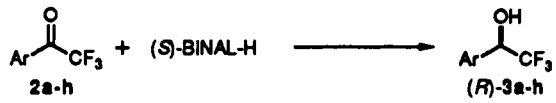
Table I. Enantioselective Reduction of Aryl Trifluoromethyl Ketones with (*S*)-BINAL-H



2a-h (*R*)-3a-h

entry	Ar	equiv of (*S*)-BINAL-H[a]	temp (°C)	time (h)	yield[b] (%)	ee[c,d] (%)
1	a: 9-anthryl	2.6	-60	72	51	93
2		2.6	-20	22	90	98
3		2.6	0	14	100	92
4		2.6	25	1	93	84
5		2.1[e]	-20	24	89	91[f]
6		2.1	25	3	99	84
7		1.6	25	3	82	75
8		1.2	25	20	97	56
9	b: 2-methyl-1-naphthyl	2.5	-60	24	85	93
10		2.5	0	3	100	85
11	c: 1-naphthyl	2.4	-60	24	93	70
12		2.3	0	3	97	65
13	d: 2,4,6-trimethylphenyl	2.3	-60	24	69	97[g]
14		2.2	0	24	94	87[g]
15	e: 2-methylphenyl	2.2	-60	24	81	74[g]
16		2.2	0	22	91	62[g]
17	f: phenyl	2.2	-60	4	97	27
18		2.2	0	4	98	23
19	g: 4-methoxyphenyl	2.0	-60	3	99	6[h]
20		2.0	0	3	98	1[h]
21	h: 4-fluorophenyl	2.1	-60	3	87	9[h,i]
22		2.2	0	3	94	14[h,i]

[a] Unless otherwise stated, 1.0 mmol of (*S*)-BINAL-H was used in each case. [b] Isolated yields. In each case, the yield based on recovered starting material was >95%. [c] Determined by HPLC analysis on a Pirkle covalent leucine column.[12] [d] Unless otherwise stated, the alcohols are of *R* configuration on the basis of the sign of the optical rotation and on the basis of the order of elution (second) on a Pirkle covalent leucine column.[12] [e] 10 mmol of (*R*)-BINAL-H was used. [f] (*S*)-Alcohol was obtained. [g] *R* configuration was corroborated by ^{1}H NMR analysis of the derived (*S*)-*O*-methylmandelate ester.[14] See text. [h] Unknown configuration. [i] Determined by GC analysis of the derived (+)-MTPA ester.

After the organic layer was dried and concentrated under reduced pressure, 2.8 g of (*R*)-binaphthol was obtained (99% recovery). HPLC analysis (same operating conditions as for alcohols **3a-b**) showed the material to be essentially 100% ee.

(*R*)-2,2,2-Trifluoro-1-(2-methylnaphthyl)ethanol [(*R*)-3b]: mp 73-74 °C; IR ($CHCl_3$) 3581, 3220 (br), 3041, 3003, 2949, 1502, 1262, 1166, 1119, 1034 cm^{-1}; ^{1}H NMR (250 MHz) δ 8.60 (br s, 1 H), 7.70 (dd, 1 H, J = 7.6, 1.6 Hz), 7.64 (d, 1 H, J = 8.4 Hz), 7.44-7.31 (m, 2 H), 7.16 (d, 1 H, J = 8.4 Hz), 5.70 (br s, 1 H), 3.07 (br s, 1 H), 2.40 (br s, 3 H); ^{13}C NMR (63 MHz) δ 136.5 (br), 133.1 (br), 131.9, 130.0, 129.3 (br), 128.5 (2 C), 126.2, 125.5 (q, J = 284 Hz), 125.0 (2 C), 70.8 (br q, J = 33 Hz), 21.0; MS m/z (relative intensity) 240 (96, M$^+$), 222 (2.5), 171 (100), 143 (62), 128 (58); 93% ee by HPLC; $[\alpha]^{25}_D$ -36° (c 0.634, $CHCl_3$). Anal. Calcd for $C_{13}H_{11}F_3O$: C, 65.00; H, 4.62. Found: C, 65.00; H, 4.73.

(*R*)-2,2,2-Trifluoro-1-(2,4,6-trimethylphenyl)ethanol [(*R*)-3d]: IR (film) 3479 (br), 2959, 1611, 1269, 1166, 1128, 849, 697 cm^{-1}; ^{1}H (250 MHz) δ 6.85 (s, 2 H), 5.47 (br q, 1 H, J = 8.0 Hz), 2.72 (br s, 1 H), 2.40 (br s, 6 H), 2.25 (s, 3 H); ^{13}C (63 MHz) δ 138.6, 138.0, 130.5 (br), 126.8, 125.5 (q, J = 283 Hz), 70.4 (q, J = 32 Hz), 20.7 (2 C); MS m/z (relative intensity) 218 (60, M$^+$), 200 (12), 149 (100), 121 (24), 105 (18); 97% ee by HPLC; $[\alpha]^{25}_D$ -30° (c 0.544, $CHCl_3$). Anal. Calcd for $C_{11}H_{13}F_3O$: C, 60.55; H, 6.00. Found: C, 60.58; H, 6.01.

(*R*)-2,2,2-Trifluoro-1-(2-methylphenyl)ethanol [(*R*)-3e]: IR (film) 3399 (br), 3031, 2935, 1266, 1172, 1134, 759, 729 cm^{-1}; ^{1}H NMR (250 MHz) δ 7.52 (br d, 1 H, J = 6.7 Hz), 7.26-7.12 (m, 3 H), 5.20 (q, 1 H, J = 6.6 Hz), 3.37 (br s, 1 H), 2.29 (s, 3 H); ^{13}C NMR (63 MHz) δ 136.5, 132.6, 130.6, 129.2, 127.0, 126.3, 124.7 (q, J = 283 Hz), 68.8 (q, J = 32 Hz), 19.1; MS m/z (relative intensity) 190 (68, M$^+$), 172 (25), 121 (100); 74% ee by HPLC; $[\alpha]^{25}_D$ -26° (c 0.664, $CHCl_3$). Anal. Calcd for $C_9H_9F_3O$: C, 56.85; H, 4.77. Found: C, 56.81; H, 5.01.

2,2,2-Trifluoro-1-(4-methoxyphenyl)ethanol (3g): IR (film) 3433 (br), 2940, 2842, 1611, 1514, 1251, 1170, 1128, 820 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.33 and 6.87 (AA'XX' system, 4 H, J_{AX} = 8.8 Hz), 4.86 (dq, 1 H, J = 6.8, 4.6 Hz), 3.75 (s, 3 H), 3.55 (d, 1 H, J = 4.6 Hz); ^{13}C NMR (63 MHz) δ 160.3, 128.8, 126.4, 124.4 (q, J = 282 Hz), 114.0, 72.4 (q, J = 32 Hz), 55.2; MS m/z (relative intensity) 206 (62, M$^+$), 170 (8.2), 137 (100), 109 (12), 94 (6.5). Anal. Calcd for $C_9H_9F_3O_2$: C, 52.43; H, 4.40. Found: C, 52.44; H, 4.58.

