757 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.16 (3 H, s), 2.34 (3 H, s); HRMS m/e 267.8559 [M$^+$], calcd for $C_6H_6Br_2S$ 267.8558.

A mixture of 110 mg (1.0 mmol) of 2,4-dimethylthiophene (4) and 500 mg (3.1 mmol) of Br_2 was stirred for 3 min at rt. The organic product was extracted with CH_2Cl_2, and the extract was washed with brine and dried ($MgSO_4$). Evaporation of the solvent afforded 260 mg (96%) of 3.

2,4-Bis(mercaptomethyl)-3,5-dibromothiophene (5). A solution of 13.6 g (40 mmol) of 2 and 7.6 g (100 mmol) of thiourea in 100 mL of DMSO was stirred at room temperature for 13 h under N_2. The mixture was poured into 130 mL of 10% aq NaOH and stirred for 1 h in an ice/water bath. The mixture was acidified with 10% aq HCl, and the organic layer was extracted with CH_2Cl_2. The extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated. Recrystallization of the residue from hexane afforded 7.3 g (55%) of 5: colorless prisms (hexane); mp 58.0–63.0 °C; IR (KBr) ν 2534, 1538, 1416, 1349, 1243, 1029, 954 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.95 (1 H, t, J = 8 Hz), 2.05 (1 H, t, J = 8 Hz), 2.64 (2 H, d, J = 8 Hz), 2.78 (2 H, d, J = 8 Hz); HRMS m/e 331.7994 [M$^+$], calcd for $C_6H_6Br_2S_3$ 331.7999.

14,17-Dibromo-2,11-dithia[3]metacyclo[3](2,4)thiophenophane (7). To a refluxing solution of 4.3 g (80 mmol) of KOH and 380 mg (10 mmol) of $NaBH_4$ in 3 L of EtOH was added dropwise a solution of 6.7 g (20 mmol) of 5 and 5.3 g (20 mmol) of 1,3-bis(bromomethyl)benzene (6) in 200 mL of EtOH:PhH = 1:1 over 23 h. The solvent was removed by distillation, and the residue was poured into ice/water. The organic layer was extracted with CH_2Cl_2, and the extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated, and the residue was subjected to column chromatography (silica gel, eluent: hexane:CH_2Cl_2 = 2:1). Recrystallization of the eluate afforded 4.8 g (55%) of 7: colorless prisms (EtOH/PhH); mp 137.0–138.0 °C; IR (KBr) ν 2902, 1542, 1443, 1409, 1342, 1212, 1025, 931, 909, 886, 771, 709 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.62 (1 H, d, J = 14 Hz), 3.65 (1 H, d, J = 15 Hz), 3.74 (1 H, d, J = 15 Hz), 3.78 (1 H, d, J = 17 Hz), 3.89 (1 H, d, J = 15 Hz), 3.92 (1 H, d, J = 14 Hz), 3.93 (1 H, d, J = 17 Hz), 4.58 (1 H, d, J = 15 Hz), 7.02–7.17 (4 H, m); MS m/e 434, 436, 438 [M$^+$]. Anal. Calcd for $C_{14}H_{12}Br_2S_3$: C, 38.54; H, 2.77. Found: C, 38.93; H, 2.89.

Hydrodebromination of 7. 1. Via Lithiation. A solution of 870 mg (2.0 mmol) of 7 in 20 mL of dry THF at −60 °C was added to 4.0 mL (6.4 mmol) of 1.6 M BuLi in hexane, and the mixture was stirred for 40 min at this temperature. The mixture was treated with 5 mL of 10% aq HCl, stirred for 1 h at room temperature, and extracted with Et_2O. The extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated, and the residue was subjected to column chromatography (silica gel eluent: hexane:CH_2Cl_2 = 3:1). Recrystallization of the first eluate afforded 120 mg (17%) of 9 and that of the second eluate afforded 180 mg (33%) of 8.

