6-methoxy-7,8-dimethylcarbazole (17). Sodium naphthalenide (0.50 M in THF, 2.5 mL, 1.25 mmol) was added to a stirred solution of **15** (78.3 mg, 0.159 mmol) in THF (8 mL). After being stirred for 2 min, the solution was quenched with saturated aqueous NH_4Cl (5 drops), diluted with H_2O, neutralized with 10% v/v HCl, and extracted with CH_2Cl_2. The organic extract was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel, using hexanes first (to elute naphthalene), and then 1:1 hexanes–EtOAc, gave **17** (25.5 mg, 65%) as an unstable, clear, homogeneous (TLC, silica, 10:1 hexanes–EtOAc) oil: FT-IR ($CHCl_3$ cast) 3370, 2930, 1460, 1450 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.36–1.96 (m, 8 H), 1.97 (s, 3 H), 2.15 (s, 3 H), 3.16 (s, 3 H), 3.25 (m, 1 H), 4.26 (broad s, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.43, 13.12, 21.29, 23.12, 27.14, 26.90, 39.55, 59.36, 61.19, 110.04, 117.06, 127.23, 139.02, 143.11, 146.34; exact mass, m/z calcd for $C_{15}H_{21}NO_2$ 247.1573, found 247.1574.

Carbazomycin B (1).[1a] A slow stream of dry argon was bubbled for 56 h through a hot (210 °C) mixture of **17** (25.5 mg, 0.1032 mmol) and 10% Pd/C (17.7 mg) in triglyme (7 mL). The mixture was cooled, filtered through silica gel, and evaporated at reduced pressure using a Kugelrohr distillation apparatus. Flash chromatography of the residue over silica gel using 10:1 hexanes–EtOAc gave **1** (17.8 mg, 71%) as an off-white, homogeneous (TLC, silica, 10:1 hexanes–EtOAc) solid: mp 148 °C [lit.[1a] mp 158.5–160 (*n*-hexane–EtOAc)]; FT-IR ($CHCl_3$ cast) 3425, 1454, 1411 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.34 (s, 3 H), 2.38 (s, 3 H), 3.81 (s, 3 H), 6.09 (s, 1 H), 7.17–7.25 (m, 1 H), 7.33–7.40 (m, 2 H), 7.76 (s, 1 H), 8.25 (d, 1 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.77, 13.18, 61.49, 109.30, 109.36, 109.99, 119.47, 122.65, 123.27, 124.74, 126.98, 136.76, 138.46, 139.26, 142.02; exact mass, m/z calcd for $C_{15}H_{15}NO_2$ 241.1102,

(18) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073.
(19) Clive, D. L. J.; Boivin, T. L. B.; Angoh, A. G. *J. Org. Chem.* **1987**, *52*, 4943.

found 241.1101. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.91; H, 6.27; N, 5.98.