2,2,2-Trifluoro-1-(4-fluorophenyl)ethanol (3h): IR (film) 3408 (br), 1608, 1512, 1271, 1230, 1175, 1129, 822 cm^{-1}; ^{1}H NMR (250 MHz) δ 7.41 and 7.06 (AA'XX' system, 4 H, J_{AX} = 8.6 Hz), 4.94 (dq, 1 H, J = 6.6, 3.9 Hz), 3.54 (d, 1 H, J = 3.9 Hz); ^{13}C NMR (63 MHz) δ 163.4 (d, J = 248 Hz), 129.9, 129.3 (d, J = 8 Hz), 124.2 (q, J = 281 Hz), 115.6 (d, J = 22 Hz), 72.2 (q, J = 32 Hz); MS m/z (relative intensity) 194 (37, M$^+$), 158 (2.7), 125 (100), 97 (36); 14% ee by GC; $[\alpha]^{25}_D$ +1.4 (±0.9)° (c 0.193, $CHCl_3$). Anal. Calcd for $C_8H_6F_4O$: C, 49.50; H, 3.12. Found: C, 49.49; H, 3.15.

Preparation of (*S*)-*O*-Methylmandelate Esters for Determination of the Absolute Configurations of 3d and 3e. To a CH_2Cl_2 solution of the trifluoromethyl carbinol (1 equiv) was added HOBT (1 equiv), (*S*)-*O*-methylmandelic acid (1 equiv), DCC (1.4 equiv), and DMAP (1 equiv). After stirring for 1 h at room temperature, the reaction mixture was concentrated under reduced pressure and chromatographed on silica gel (petroleum ether-ether, 20:1), affording the (*S*)-*O*-methylmandelate ester.

Acknowledgment. We thank the Natural Sciences and Engineering Council of Canada for financial support and a postgraduate scholarship (to E.K.M.).

Annulation of Heterocycles via Intramolecular Nitrile Oxide-Heterocycle Cycloaddition Reaction[1]

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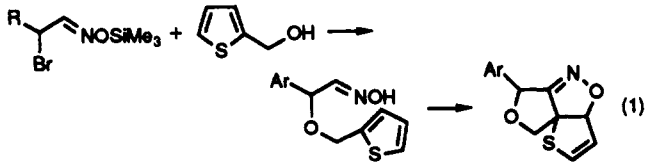
In recent years the INOC (intramolecular nitrile oxide-olefin cycloaddition) reaction has received a great deal

of attention, especially in the synthesis of functionalized rings.[2] Reports on systems where the olefin is a part of a heterocyclic ring are rather scarce in the literature.[3] In the course of work performed in this laboratory on intramolecular nitrile oxide–olefin cycloadditions,[4] we found that furan and thiophene substituted systems can also be used as substrates for the INOC reactions (see eq 1).[5]



(1)

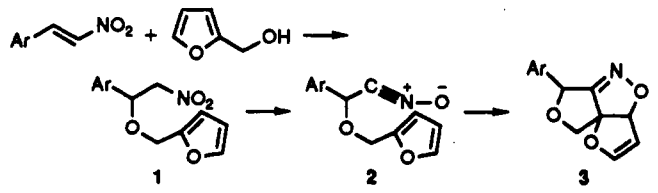
N–O bond cleavage in isoxazolines can lead further to functionalized ring systems.[2,4]

We wished to see if such an intramolecular nitrile oxide–heterocycle cycloaddition (INHC) would also take place with nitrogen-containing heterocycles and to determine the scope of such ring formation.

Although related intermolecular cycloadditions have been reported,[6] nothing is known about the intramolecular mode involving pyrroles or indoles. Our interest in such reactions was further stimulated by the possibility of using INHC reactions to generate the skeleton found in mitomycin[7] (cf. **8a**), in indolizidines (cf. **16b**), or in the rather novel fused cycloheptano[1,2-*a*]indoles **10**.

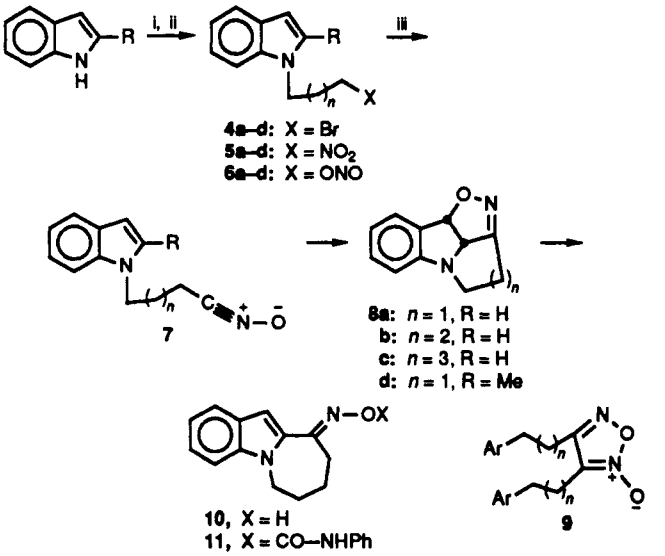
Results

First, we decided to examine the INHC reaction of the furan nitrile oxide **2** and to establish a convenient route to such systems via nitro compounds. The furfuryl derivative **1** was prepared via Michael addition of furfuryl alcohol to 4-methoxy-β-nitrostyrene and was subsequently transformed (PhNCO–Et_3N[8] in benzene at room temperature), without isolation of the intermediate nitrile oxide **2**, to the triheterocyclic isoxazoline **3** as a 5:1 mixture of isomers (stereochemistry undetermined) in high yield.



Indole was converted by monosubstitution of α,ω-dibromoalkanes under ambient conditions in moderate yields to the ω-bromoalkyl heterocycles **4a–c** (*n* = 1–3, R = H).

Scheme I[a]



[a] (i) DMF, KOH, $BrCH_2(CH_2)_nCH_2$ Br, room temperature; (ii) $AgNO_2$, ether, room temperature, 2 days. (iii) PhNCO, Et_3N, benzene, room temperature or heat.

Attempted substitution of the latter with $NaNO_2$ in DMF[9] only gave tar and nitrites **6** in low yields. Substitution of the halide in **4** was accomplished with silver nitrite in ether and led to ω-nitroalkyl compounds **5a–c** (*n* = 1–3, R = H) contaminated with a minor amount (10–20%) of the unstable alkyl nitrites **6a–c**. The nitro compounds **5** were purified by flash chromatography. The reactive nitrile oxides **7a–c** were generated in situ with PhNCO–Et_3N in benzene,[8] and their chemical behavior was found to depend strongly on the size of the alkyl chain (Scheme I).

To our disappointment, nitrile oxide **7a** (*n* = 1), formed in situ from **5a**, did not produce cycloadduct **8a** but instead led to a dimeric furoxan **9a**. Higher temperatures, or higher dilution to prevent dimerization, did not change the outcome of the reaction. However, we were gratified that the homologue **7b** (*n* = 2) gave cycloadduct **8b** at room temperature and in high yield.