2,11-Dithia[3]metacyclo[3](2,4)thiophenophane (8): colorless prisms (hexane) mp 133.0–135.0 °C; IR (KBr) ν 2900, 1489, 1442, 1408, 1249, 1116, 1082, 803, 758, 722, 707 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.70 (2 H, s), 3.80 (2 H, s), 3.81 (2 H, s), 4.01 (2 H, s), 6.56 (1 H, m), 6.74 (1 H, s), 6.79 (1 H, s), 6.87 (1 H, dt, J = 6, 2 Hz), 7.04–7.07 (2 H, m); MS m/e 278 [M$^+$]. Anal. Calcd for $C_{14}H_{14}S_3$: C, 60.39; H, 5.07. Found: C, 60.72; H, 5.34.

17-Bromo-2,11-dithia[3]metacyclo[3]-(2,4)-thiophenophane (9): colorless prisms (hexane); mp 141.0–143.0 °C; IR (KBr) ν 2900, 1528, 1488, 1442, 1410, 1364, 1219, 1084, 992, 892, 769, 720; ^{1}H NMR ($CDCl_3$) δ 3.71 (1 H, d, J = 15 Hz), 3.74 (1 H, d, J = 15 Hz), 3.75 (1 H, d, J = 15 Hz), 3.84 (1 H, d, J = 15 Hz), 3.85 (1 H, d, J = 15 Hz), 3.86 (1 H, d, J = 15 Hz), 3.90 (1 H, d, J = 15 Hz), 4.57 (1 H, dd, J = 15, 2 Hz), 6.68 (1 H, s), 6.91–6.97 (2 H, m), 7.03–7.13 (2 H, m); MS m/e 356, 358 [M$^+$]. Anal. Calcd for $C_{14}H_{13}BrS_3$: C, 47.05; H, 3.67. Found: C, 47.37; H, 3.97.

2. Treatment with Zn. A mixture of 2.0 g (4.5 mmol) of 7, 860 mg (13.5 mmol) of Zn, and 1.08 g (18 mmol) of NaOH in 9 mL of water and 45 mL of dioxane was refluxed for 24 h. The mixture was acidified with 10% aq HCl and filtered. The filtrate was extracted with CH_2Cl_2, and the extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated. Recrystallization of the residue afforded 1.14 g (69%) of 9.

2,11-Dithia[3]metacyclo[3](2,4)thiophenophane *S,S,S',S'*-*S'*-Tetraoxide (10). To a solution of 140 mg (0.50 mmol) of 8 in 15 mL of CH_2Cl_2 was added portionwise 540 mg (2.5 mmol) of 80% *m*-CPBA, and the mixture was stirred at room temperature for 13 h. To the mixture was added 30 mL of MeOH, and the white precipitate was filtered and washed with MeOH and hot $CHCl_3$ to afford 130 mg (76%) of 10: colorless prisms; mp 320.0 °C dec; IR (KBr) ν 2914, 1406, 1310, 1269, 1168, 1110, 525, 463 cm^{-1}; a ^{1}H NMR spectrum was not recorded because 10 is insoluble in any solvent; MS m/e 342 [M$^+$]. Anal. Calcd for $C_{14}H_{14}O_4S_3$: C, 49.10; H, 4.12. Found: C, 48.75; H, 4.26.

17-Bromo-2,11-dithia[3]metacyclo[3](2,4)thiophenophane *S,S,S',S'*-tetraoxide (11) was obtained in a similar manner to that described above for 10. 11: colorless prisms mp 295.0 °C dec; IR (KBr) ν 2974, 2914, 1404, 1317, 1274, 1168, 1115, 861, 460 cm^{-1}; a ^{1}H NMR spectrum was not recorded because 11 is insoluble in any solvent; MS m/e 420, 422 [M$^+$]. Anal. Calcd for $C_{14}H_{13}BrO_4S_3$: C, 39.91; H, 3.11. Found: C, 40.37; H, 3.25.