***N*-(3-Acetoxy-2-bromo-4-methoxy-5,6-dimethylphenyl)-*N*-[3-(phenylsulfonyl)-2-cyclohexenyl]-4-methylbenzenesulfonamide (20).** A mixture of **11** (550.1 mg, 1.24 mmol), bromide **19** (451.1 mg, 1.50 mmol), and anhydrous K_2CO_3 (0.99 g, 7.2 mmol) in anhydrous acetone (15 mL) was refluxed under argon for 18 h. The solvent was evaporated, and the residue was partitioned between CH_2Cl_2 and water. The aqueous phase was extracted with CH_2Cl_2, and the combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel using 100:1 CH_2Cl–ether gave **20** (800.0 mg, 97%) as a white solid composed of two isomers (TLC, silica, 2:1 hexanes–EtOAc). The material was subjected four times to flash chromatography over silica gel using 100:1 CH_2Cl_2–ether in order to effect partial separation of the isomers. The less polar isomer was obtained pure (^{1}H NMR, 400 MHz): mp 208–208.5 °C (after crystallization from CH_2Cl_2–petroleum ether); FT-IR ($CHCl_3$ cast) 1774, 1152 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.49 (m, 1 H), 1.88 (m, 1 H), 1.98–2.15 (m, 3 H), 2.20 (s, 3 H), 2.25 (m, 1 H), 2.34 (s, 3 H), 2.37 (s, 3 H), 2.43 (s, 3 H), 3.78 (s, 3 H), 4.39 (m, 1 H), 7.32 (d, 2 H, J = 8 Hz), 7.46 (s, 1 H), 7.58 (t, 2 H, J = 8 Hz), 7.62 (d, 1 H, J = 8 Hz), 7.68 (d, 2 H, J = 8 Hz), 7.92 (d, 2 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 13.39, 19.21, 20.56, 21.42, 21.58, 22.53, 28.83, 61.02, 61.92, 118.42, 127.95, 129.25, 129.72, 129.88, 131.93, 133.42, 133.90, 137.55, 138.84, 138.87, 140.63, 140.84, 140.89, 143.65, 151.09, 167.83; exact mass, m/z calcd for $C_{30}H_{32}BrNO_7S_2$ 663.0783, found 663.0784.

The more polar isomer was also obtained pure (^{1}H NMR, 300 MHz): mp 189–191 °C (after crystallization from CH_2Cl_2–petroleum ether); FT-IR ($CHCl_3$ cast) 1774, 1151 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24 (m, 1 H), 1.56 (m, 1 H), 1.83 (m, 3 H), 2.19 (s, 3 H), 2.22 (m, 1 H), 2.28 (s, 3 H), 2.33 (s, 3 H), 2.47 (s, 3 H), 3.77 (s, 3 H), 4.98 (m, 1 H), 7.31 (m, 3 H), 7.48 (m, 2 H), 7.58 (m, 1 H), 7.76 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.39, 19.13, 20.59, 21.36, 21.65, 22.32, 26.60, 58.37, 61.02, 119.52, 128.11, 129.13, 129.70, 131.60, 132.12, 133.30, 138.40, 138.76, 138.93, 140.42, 140.71, 141.03, 143.86, 151.30, 167.67; exact mass, m/z calcd for $C_{30}H_{32}BrNO_7S_2$ 663.0783, found 663.0779. Analysis was performed on the isomer mixture. Anal. Calcd for $C_{30}H_{32}BrNO_7S_2$: C, 54.38; H, 4.87; N. 2.11; O, 16.90; S, 9.68. Found: C, 54.25; H, 4.89; N, 1.95; O, 16.83; S, 9.74.

Fragmentation of *N*-(3-Acetoxy-2-bromo-4-methoxy-5,6-dimethylphenyl)-*N*-[3-(phenylsulfonyl)-2-cyclohexenyl]-4-methylbenzenesulfonamide (20) (major isomer). Triphenyltin hydride (0.15 mL, 0.59 mmol) in anhydrous benzene (5 mL) and AIBN (30.5 mg, 0.189 mmol) in benzene (5 mL) were each added over 10 h (double syringe pump) to a refluxing solution of **20** (major isomer) (252.2 mg, 0.381 mmol) in the same solvent (50 mL). The mixture was refluxed for a further 10 h, cooled, and evaporated. Flash chromatography of the residue over silica gel using 4:1 hexanes–EtOAc (to elute **22**), and then 2:1 hexanes–EtOAc (to elute **21**), gave **22** (34.4 mg, 41%) and **21** (55.6 mg, 40%), each as a white, homogeneous (TLC, silica, 2:1 hexanes–EtOAc) solid. Compound **22** had mp 90–91 °C [lit.[20] mp 92–93 °C]; FT-IR ($CHCl_3$ cast) 1303, 1149 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.31 (m, 4 H), 6.08, 6.11 (two s, 2 H), 7.04 (m, 1 H), 7.47–7.65 (m, 3 H); 7.88 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.13, 22.92, 122.76, 127.89, 129.18, 131.76, 133.22, 133.33, 136.34, 139.78; exact mass, m/z calcd for $C_{12}H_{12}O_2S$ 220.0558, found 220.0549. Compound **21** had: mp 139–140 °C; FT-IR ($CHCl_3$ cast) 3275, 1768, 1162 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.90 (s, 3 H), 2.13 (s, 3 H), 2.29 (s, 3 H), 2.40 (s, 3 H), 3.70 (s, 3 H), 6.56 (s, 1 H), 6.85 (s, 1 H), 7.22 (d, 2 H, J = 8 Hz), 7.40 (d, 2 H, J = 8 Hz); exact mass, m/z calcd for $C_{18}H_{21}NO_5S$ 363.1141, found 363.1148. An authentic sample, made by a different route, had: ^{13}C NMR ($CDCl_3$, 75.5 Hz) δ 13.06, 14.24, 20.73, 21.55, 60.84, 118.57, 127.29, 129.61, 129.76, 131.54, 132.07, 136.61, 141.49, 143.73, 148.70, 169.00.