Cycloaddition of **7c** (*n* = 3) to the seven-membered compound **8c** occurred, albeit somewhat less smoothly. Refluxing **5c** in benzene at high dilution with PhNCO–Et_3N was needed. Under these reaction conditions the isoxazoline **8c** underwent partial rearomatization to oxime **10**, which added to phenyl isocyanate to form carbamate **11**. Thus, a 1:1 mixture of cycloadduct **8c** and ring-opened product **11** was formed in fair combined yield.

The same sequence was attempted, starting from 2-methylindole, since we envisaged that the 2-methyl substituent would prevent rearomatization. Bromoalkylation and nitration occurred smoothly to form products **4d** and **5d** (*n* = 1, R = Me), respectively, but the resulting nitrile oxide **7d** failed to cycloadd to produce **8d** and gave only furoxan **9d**.

Analogously, pyrrole gave ω-bromoalkyl and ω-nitroalkyl derivatives **12a–c** and **13a–c**, which were converted in situ to nitrile oxides **14a–c** with PhNCO–Et_3N. Again, for *n* = 1, nitrile oxide **14a** failed to cycloadd to the five-membered ring annulated pyrrole **15a**, and only furoxan **9** was isolated. Starting from the higher homologues **13b,c**, ring closure did occur with formation of carbamates **16b,c** in

(1) Cycloadditions. 45. For the previous paper in the series, see: Hassner, A.; Dehaen, W.; M. L. *J. Org. Chem.* **1990**, *55*, 5505.

(2) For recent reviews, see: (a) Kozikowski, A. P. *Acc. Chem. Res.* **1984**, *17*, 410. (b) Padwa, A. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley-Interscience: New York, 1984; Vol 2. (c) Torsell, K. B. G. *Nitrile Oxides Nitrones and Nitronates in Organic Synthesis*; VCH Publishers: New York, 1988.

(3) Heinze, I.; Eberbach, W. *Tetrahedron Lett.* **1988**, *29*, 2051. Prajapati, D.; Sandhu, D. S. *Synthesis* **1988**, 342.

(4) (a) Hassner, A.; Murthy, K. S. K. *Tetrahedron Lett.* **1986**, *27*, 1407; (b) **1987**, *28*, 693. (c) Hassner, A.; Amarasekara, A. S.; Padwa, A.; Bullock, W. H. *Tetrahedron Lett.* **1988**, *28*, 716.

(5) Hassner, A.; Murthy, K. S. K.; Padwa, A.; Chiacchio, V.; Dean, D. C.; Schoffstall, A. M. *J. Org. Chem.* **1989**, *54*, 5277.

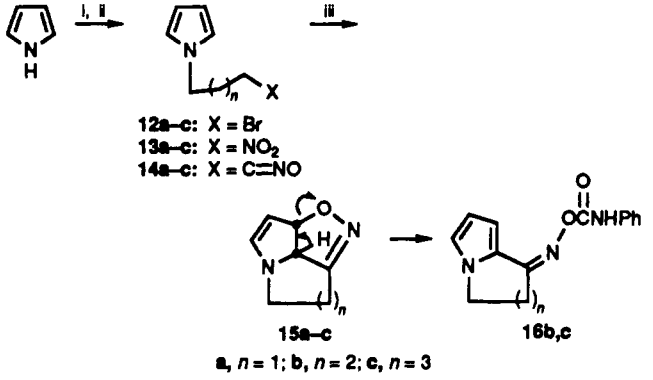
(6) Caramella, P.; Coda Corsico, A.; Corsaro, A.; Del Monte, D.; Albini, F. M. *Tetrahedron* **1982**, *38*, 173; ref 2b, p 335.

(7) See, for instance: Nakatsubo, F.; Fukuyama, T.; Cocuzza, A. J.; Kishi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 8115.

(8) Hoshino, T.; Mukaiyama, T. *J. Am. Chem. Soc.* **1960**, *82*, 5339.

(9) For recent examples of successful substitution of bromoalkyl compounds with DMF/$NaNO_2$, see: Hassner, A.; Murthy, K. S. K.; Padwa, A.; Bullock, W. H.; Still, P. D. *J. Org. Chem.* **1988**, *53*, 5063; and ref 4c.

moderate yields. Pyrroles **15** could not be isolated but showed as expected, a greater tendency toward rearomatization than the annulated indoles **8**.



In summary, the results show that indoles and pyrroles, like the more reactive furans, can be used in an INHC reaction. The annulation is successful when pyrroles or indoles become fused to six- and seven-membered rings but leads to nitrile oxide dimerization instead of formation of the rather strained polycycles **8a** or **15a**.

Experimental Section

2-[(Furylmethyl)oxy]-2-(4-methoxyphenyl)-1-nitroethane (1). To a stirred solution of 0.288 g (3 mmol) of furfuryl alcohol in 10 mL of THF at −20 °C was added 0.33 g (3 mmol) of potassium *tert*-butoxide in small portions followed by a solution of 0.179 g (1 mmol) of *p*-methoxy-β-nitrostyrene in 5 mL of THF dropwise over 10 min, while maintaining the temperature at −20 °C. After 10 additional minutes of stirring, a solution of 0.2 g of acetic acid in 20 mL of ether was added, the resulting emulsion was filtered, and the potassium salts were washed several times with ether. The combined filtrates were concentrated and the residue was chromatographed on silica gel with 2:1 petroleum ether/ether as the eluent, giving 193 mg of **1** (70%) as a light yellow oil: ^{1}H NMR δ 3.81 (s, 3 H, CH_3O), 4.26 (d, J = 13 Hz, 1 H, CH_2O), 4.35 (dd, J = 13, 4 Hz, 1 H, CH_2NO_2), 4.45 (d, J = 13 Hz, 1 H, CH_2O), 4.64 (dd, J = 13, 10 Hz, 1 H, CH_2NO_2), 5.09 (dd, J = 10, 4 Hz, 1 H, CHO), 6.25 (dd, J = 3, 1 Hz, 1 H, furyl-3), 6.33 (dd, J = 3, 2 Hz, 1 H, furyl-4), 6.94 (dt, J = 9, 2 Hz, 2 H, Ar), 7.31 (dt, J = 9, 2 Hz, 2 H, Ar), 7.39 (dd, J = 2, 1 Hz, 1 H, furyl-5); ^{13}C NMR δ 55.36 (CH_3O), 62.66 (CH_2O), 76.77 (CHO), 80.24 (CH_2NO_2), 109.71, 110.26 (furyl), 114.53, 127.89, 128.31 (Ar), 142.93, 150.79 (furyl), 160.30 (Ar). Anal. Calcd for $C_{14}H_{15}NO_5$: C, 60.65; H, 5.41. Found: C, 60.79; H, 5.61.