Pyrolysis of 10. Pyrolysis of 120 mg (0.35 mmol) of 10 was performed in similar manner to that described in the literature.[7] The products were extracted with CH_2Cl_2, and the insoluble ash was filtered off. The solvent was evaporated, and recyrstallization of the residue afforded 53 mg (71%) of **[2]metacyclo[2](2,4)-thiophenophane (12)**: colorless prisms (60% MeOH); mp 92.0–93.0 °C; IR (KBr) ν 2938, 2846, 1439, 1238, 1169, 791, 716 670 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.23–2.49 (4 H, m), 2.95–3.15 (4 H, m), 4.08 (1 H, d, J = 1 Hz), 4.63 (1 H, t, J = 2 Hz), 6.99 (1 H, s), 7.02 (2 H, t, J = 7 Hz), 7.20 (1 H, t, J = 7 Hz); MS m/e 214 [M$^+$]. Anal. Calcd for $C_{14}H_{14}S$: C, 78.46; H, 6.58. Found: C, 78.22; H, 6.52.

Pyrolysis of 420 mg (1.0 mmol) of 11 was carried out in a similar manner to that described above, and the extract was subjected to column chromatography (*silica gel, eluent: hexane*). Recrystallization of first eluate afforded 40 mg (19%) of 13, and that of second eluate afforded 50 mg (24%) of 14.

8,9-Dihydrophenaleno[1,9-*bc*]thiophene (13): colorless plates (60% MeOH); mp 120.0–123.0 °C; IR (KBr) ν 2930, 1396, 819, 762, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.21–3.27 (2 H, m), 3.31–3.38 (2 H, m), 7.15 (1 H, s), 7.38–7.49 (2 H, m), 7.72 (1 H, d, J = 9 Hz), 7.76–7.79 (1 H, m), 7.85 (1 H, d, J = 9 Hz); MS m/e 210 [M$^+$]. Anal. Calcd for $C_{14}H_{10}S$: C, 79.96; H, 4.79. Found: C, 80.21; H, 5.02.

3,4,8,9-Tetrahydrophenaleno[1,9-*bc*]thiophene (14): colorless plates (60% MeOH); mp 134.0–140.0 °C IR (KBr) ν 2930, 2890, 1601, 1560, 1494, 1428, 1110, 794, 769, 735, 686 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.84–2.95 (4 H, m), 2.94–3.08 (4 H, m), 6.74 (1 H, s), 7.06–7.07 (3 H, m); MS m/e 212 [M$^+$]. Anal. Calcd for $C_{14}H_{12}S$: C, 79.20; H, 5.70. Found: C, 78.98; H, 5.74.

Registry No. 1, 3141-27-3; 2, 7311-54-8; 3, 63862-00-0; 4, 638-00-6; 5, 137434-94-7; 6, 626-15-3; 7, 137434-95-8; 8, 137434-96-9; 9, 137434-97-0; 10, 137434-98-1; 11, 137434-99-2; 12, 137435-00-8; 13, 137435-01-9; 14, 137435-02-0; chloromethyl methyl ether, 107-30-2; thiourea, 62-56-6.

Cyanoacylation of 1-Substituted Isoquinolines and 3,4-Dihydroisoquinolines

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Reissert compounds such as 2-acyl-1-cyano-1,2-dihydroisoquinolines, their reactions, and, to a lesser extent, dihydro-Reissert compounds such as 2-acyl-1-cyano-1,2,3,4-tetrahydroisoquinolines have been well documented.[1] Reissert compounds are typically formed by treating an isoquinoline or 3,4-dihydroisoquinoline with an acyl halide in the presence of potassium cyanide in biphasic aqueous dichloromethane.[2] It was shown that