5-Acetoxy-1,2,3,4,4a,9a-hexahydro-6-methoxy-7,8-dimethyl-9-[(4-methylphenyl)sulfonyl]-4-(phenylsulfonyl)carbazole (23). Triphenyltin hydride (0.028 mL, 0.11 mmol) in anhydrous benzene (2.5 mL) and AIBN (7.2 mg, 0.044 mmol) in benzene (2.55 mL) were each added over 10 h (double syringe pump) to a refluxing solution of crude **20** (minor isomer) (45.5 mg, 0.0687 mmol) in the same solvent (12 mL). The mixture was refluxed a further 10 h, cooled, and evaporated. Flash chromatography of the residue over silica gel using 2:1 hexanes–EtOAc gave crude **23** (25.7 mg) as an off-white solid, which was recrystallized from CH_2Cl_2–hexanes to afford **23** (20.4 mg, 51%) as a single isomer. The material was a colorless, homogeneous (TLC, 2:1 hexanes–EtOAc) crystalline solid: mp 225–227 °C; FT-IR ($CHCl_3$ cast) 1773, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.41 (m, 2 H), 1.66–1.88 (m, 1 H), 1.93 (s, 3 H), 2.03–2.18 (m, 3 H), 2.22 (s, 3 H), 2.40 (s, 3 H), 2.46 (s, 3 H), 3.24 (m, 1 H), 3.64 (s, 3 H), 3.80 (m, 1 H), 4.72 (dt, 1 H, J = 12, 6 Hz), 7.29 (d, 2 H, J = 8 Hz), 7.53 (d, 4 H, J = 8 Hz), 7.64 (d, 3 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.04, 17.69, 18.26, 20.07, 21.27, 21.83, 28.28, 38.50, 59.88, 60.92, 62.32, 125.54, 127.68, 128.26, 129.36, 130.01, 131.71, 132.21, 133.77, 135.71, 137.33, 138.58, 138.70, 144.15, 148.92, 167.39; exact mass, m/z calcd for $C_{30}H_{33}NO_7S_2$ 583.1699, found 583.1691. Anal. Calcd for $C_{30}H_{33}NO_7S_2$: C, 61.73; H, 5.70; N, 2.40; S, 10.98. Found: C, 61.46; H, 5.66; N, 2.41; S, 10.91.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada and the University of Alberta for financial support, NSERC for a postgraduate fellowship (N.E.), and Drs. B. D. Santarsiero and R. McDonald for determining the X-ray structure.

Supplementary Material Available: X-ray crystallographic data for **20** (major isomer); experimental procedures for **3**, **5**, **7–13**, and **19**, and details of the calculations (27 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(20) Truce, W. E.; Goralski, C. T.; Christensen, L. W.; Barry, R. H. *J. Org. Chem.* **1970**, *35*, 4217. Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208.