General Procedure for Cyclization Starting from the Nitro Compounds. Triheterocycle 3. To a solution of 50 mg (0.18 mmol) of nitro compound **1** in 10 mL of benzene containing 1 drop of triethylamine was added 60 mg (0.50 mmol) of phenyl isocyanate. The mixture was allowed to react for 2 days at room temperature. Diphenylurea was filtered and washed with some solvent. The combined filtrates were concentrated and the resulting oil was chromatographed over silica gel with dichloromethane as the eluent to yield 38 mg (84%) of product **3** as a 5:1 mixture of cis/trans isomers (oil). ***cis*-3**: ^{1}H NMR δ 3.80 (s, 3 H, CH_3O), 4.01 and 4.42 (d, J = 10 Hz, 1 H, CH_2O), 5.40 (t, J = 3 Hz, 1 H, dihydrofuran), 5.70 (s, 1 H, CH–Ar), 5.78 (d, J = 3 Hz, 1 H, dihydrofuran CHO), 6.69 (d, J = 3 Hz, 1 H, dihydrofuran), 6.91 and 7.41 (dt, J = 9, 2 Hz, 2 H, Ar); ^{13}C NMR δ 55.12 (CH_3O), 71.95, (CH_2O), 74.11 (CH–Ar), 89.62 (CHO dihydrofuran), 100.51, 105.50 (dihydrofuran), 113.93, 128.08, 128.37 (Ar), 149.89 (dihydrofuran), 159.76 (Ar), 163.06 (C=N). ***trans*-3**: ^{1}H NMR δ 3.80 (s, 3 H, CH_3O), 4.19 and 4.36 (d, J = 10 Hz, 1 H, CH_2O), 5.42 (t, J = 3 Hz, 1 H, dihydrofuran), 5.70 (s, 1 H, (CH–Ar), 5.83 (d, J = 3 Hz, 1 H, CHO dihydrofuran), 6.73 (d, J = 3 Hz, 1 H, dihydrofuran), 6.91 and 7.37 (dt, J = 9, 2 Hz, 2 H, Ar); ^{13}C NMR δ 55.12 (CH_3O), 70.82 (CH_2O), 73.59 (CH–Ar), 90.02 (CHO dihydrofuran), 100.94, 105.50 (dihydrofuran), 113.93, 128.86, 129.09 (Ar), 149.72 (dihydrofuran), 159.76 (Ar), 162.82 (C=N); MS (*m*/*z* relative intensity, mixture of isomers, CI, CH_4) 260 (MH^+, 82), 230 ($MH^+ - CH_2O$, 100), 152 ($M^{\bullet+}$ − Ar, 40). Anal. (mixture of isomers). Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.01. Found: C, 65.14; H, 5.30.

General Method for Synthesis of *N*-(ω-Bromoalkyl) Heterocycles 4 and 12. *N*-(3-Bromopropyl)indole (4a). To a stirred solution of 6.06 g (30 mmol) of 1,3-dibromopropane in 50 mL of DMF were added 1.17 g (10 mmol) of indole and 0.57 g (10 mmol) of ground KOH powder. The mixture evolved a moderate amount of heat and stirring was continued overnight. Water (100 mL) was added and the product was extracted into ether (3 × 50 mL). The ether extracts were washed with H_2O, dried ($MgSO_4$), and evaporated. The residue was chromatographed on silica gel. First the excess 1,3-dibromopropane (3.3 g) was eluted with petroleum ether and then chromatography was continued with 10:1 petroleum ether/ether to give 1.8 g (75%, oil) of **4a** in the first fraction. A second fraction (180 mg) consisted of a mixture of indole and 1,3-bis(*N*-indolyl)propane. **4a**: ^{1}H NMR δ 2.20 (quintet, J = 6.5 Hz, 2 H, CH_2CH_2N), 3.17 (t, J = 6.5 Hz, 2 H, CH_2Br), 4.18 (t, J = 6.5 Hz, 2 H, CH_2N), 6.45 (dd, J = 3, 1 Hz, 1 H, Ind.), 7.02 (d, J = 3 Hz, 1 H, Ind.), 7.08 and 7.18 (td, J = 8, 1 Hz, 1 H, Ind.), 7.29 (dq, J = 8, 1 Hz, 1 H, Ind.), 7.60 (dt, J = 8, 1 Hz, 1 H, Ind.); ^{13}C NMR δ 30.30 (CH_2Br), 32.65 (CH_2CH_2Br), 43.86 (CH_2N), 101.48, 109.18, 119.44, 121.00, 121.57, 127.81, 128.69, 135.62 (Ind.); MS (*m*/*z*, relative intensity, EI) 239 and 237 ($M^{\bullet+}$, 90 and 82), 130 ($M^{\bullet+} - C_2H_4Br$, 100). Anal. Calcd for $C_{11}H_{12}BrN$: C, 55.46; H, 5.04. Found: C, 55.44; H, 5.24.

***N*-(4-Bromobutyl)indole (4b)** was prepared analogously in 67% yield (oil): ^{1}H NMR δ 1.94 and 2.02 (m, 2 H, $CH_2CH_2CH_2Br$), 3.38 (t, J = 6.5 Hz, 2 H, CH_2Br), 4.18 (t, J = 7 Hz, 2 H, CH_2N), 6.50 (dd, J = 3, 1 Hz, Ind.), 7.08 (d, J = 3 Hz, 1 H, Ind.), 7.10 and 7.21 (dt, J = 7.5, 1 Hz, 1 H, Ind.), 7.34 (dq, J = 7.5, 1 Hz, 1 H, Ind.), 7.63 (dt, J = 7.5, 1 Hz, 1 H, Ind.); ^{13}C NMR δ 28.79 and 29.95 ($CH_2CH_2CH_2Br$), 32.93 (CH_2Br), 45.43 (CH_2N), 101.27, 109.18, 119.30, 120.99, 121.46, 127.51, 128.57, 135.85 (Ind.); MS (*m*/*z*, relative intensity, EI) 253 and 251 ($M^{\bullet+}$, 100 and 85), 172 ($M^{\bullet+}$ − Br, 26), 130 ($M^{\bullet+} - C_2H_6Br$, 99). Anal. Calcd for $C_{12}H_{14}BrN$: C, 57.14; H, 5.56. Found: C, 56.86; H, 5.79.

***N*-(5-Bromopentyl)indole (4c)** was prepared in a similar manner in 79% yield (oil): ^{1}H NMR δ 1.47 (quintet, J = 7 Hz, 3 H, $CH_2CH_2CH_2Br$), 1.85 (quintet, J = 7 Hz, 6 H, $CH_2CH_2CH_2CH_2Br$), 3.35 (t, J = 7 Hz, 2 H, CH_2Br), 4.12 (t, J = 7 Hz, 2 H, CH_2N), 6.49 (dd, J = 3, 1 Hz, 1 H, Ind.), 7.09 (m, 2 H, Ind.), 7.20 (td, J = 8, 1 Hz, 1 H, Ind.), 7.32 (dq, J = 8, 1 Hz, 1 H, Ind.), 7.62 (dt, J = 8, 1 H, Ind.); ^{13}C NMR δ 25.60, 29.41, 32.29, 33.30 ($CH_2CH_2CH_2CH_2Br$), 116.13 (CH_2N), 101.05, 109.22, 119.21, 120.95, 121.37, 127.64, 128.56, 135.85 (Ind.); MS (*m*/*z*, relative intensity, EI) 267 and 265 ($M^{\bullet+}$, 100 and 98), 186 ($M^{\bullet+}$ − Br, 29), 130 ($M^{\bullet+} - C_4H_8Br$, 88). Anal. Calcd for $C_{13}H_{16}BrN$: C, 58.65; H, 6.02. Found: C, 58.60; H, 6.30.