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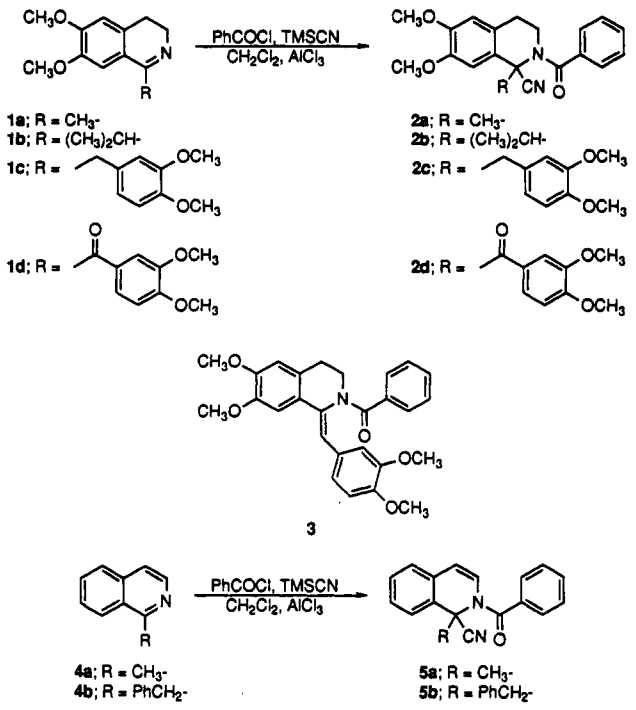
0022-3263/92/1957-0748$03.00/0

Scheme I



1-alkylisoquinolines do not react under these conditions.[3] The use of trimethylsilyl cyanide (TMSCN) as the cyanide source in Reissert reactions has more recently been established.[4] Reissert compounds undergo proton abstraction to give the anions which can be quenched with alkyl halides to give the alkylated derivatives **2** or **5**. Their utility in synthesis of isoquinoline alkaloids has also been shown.[5] The reactions of dihydro-Reissert compounds have been utilized in the synthesis of the 1,1-disubstituted spirobenzylisoquinoline alkaloids, but without regard to control of the stereochemistry at C1.[6] It has also been demonstrated that the nitrile functionality of the alkylated compound **2** can be hydrolyzed to the acid[6] to give the corresponding amino acids, thus demonstrating the conversion of the nitrile functionality into other useful functionalities. It is our belief that the stereochemistry at C1 can be controlled in the alkylation by the use of a chiral acyl auxiliary, and we are currently exploring this avenue. This potentially can be a simple way to build 1,1-disubstituted isoquinolines with control of the stereochemistry at C1.

As an alternative to the alkylations of the anions of Reissert compounds, we also are seeking to utilize direct cyanoacylation of 1-substituted isoquinolines and 3,4-dihydroisoquinolines with the ultimate aim of achieving stereoselective control at C1 by use of chiral acyl moieties. We therefore examined model reactions of some simple 1-substituted isoquinolines and 1-substituted 3,4-dihydroisoquinolines using benzoyl chloride as the acylating agent and TMSCN as the cyanide source in CH_2Cl_2. *Here we report for the first time the cyanoacylation of 1-substituted isoquinolines and 1-substituted 3,4-dihydroisoquinolines.* The cyanoacylation reaction gives the desired products in good to quantitative yields.

In our first experiment, the single-phase cyanoacylation reaction of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline (**1a**) gave 2-benzoyl-1-cyano-1-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**2a**) in 94 % yield (Scheme I). In order to test whether cyanoacylation would occur when there is a larger substituent at C1, cyanoacylation of 6,7-dimethoxy-1-(methylethyl)-3,4-dihydroisoquinoline (**1b**) was carried out; it gave 2-benzoyl-1-cyano-1-(methylethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**2b**) in 63 % yield. *These are the first reports of cyanoacylation of 1-alkyl-3,4-dihydroisoquinolines*, to our knowledge.

This led us to examine the reaction with other substituents at C1. The 1-veratryl analogue **1c** was subjected to the cyanoacylation conditions in an effort to produce **2c**. However, formation of **2c** apparently was followed by elimination of hydrogen cyanide; enamide **3** was isolated. To circumvent this problem, the enamine **1c** was oxidized in air in a solution of ethanol to give the 1-acyl-3,4-dihydroisoquinoline **1d**.[7] When **1d** was subjected to the cyanoacylation conditions, product **2d** formed in quantitative yield. *This is the first report of the cyanoacylation of a 1-acylisoquinoline.*

We then explored the utility of this reaction with fully aromatic isoquinolines. The single-phase cyanoacylation reaction on 1-methylisoquinoline (**4a**) gave 2-benzoyl-1-cyano-1-methyl-1,2-dihydroisoquinoline (**5a**) in 56% yield. The cyanoacylation reaction on 1-benzylisoquinoline (**4b**) gave the corresponding analogue **5b** in 85% yield.

To our knowledge, these are the first reported cyanoacylations of 1-substituted isoquinolines and 3,4-dihydroisoquinolines. We anticipate that this methodology may be useful in alkaloid syntheses, particularly in the synthesis of 1,1-disubstituted 1,2,3,4-tetrahydroisoquinolines. Presently, efforts are underway to control the stereochemistry of such cyanoacylations.

Experimental Section

All melting points were taken on an Haake Buchler Digital Melting Point Apparatus and are uncorrected. Unless otherwise noted, all IR spectra were obtained with KBr pellets on a Perkin-Elmer 1600 series FT-IR. ^1H NMR and ^{13}C NMR were obtained on a Bruker WP-270 MHz instrument using chloroform-*d* as the solvent. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, GA. All reactions involving TMSCN were conducted in an efficient fume hood.

Preparation of Starting Materials. Compounds **1a** and **1b** were made using 3,4-dimethoxyphenethylamine and acetic acid (**1a**) and isobutyric acid (**1b**), respectively, using a procedure reported[8] for the synthesis of 1, R = H.

Cyanoacylation of 1-Substituted Isoquinolines and 1-Substituted 3,4-Dihydroisoquinolines: General Procedures. Method A. To a stirred solution of 0.50 g of the substituted isoquinoline, 1.1 equiv of TMSCN, and 0.10 equiv of anhydrous aluminum chloride in dichloromethane (20 mL) was added 1.1 equiv of benzoyl chloride. After 3–5 days of stirring at room temperature, 1 mL of water was added and stirring was continued for an additional day. The organic phase was washed with three portions each of water, 10% HCl, water, 10% NaOH, and water and then once with brine. The organic phase was dried over anhydrous sodium sulfate and evaporated to give the crude product.

Method B. The procedure was the same as method A except 1.5 equiv of TMSCN and 2.0 equiv of benzoyl chloride were used. All other ratios remained the same.

2-Benzoyl-1-cyano-6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline (2a). This was made by cyanoacylation

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method A from **1a** in 94% yield: mp 205.2–207.1 °C (lit.[9] mp 205–206 °C); IR 2233, 1631 cm^{-1}; ^1H NMR δ 2.11 (s, 3 H), 2.88 (m, 2 H), 3.61 (m, 2 H), 3.88 (s, 3 H), 3.93 (s, 3 H), 6.61 (s, 1 H), 7.08 (s, 1 H), 7.50 (m, 5 H); ^{13}C NMR δ 27.86, 29.28, 44.73, 54.50, 56.06, 56.29, 110.20, 111.23, 120.52, 126.06, 127.39, 128.73, 130.76, 135.69, 148.88, 149.27, 172.10. A sample made by alkylation of the anion of 2-benzoyl-1-cyano-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline was essentially identical as reported.[9]

2-Benzoyl-1-cyano-6,7-dimethoxy-1-(methylethyl)-1,2,3,4-tetrahydroisoquinoline (2b). This compound was produced by cyanoacylation method B from **1b** in 63% yield: mp 181.1–182.3 °C (EtOH); IR 2232, 1655 cm^{-1}; ^1H NMR δ 0.70 (d, 3 H), 1.19 (d, 3 H), 2.60 (dt, 1 H), 2.95 (dt, 1 H), 3.24 (dt, 1 H), 3.38 (m, 1 H), 3.88 (s, 3 H), 3.92 (s, 3 H), 4.00 (dt, 1 H), 6.63 (s, 1 H), 7.10 (s, 1 H), 7.47 (m, 5 H); ^{13}C NMR δ 16.33, 19.04, 29.59, 35.10, 45.89, 55.99, 56.18, 62.84, 111.15, 112.13, 119.34, 122.42, 126.95, 128.37, 128.75, 130.30, 136.57, 147.42, 149.07, 172.19. A sample was also prepared by alkylation of 2-benzoyl-1-cyano-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline[12] using a reported method;[10] its mp and spectral data were identical to the compound prepared by cyanoacylation. Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.51; H, 6.64. Found: C, 72.39; H, 6.64.