***N*-(4-Bromobutyl)-2-methylindole (4d)** was prepared analogously in 73% yield (oil): ^{1}H NMR δ 1.90 (m, 4 H, $CH_2CH_2CH_2Br$), 2.43 (s, 3 H, CH_3), 3.37 (m, 2 H, CH_2Br), 4.09 (m, 2 H, CH_2N), 6.27 (t, J = 1 Hz, 1 H, Ind.), 7.06 and 7.14 (td, J = 7.5, 1 Hz, 1 H, Ind.), 7.26 and 7.51 (br d, J = 8 Hz, 1 H, Ind.); ^{13}C NMR δ 12.75 (CH_3), 28.81, 30.09 ($CH_2CH_2CH_2Br$), 32.87 (CH_2Br), 42.29 (CH_2N), 100.30, 108.61, 119.29, 119.74, 120.51, 136.03, 136.64 (Ind.); MS (*m*/*z*, relative intensity, EI) 267 and 265 ($M^{\bullet+}$, 40 and 25), 186 ($M^{\bullet+}$ − Br, 8), 144 ($M^{\bullet+} - C_3H_6Br$, 100). Anal. Calcd for $C_{13}H_{16}BrN$: C, 58.65; H, 6.02. Found: C, 58.39; H, 6.28.

***N*-(3-Bromopropyl)pyrrole (12a)** was prepared analogously in 64% yield (oil): ^{1}H NMR δ 2.23 (quintet, J = 6.5 Hz, 2 H, $CH_2CH_2CH_2$), 3.28 (t, J = 6.5 Hz, 2 H, CH_2Br), 4.05 (t, J = 6.5 Hz, 2 H, CH_2N), 6.14 and 6.65 (t, J = 2 Hz, 2 H, pyrrole); ^{13}C NMR δ 30.13 (CH_2Br), 34.23 ($CH_2CH_2CH_2$) 47.07 (CH_2N), 108.46 and 120.61 (pyrrole); MS (*m*/*z*, relative intensity, EI) 189 and 187 ($M^{\bullet+}$, 63 and 67), 108 ($M^{\bullet+}$ − Br, 26), 81 ($M^{\bullet+} - C_2H_3Br$, 100), 80 ($M^{\bullet+} - C_2H_4Br$, 83). Anal. Calcd for $C_7H_{10}BrN$: C, 44.68; H, 5.32. Found: 44.95; H, 5.59.

***N*-(4-Bromobutyl)pyrrole (12b)** was prepared analogously in 57% yield (oil); ^{1}H NMR δ 1.83 (m, 2 H, CH_2CH_2Br), 1.92 (m, 2 H, CH_2CH_2N), 3.37 (t, J = 6 Hz, 2 H, CH_2Br), 3.91 (t, J = 6.5 Hz, 2 H, CH_2N), 6.14 and 6.64 (t, J = 2 Hz, 2 H, pyrrole); ^{13}C NMR δ 29.88, 30.08 ($CH_2CH_2CH_2Br$), 32.88 (CH_2Br), 48.73 (CH_2N), 108.27, 120.43 (pyrrole); MS (*m*/*z*, relative intensity, EI) 203 and 201 ($M^{\bullet+}$, 27 and 28), 122 ($M^{\bullet+}$ − Br, 100), 80 ($M^{\bullet+} - C_3H_6Br$, 74).

Anal. Calcd for $C_8H_{12}BrN$: C, 47.52; H, 5.94. Found: C, 47.24; H, 6.20.

***N*-(5-Bromopentyl)pyrrole (12c)** was similarly prepared in 61% yield (oil): ^{1}H NMR δ 1.35–1.50 (m, 2 H, $CH_2CH_2CH_2Br$), 1.70, 1.90 (m, 4 H, $CH_2CH_2CH_2CH_2Br$), 3.42 (t, J = 6.5 Hz, 2 H, CH_2Br), 3.87 (t, J = 7 Hz, 2 H, CH_2N), 6.13 and 6.63 (t, J = 2 Hz, 2 H, pyrrole); ^{13}C NMR δ 25.42 ($CH_2CH_2CH_2Br$), 30.75, 32.32 ($CH_2CH_2CH_2CH_2Br$), 33.27 (CH_2Br), 49.34 (CH_2N), 108.02, 120.41 (pyrrole); MS (m/z, relative intensity, EI) 217 and 215 ($M^{\bullet+}$, 22 and 20), 136 ($M^{\bullet+}$ – Br, 100), 81 ($M^{\bullet+}$ – C_4H_7Br, 53), 80 ($M^{\bullet+}$ – C_4H_8Br, 55). Anal. Calcd for $C_9H_{14}BrN$: C, 50.00; H, 6.48. Found: C, 49.69; H, 6.62.

General Procedure for the Synthesis of Nitro Compounds 5 and 13. *N*-(3-Nitropropyl)indole (5a). Silver nitrite (1 g, 6.5 mmol) was added to a stirred solution of 0.476 g (2 mmol) of **4a** in 20 mL of ether. Stirring was continued in the dark for 2 days. The silver salts were filtered off and washed several times with ether. The combined filtrates were concentrated at 0 °C to a volume of approximately 5 mL. (On further concentration, or at higher temperatures, rapid decomposition to a tarry substance took place.) Flash chromatography of the above concentrate on silica gel with 2:1 petroleum ether/ether as the eluent gave a first fraction on an unstable nitrite (10%), followed by a second fraction of the desired nitro compound **5a** (270 mg, 67%, oil): ^{1}H NMR δ 2.51 (quintet, J = 6.5 Hz, 2 H, $CH_2CH_2NO_2$), 4.28 and 4.30 (t, J = 6.5 Hz, 2 H, CH_2NO_2 + CH_2N), 6.53 (dd, J = 3, 1 Hz, 1 H, Ind.), 7.07 (d, J = 3 Hz, 1 H, Ind.), 7.13 (td, J = 7.5, 1, 1 H, Ind.), 7.23 (td, J = 7.5, 1 Hz, 1 H, Ind.), 7.31 (dq, J = 7.5, 1 Hz, 1 H, Ind.), 7.64 (dt, J = 7.5, 1, 1 H, Ind.); ^{13}C NMR 27.80 ($CH_2CH_2NO_2$), 42.87 (CH_2N). 72.24 (CH_2NO_2), 102.28, 108.93, 119.83, 121.32, 122.05, 127.60, 128.90, 135.86; MS (m/z, relative intensity, EI) 204 ($M^{\bullet+}$, 65), 139 ($M^{\bullet+}$ – $C_2H_4NO_2$, 100). Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.71; H, 5.88. Found: C, 64.42; H, 6.08.