Attempted Cyanoacylation of 6,7-Dimethoxy-1-(3′,4′-dimethoxybenzyl)-3,4-dihydroisoquinoline. The reaction (method B) of **1c** gave a quantitative yield of the elimination product **3** as white needle crystals from ethyl acetate: mp 222.5–223.3 °C; IR 3005, 2934, 2912, 2885, 2883, 1640 cm^{-1}; ^1H NMR δ 2.86 (m, 1 H), 3.31 (m, 2 H), 3.76 (s, 3 H), 3.86 (s, 3 H), 3.91 (s, 3 H), 3.94 (s, 3 H), 5.12 (m, 1 H), 6.35 (d, 2 H), 6.56 (d, 1 H), 6.70 (m, 2 H), 6.86 (d, 2 H), 7.01 (m, 3 H), 7.17 (m, 1 H); ^{13}C NMR δ 28.85, 42.21, 55.68, 55.83, 56.30, 106.72, 111.65, 112.17, 118.26, 121.07, 125.69, 126.62, 127.17, 127.61, 128.34, 129.12, 134.99, 135.85, 148.18, 148.32, 149.83, 150.06, 169.20. Anal. Calcd for $C_{27}H_{27}NO_5$: C, 72.79; H, 6.11; N, 3.14. Found: C, 73.07; H, 6.22; N, 3.20.

2-Benzoyl-1-cyano-6,7-dimethoxy-1-(3′,4′-dimethoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline (2d). This new compound was prepared from **1d** by cyanoacylation method B in quantitative yield: mp 219.2–220.7 °C (toluene); IR 2234, 1683, 1646 cm^{-1}; ^1H NMR δ 3.00 (d, 1 H), 3.56 (m, 2 H), 3.79 (s, 3 H), 3.81 (s, 6 H), 3.90 (s, 3 H), 4.27 (dt, 1 H), 6.76 (d, 1 H), 6.83 (s, 1 H), 6.97 (s, 1 H), 7.42 (m, 7 H); ^{13}C NMR δ 28.32, 45.04, 55.83, 55.98, 109.42, 109.75, 112.09, 117.55, 119.67, 122.16, 125.76, 126.30, 127.16, 128.02, 128.65, 131.15, 133.49, 148.65, 149.04, 150.29, 152.95, 172.33, 188.19. Anal. Calcd for $C_{28}H_{26}N_2O_6$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.94; H, 5.43; N, 5.70.

1-Methylisoquinoline (4a). Compound **5a**[11] (1.25 g, 4.56 mmol) was refluxed for 6 h with potassium hydroxide (0.54 g, 9.59 mmol) in 95% ethanol (30 mL) and water (4 mL). To the cooled amber solution was added 15 mL of water. The solution was extracted with dichloromethane, and the organic phase was washed with water and then brine. The organic phase was dried over anhydrous sodium sulfate and then evaporated to give 0.65 g of a yellow oil: quantitative yield; IR (neat) 3051, 2993, 2967, 2920, 2863 cm^{-1}; ^1H NMR δ 2.95 (s, 3 H), 7.50 (d, 1 H), 7.57 (t, 1 H), 7.66 (t, 1 H), 7.80 (d, 1 H), 8.11 (d, 1 H), 8.40 (d, 1 H); ^{13}C NMR δ 22.00, 118.96, 125.29, 126.70, 126.86, 127.25, 129.59, 141.47.

2-Benzoyl-1-cyano-1-methyl-1,2-dihydroisoquinoline (5a). This compound was made by cyanoacylation (method A) of **4a** and purified by flash chromatography and subsequent recrystallization from ethanol in 56% yield: mp 123.6–125.2 °C (lit.[11] mp 119–121 °C); IR 2237, 1662 cm^{-1}; ^1H NMR δ 2.00 (s, 3 H), 5.77 (d, 1 H), 6.46 (d, 1 H), 7.10 (m, 1 H), 7.55 (m, 8 H); ^{13}C NMR δ 26.52, 57.00, 106.62, 118.72, 125.19, 125.91, 128.34, 128.58, 129.27, 129.43, 131.08, 131.93, 133.26, 169.35. A sample made by alkylation[10] of 2-benzoyl-1-cyano-1,2-dihydroisoquinoline[2] was identical.

1-Benzylisoquinoline (4b). This compound was made from **5b**[10] by the method given for **4a** as a yellow oil in 91% yield: IR (neat) 3084, 3053, 3027 cm^{-1}; ^1H NMR δ 4.69 (s, 2 H), 7.26 (m, 5 H), 7.55 (m, 3 H), 7.81 (d, 1 H), 8.15 (d, 1 H), 8.51 (d, 1 H); ^{13}C NMR δ 42.00, 119.67, 125.76, 126.20, 127.09, 127.32, 128.43, 128.56, 129.75, 136.62, 139.44, 142.01, 160.14.

2-Benzoyl-1-cyano-1-benzyl-1,2-dihydroisoquinoline (5b). Prepared by cyanoacylation method B from **4b**, the yield of **5b** was 85%: mp 133.6–135.0 °C (lit.[10] mp 123.5–125.0 °C); IR 2235, 1667 cm^{-1}; ^1H NMR δ 3.54 (d, J = 13 Hz, 1 H), 3.74 (d, J = 13 Hz, 1 H), 5.54 (d, J = 8 Hz, 1 H), 6.35 (d, J = 8 Hz, 1 H), 6.81 (d, 2 H), 7.04 (d, 1 H), 7.01 (m, 1 H), 7.21 (m, 5 H), 7.51 (m, 3 H), 7.61 (m, 2 H); ^{13}C NMR δ 43.64, 61.45, 106.54, 117.75, 124.82, 126.54, 127.54, 127.79, 127.95, 128.73, 129.20, 129.50, 130.99, 131.85, 133.18, 133.49, 169.51. A sample made in 56% yield by alkylation of 2-benzoyl-1-cyano-1,2-dihydroisoquinoline[2] according to the literature[10] was identical.

Registry No. **1a**, 4721-98-6; **1b**, 58735-47-0; **1c**, 6957-27-3; **1d**, 20345-69-1; **2a**, 73154-69-5; **2b**, 137465-61-3; **2d**, 137465-62-4; **3**, 137465-63-5; **4a**, 1721-93-3; **4b**, 6907-59-1; **5a**, 16576-32-2; **5b**, 16576-35-5; TMSCN, 7677-24-9; PhCOCl, 98-88-4; 2-benzoyl-1-cyano-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline, 10174-83-1; 2-benzoyl-1-cyano-1,2-dihydroisoquinoline, 844-25-7.

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One-Step Synthesis of Substituted 6,8-Dioxabicyclo[3.2.1]octanes: Easy Preparation of Racemic Frontalin, Brevicomins, and Related Systems

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Substituted 6,8-dioxabicyclo[3.2.1]octanes are important beetle aggregation pheromones,[1] and their biological activity in racemic or enantiomeric form is pertinent to the protection of ecologically important coniferous forests.[2] In general, the activity of both enantiomers is different; nevertheless, the racemic mixtures are sufficiently potent for their practical application.[3] From this family of compounds, frontalin[4] and brevicomins[5] are the best known, and numerous syntheses for both and related molecules have been reported.[6] However, in general, their preparation takes place through a multistep process and the procedures are rarely of general use. On the other hand, we have recently described the preparation and reactivity[7] of masked lithium bishomoenolates of the type **1**, which are easily prepared from the corresponding chlorinated precursors by stoichiometric[7] or catalytic[8] lithiation at low temperature. In this paper, we report the one-step preparation of the bicyclic skeleton of the frontalin type by direct reaction of intermediates **1** with protected 2-hydroxy carbonyl compounds.

The reaction of the lithiated ketal **1a**[7] (prepared by lithiation of 2-(3-chloropropyl)-1,3-dioxolane with lithium

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