***N*-(4-Nitrobutyl)indole (5b)** was prepared analogously in 62% yield (oil): ^{1}H NMR δ 1.95–2.05 (m, 4 H, $CH_2CH_2CH_2NO_2$), 4.13 (m, 2 H, CH_2N), 4.26 (m, 2 H, CH_2NO_2), 6.50 (dd, J = 3, 1 Hz, 1 H, Ind.), 7.04 (d, J = 3 Hz, 1 H, Ind.), 7.10 and 7.21 (td, J = 7.5, 1 Hz, 1 H, Ind.), 7.30 (dq, J = 8, 1 Hz, 1 H, Ind.), 7.62 (dt, J = 8, 1 Hz, 1 H, Ind.); ^{13}C NMR δ 24.73 (CH_2CH_2N), 26.98 ($CH_2CH_2NO_2$), 45.36 (CH_2N), 74.91 (CH_2NO_2), 101.63, 109.08, 119.47, 121.12, 121.67, 127.46, 128.65, 135.61 (Ind.); MS (m/z, relative intensity, EI) 218 ($M^{\bullet+}$, 73), 172 ($M^{\bullet+}$ – NO_2, 12), 144 ($M^{\bullet+}$ – $C_2H_4NO_2$, 11), 130 ($M^{\bullet+}$ – $C_3H_6NO_2$, 100). Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.06; H, 6.42. Found: C, 65.64, H, 6.08.

***N*-(5-Nitropentyl)indole (5c)** was obtained analogously in 68% yield (oil): ^{1}H NMR δ 1.38 (m, 2 H, $CH_2CH_2CH_2NO_2$), 1.85–2.05 (m, 4 H, $CH_2CH_2CH_2CH_2NO_2$), 4.14 (t, J = 7 Hz, 2 H, CH_2N), 4.31 (t, J = 7 Hz, 2 H, CH_2NO_2), 6.49 (dd, J = 3.1 Hz, 1 H, Ind.), 7.06 (d, J = 3 Hz, 1 H, Ind.), 7.10 and 7.21 (td, J = 8, 1 Hz, 1 H, Ind.), 7.31 (dq, J = 8, 1 Hz, 1 H, Ind.), 7.63 (dt, J = 8, 1 Hz, 1 H, Ind.); ^{13}C NMR δ 23.85 ($CH_2CH_2CH_2NO_2$), 26.97, 29.56 ($CH_2CH_2CH_2CH_2NO_2$), 45.94 (CH_2N), 75.29 (CH_2NO_2), 101.41, 109.21, 119.42, 121.13, 121.59, 127.61, 128.77. 136.01 (Ind.); MS (m/z, relative intensity, EI) 232 ($M^{\bullet+}$, 64), 186 ($M^{\bullet+}$ – NO_2, 9), 130 ($M^{\bullet+}$ – $C_4H_8NO_2$, 100). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.24; H, 6.90. Found: C, 66.99; H, 7.20.

2-Methyl-*N*-(4-nitrobutyl)indole (5d) was prepared analogously in 70% yield (oil): ^{1}H NMR δ 1.80–2.05 (m, 4 H, $CH_2CH_2NO_2$), 2.41 (d, J = 1 Hz, 3 H, CH_3), 4.12 (t, J = 7 Hz, 2 H, CH_2, N), 4.29 (t, J = 7 Hz, 2 H, CH_2NO_2), 6.24 (br s, 1 H, Ind.), 7.06 and 7.13 (td, J = 7.5, 1 Hz, 1 H, Ind.), 7.24 (dq, J = 8, 1 Hz, 1 H, Ind.), 7.71 (dt, J = 8, 1 Hz, 1 H, Ind.); ^{13}C NMR δ 12.72 (CH_3), 24.82 (CH_2CH_2N), 26.97 ($CH_2CH_2NO_2$), 42.17 (CH_2N), 75.03, (CH_2NO_2), 100.60, 108.69, 119.47, 119.47, 119.86, 120.69, 128.21, 135.93, 136.59 (Ind.); MS (m/z, relative intensity, EI) 232 ($M^{\bullet+}$, 25), 186 ($M^{\bullet+}$ – NO_2, 7), 171 ($M^{\bullet+}$ – CH_3 – NO_2, 10), 144 ($M^{\bullet+}$ – $C_3H_6NO_2$, 100). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.24; H, 6.90. Found: C, 67.01; H, 7.19.

***N*-(3-Nitropropyl)pyrrole (13a)** was prepared in the same manner in 58% yield (oil): ^{1}H NMR δ 2.40 (quintet, J = 6.5 Hz, 2 H, $CH_2CH_2NO_2$), 4.02 (t, J = 6.5 Hz, 2 H, CH_2N), 4.24 (t, J = 6.5 Hz, 2 H, CH_2N), 6.18 and 6.62 (t, J = 2 Hz, 2 H, pyrrole; ^{13}C NMR δ 29.06 ($CH_2CH_2NO_2$), 45.77 (CH_2N), 72.08 (CH_2NO_2), 108.93, 120.49 (pyrrole); MS (m/z, relative intensity, EI) 154 ($M^{\bullet+}$, 100), 108 ($M^{\bullet+}$ – NO_2, 18), 80 ($M^{\bullet+}$ – $C_2H_4NO_2$, 78). Anal. Calcd for $C_7H_{10}N_2O_2$: C, 54.55; H, 6.49. Found: C, 54.38; H, 6.62.

***N*-(4-Nitrobutyl)pyrrole (13b)** was prepared analogously in 57% yield (oil): ^{1}H NMR δ 1.80–2.00 (m, 4 H, $CH_2CH_2CH_2NO_2$), 3.93 (t, J = 6.5 Hz, 2 H, CH_2N), 4.28 (t, J = 6.5 Hz, 2 H, CH_2NO_2), 6.15 and 6.63 (t, J = 2 Hz, 2 H, pyrrole); ^{13}C NMR δ 24.60 and 28.20 ($CH_2CH_2CH_2NO_2$), 48.62 (CH_2N), 74.93 (CH_2NO_2), 108.56, 120.37 (pyrrole); MS (m/z, relative intensity, EI) 168 ($M^{\bullet+}$, 91), 122 ($M^{\bullet+}$ – NO_2, 59), 80 ($M^{\bullet+}$ – $C_3H_6NO_2$). Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.14; H, 7.14. Found: C, 56.78, H, 7.35.

***N*-(5-Nitropentyl)pyrrole (13c)** was prepared analogously in 61% yield (oil): ^{1}H NMR δ 1.32–1.45 (m, 2 H, $CH_2CH_2CH_2NO_2$), 1.75–1.87 (m, 2 H, CH_2CH_2N), 1.95–2.00 (m, 2 H, CH_2NO_2), 3.95 (t, J = 7 Hz, 2 H, CH_2N), 4.35 (t, J = 7 Hz, 2 H, CH_2NO_2), 6.14 and 6.63 (t, J = 3 Hz, 2 H, pyrrole); ^{13}C NMR δ 23.56 ($CH_2CH_2CH_2NO_2$), 26.91 (CH_2CH_2N), 30.83 ($CH_2CH_2NO_2$), 49.08 (CH_2N), 75.31 (CH_2NO_2), 108.15, 120.36 (pyrrole); MS (m/z, relative intensity, EI) 187 ($M^{\bullet+}$, 69), 136 ($M^{\bullet+}$ – NO_2, 37), 81 ($M^{\bullet+}$ – $C_4H_7NO_2$, 51), 80 ($M^{\bullet+}$ – $C_4H_8NO_2$, 100).

Tetracycle 8b was obtained starting from **5b** as shown for the preparation of **3** (77%): mp 146 °C (crystallization from dichloromethane/hexane); ^{1}H NMR δ 1.52 (qt, J = 13, 5 Hz, 1 H, H_{ax}), 1.78 (m, 1 H, H_{eq}), 2.40 (tdd, J = 13, 5, 1 Hz, H_{ax}-CH_2 (C=N), 2.85 (dm, J = 13 Hz, 1 H, H_{eq}-CH_2C=N), 3.32 (ddd, J = 14, 13, 3 Hz, 1 H, H_{ax}-CH_2N), 3.82 (m, 1 H, H_{eq}-CH_2N), 4.83 (d, J = 8 Hz, 1 H, CHO), 5.97 (d, J = 8 Hz, 1 H, NCHC=N), 6.63 (d, J = 8 Hz, 1 H, Ar), 6.82 and 7.22 (td, J = 7, 1 Hz, 1 H, Ar), 7.38 (dt, J = 7, 1 Hz, 1 H, Ar); ^{13}C NMR δ 23.28 (NCH$_2$$CH_2$$CH_2$C=N), 24.65 ($CH_2$C=N), 44.53 ($CH_2$–O), 82.07 (CHN), 109.15, 119.79, 126.72, 128.01, 130.45, 149.34 (Ar), 156.06 (C=N); MS (m/z, relative intensity, EI) 200 ($M^{\bullet+}$, 100), 183 ($M^{\bullet+}$ – OH, 17), 155 ($M^{\bullet+}$ – CH_2NOH, 38), 146 ($M^{\bullet+}$ – C_2H_4CN, 29), 130 ($M^{\bullet+}$ – C_2H_4CNO, 46). Anal. Calcd for $C_{12}H_{12}N_2O$: C, 72.00; H, 6.00. Found: C, 71.88; H, 6.30.

Tetracycle 8c and Carbamate 11c. Heating of a solution of 0.232 g (1 mmol) of **5c**, 0.48 g (4 mmol) of phenyl isocyanate, and a catalytic amount of triethylamine in 100 mL of benzene for 6 h gave after the usual workup two fractios on chromatography (SiO_2, $CHCl_3$). The first fraction contained 43 mg (20%, oil) of **8c**: ^{1}H NMR δ 1.58–1.70 (m, 1 H, axial CH), 1.85–1.95 (m, 1 H, axial CH), 2.02–2.20 (m, 2 H, equatorial, CH), 2.36 (ddd, J = 15, 11, 5 Hz, 1 H, CH_2C=N axial), 2.96 (dt, J = 15, 3 Hz, 1 H, CH_2C=N equatorial), 3.33 (dt, J = 13, 5 Hz, 1 H, CH_2N equatorial), 3.46 (td, J = 13, 5 Hz, 1 H, CH_2N axial), 5.13 (d, J = 9 Hz, 1 H, CHO), 6.05 (d, J = 9 Hz, 1 H, NCHC=N), 6.46 (d, J = 8 Hz, 1 H, Ar), 6.71 (td, J = 7, 1 Hz, 1 H, Ar), 7.24 (dddd, J = 8, 7.1 Hz, 1 H, Ar), 7.38 (dd, J = 7, 1 Hz, 1 H, Ar); ^{13}C NMR δ 24.47, 27.02, 27.39 ($CH_2CH_2CH_2$N), 45.48 (CH_2N), 74.86 (CHO), 84.10 (NCHC=N), 106.14, 117.28, 126.50, 127.63, 130.74 (Ar), 157.08 (C=N); MS (m/z, relative intensity, EI) 214 ($M^{\bullet+}$, 100), 197 ($M^{\bullet+}$ – OH, 36), 155 ($M^{\bullet+}$ – C_2H_5NO, 16), 130 ($M^{\bullet+}$ – C_4H_7NO, 9).

A second fraction was 68 mg (20%) of carbamate **11c**: mp 152 °C dec (crystals from ethanol); ^{1}H NMR δ 1.95–2.09 (m, 4 H, NCH$_2$$CH_2$$CH_2$), 2.80–2.85 (m, 2 H, CH_2 C=N), 4.15–4.22 (m, 2 H, CH_2N), 7.05–7.65 (m, 10 H, Ind. + Ar), 8.11 (s, 1 H, NH); ^{13}C NMR δ 26.00, 27.65 (NCH, CH_2CH_2), 33.56 (CH_2C=N), 45.02 (CH_2N), 109.61, 119.49, 120.57, 122.16, 124.13, 124.41, 126.64, 129.01, 129.73, 137.98 (Ph + Ind.), 152.02 (Ind.), 153.36 (C=N), 155.32 (C=O). Anal. Calcd for $C_{20}H_{19}N_3O_2$ (MW = 333): C, 72.07; H, 5.71. Found: C, 72.41; H, 5.66.

Carbamate 16b was prepared from **13b**, as described for **3**, in 67% yield after crystallization from ethanol: mp 149–150 °C; ^{1}H NMR δ 2.09–2.18 (m, 2 H, CH_2CH_2N), 2.66–2.70 (m, 2 H, CH_2C=N), 4.00–4.05 (m, 2 H, CH_2N), 6.28 (dd, J = 4, 3 Hz, 1 H, pyrrole), 6.82 (dd, J = 3, 1 Hz, pyrrole), 7.07–7.12 (m, 1 H, Ph), 7.29–7.34 (m, 2 H, Ph), 7.48 (dd, J = 4, 1 Hz, pyrrole), 7.51–7.55 (m, 2 H, Ph), 8.49 (s, 1 H, NH); ^{13}C NMR δ 22.97 (CH_2CH_2N), 27.86 (CH_2C=N), 45.62 (CH_2N), 110.27, 119.53, 119.92, 123.86, 124.94, 128.66, 128.93, 137.33 (Ph + pyrrole), 148.48 (C=N), 152.53 (C=O); MS (m/z, relative intensity, EI) 269 ($M^{\bullet+}$, 0.1), 150 ($M^{\bullet+}$ – PhN=C=O, 100), 133 ($M^{\bullet+}$ – $PhNHCO_2$, 12), 119 ($PhNCO^{\bullet+}$, 92). Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.91; H, 5.58. Found: C, 66.62; H, 5.82.

Carbamate 16c was prepared as described for **8c/11c**, starting from **13c**, in 36% yield after crystallization from ethanol: mp 132 °C; ^{1}H NMR δ 1.88–2.05 (m, 4 H, $CH_2CH_2CH_2$N), 2.72–2.78

(m, 2 H, $CH_2C{=}N$), 4.18-4.23 (m, 2 H, CH_2N), 6.19 (dd, J = 4, 3 Hz, 1 H, pyrrole), 6.73 (dd, J = 3, 1 Hz, 1 H, pyrrole), 7.07-7.13 (m, 1 H, Ph), 7.19 (dd, J = 4, 1 Hz, 1 H, pyrrole), 7.30, 7.35 (m, 2 H, Ph), 7.49-7.54 (m, 2 H, Ph), 8.25 (s, 1 H, NH); ^{13}C NMR δ 24.26, 27.56 ($CH_2CH_2CH_2N$), 32.63 ($CH_2C{=}N$), 49.56 (CH_2N), 108.56, 119.53, 119.92, 123.93, 127.09, 129.03, 137.39 (pyrrole + Ph), 152.36 (C=N), 153.90 (C=O).

Furoxans 9 from Reaction of Nitro Heterocycles 5a, 5d, and 13a with Phenyl Isocyanate-Triethylamine. 9a from **5a** (yield 35%, oil): ^1H NMR δ 2.10 (t, J = 7 Hz, 2 H, $CH_2C{=}N$), 2.25 (m, 2 H, $CH_2C{=}N{\rightarrow}O$), 4.02 (t, J = 7 Hz, 2 H, CH_2N), 4.18 (m, CH_2N), 6.51 (d, J = 3 Hz, 2 H, Ind.), 6.66 and 6.68 (d, J = 3 Hz, 1 H, Ind.), 7.20-7.40 (m, 6 H, Ind.), 7.57-7.62 (m, 2 H, Ind.).

9d from **5d** (yield 42%, oil): δ 1.80-2.00 (m, 4 H, CH_2CH_2N), 2.03 (t, J = 7 Hz, 2 H, $CH_2C{=}N$), 2.15 (t, J = 7 Hz, 2 H, CH_2N), 4.62 (t, J = 7 Hz, 2 H, CH_2N), 6.24 (s, 2 H, Ind.), 7.05-7.52 (m, 8 H, Ind.).

9e from 13a (yield 32%, oil): δ 2.40 and 2.52 (t, J = 7 Hz, 2 H, $CH_2C{=}N$), 3.92 and 3.96 (t, J = 7 Hz, 2 H, CH_2N), 6.12 and 6.60 (m, 4 H, pyrrole).

Preparation of 3,3-Difluoroacrylic Acid Derivatives by Dehydrohalogenation of Activated Acyl Compounds. Synthesis of Two Potential Precursors to Difluoropropadienone

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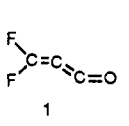
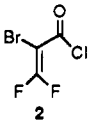
We have recently reported the successful preparation of difluoropropadienone (**1**) by flash vacuum pyrolysis of 3,3-difluoroacrylic anhydride.[1] Attempts to prepare this anhydride directly from 3,3-difluoroacrylic acid[2] were unsuccessful under a variety of conditions and invariably led to destruction of the starting material, presumably due to conjugate addition and polymerization.

Due to the difficulty in obtaining 3,3-difluoroacrylic anhydride, other possible methods for making difluoropropadienone were explored. One of these routes was the zinc reduction of 2-bromo-3,3-difluoroacryloyl chloride (**2**). Zinc reduction of 2,2-dibromomalonyl chloride has been used to prepare carbon suboxide in good yield.[3] More recently, alkyl- and arylpropadienones have been trapped in solution by the in situ reduction of 2-bromoacryloyl chlorides using $Mn(CO)_5^-$.[4]



1

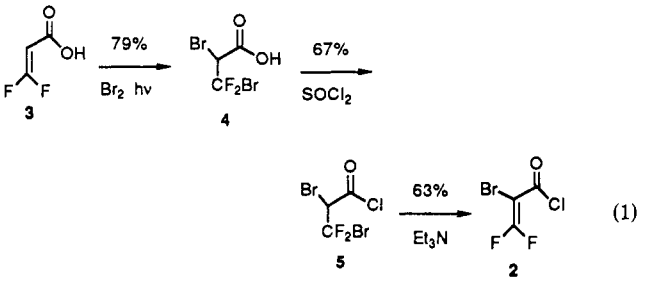


2

In our efforts to synthesize **2** as a precursor to difluoropropadienone, we discovered that it was possible to prepare this, as well as several other 3,3-difluoroacrylic acid derivatives, including 3,3-difluoroacrylic anhydride, by dehydrohalogenation of 3-bromo-3,3-difluoropropionate derivatives. While this elimination reaction has been reported for the preparation of ethyl 3,3-difluoroacrylate from ethyl 3-bromo-3,3-difluoropropionate,[5] there are no reports of this reaction being attempted on activated acyl derivatives.

Results and Discussion

It was possible to prepare 2-bromo-3,3-difluoroacryloyl chloride (**2**) in good yield by the route shown in eq 1.

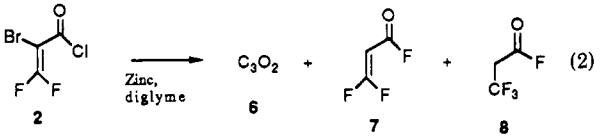


(1)

Photochemical addition of bromine to 3,3-difluoroacrylic acid (**3**)[2] gave **4**, which could be converted to the corresponding acid chloride **5** by heating with excess thionyl chloride. Acid chloride **5** can be dehydrohalogenated to give **2** in 63% yield by treatment with slightly less than 1 equiv of triethylamine in dichloromethane at 0 °C under rigorously anhydrous conditions.

Dehydrohalogenation of an acid chloride with a tertiary amine is a standard method for the formation of a ketene, presumably via an acylammonium intermediate,[6] and this pathway was considered as a potentially serious side reaction. Apparently the increased acidity of the proton adjacent to the two neighboring fluorine atoms together with the leaving group ability of bromine favors elimination to give the desired product rather than the undesired ketene.

With **2** in hand, we were in a position to investigate the zinc reduction reaction. Treatment of **2** with activated zinc dust in the absence of solvent resulted in loss of starting material without the formation of any new volatile products. Addition of **2** to a mixture of activated zinc dust in diglyme at 80 °C resulted in the formation of carbon suboxide (**6**) and 3,3-difluoroacryloyl fluoride (**7**) along with a small amount of 3,3,3-trifluoropropionyl fluoride (**8**) in about a 10% combined yield (eq 2).



(2)

These compounds have been reported in the literature,[7] but we prepared them by independent synthesis for comparison with the reaction product mixture. Carbon suboxide was prepared by treatment of malonic acid with P_2O_5.[8] Compounds **7** and **8** were prepared by the routes shown in eqs 3 and 4.

3-Bromo-3,3-difluoropropionic acid[9] (**9**) was converted to acid chloride **10**, which in turn was converted to the corresponding acid fluoride **11** with use of neat HF-

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