stirring bar. The flask was cooled to −40 °C and Cl_2 gas was slowly bubbled into the stirred solution by evaporation of 27.6 g (0.39 mol) of precondensed chlorine at such a rate that the temperature did not exceed −30 °C. After addition was completed the reaction mixture was stirred at −30 °C for an hour. The acetyl chloride was removed by rotary evaporation from a water bath at 60 °C with the aid of a water aspirator, and the residual oil was distilled to yield 45.4 g (78%) of the sulfinyl chloride: bp 68 °C (22 mm) (lit.[13] bp 36–38 °C (3.7 mm)); IR ($CHCl_3$) 1150 cm^{-1} (S=O); NMR ($CDCl_3$) δ 1.91 (d, 3, CH_3), 5.14, 5.20 (q, 1, CH). The infrared and NMR spectra were identical to those obtained from a sample of the material prepared from 1-chloroethanesulfonyl chloride by the method of King.[7]

Treatment of 1-Chloroethanesulfinyl Chloride (4) with Triethylamine. Trapping of the Intermediate Thioacetyl Chloride *S*-Oxide (2) with Chlorine. Into a 250-mL three-neck flask equipped with an addition funnel, gas in- and outlet tubes, and a magnetic stirrer was placed 100 mL of hexane and 8.10 g (0.080 mol) of triethylamine. To this stirred solution at −30 °C was added dropwise a solution of 11.80 g (0.080 mol) of 1-chloroethanesulfinyl chloride in 50 mL of hexane. After addition was completed, the precipitate of triethylammonium chloride was filtered and washed with two 50-mL portions of cold (−30 °C) hexane, and the combined filtrate and washings were quickly returned to the cooling bath. All attempts to use this solution of thioacetyl chloride *S*-oxide in reactions with diazoalkanes were unsuccessful. To prove its intermediacy in the solution it was treated with Cl_2 in the cold. While maintaining the temperature at −30 °C, Cl_2 was flashed over the stirred solution by evaporation of 7.1 g (0.10 mol) of precondensed chlorine. Evaporation of the solvent in vacuo with a water aspirator from a 50 °C water bath and distillation of the residual brown oil yielded 7.3 g (50%) of a colorless liquid, bp 59 °C (14 mm), identified by its spectral data as 1,1-dichloroethanesulfinyl chloride (**5**) [IR ($CHCl_3$) 1175 cm^{-1} (S=O); NMR ($CDCl_3$) δ 2.42, (s, CH_3)]. For identification 2.28 g (0.013 mol) of the 1,1-dichloroethanesulfinyl chloride was added to 60 mL of ethereal perphtalic acid[14] (0.047 M; 0.028 mol) at 0 °C. The phthalic acid formed was filtered and rinsed with ice-cold chloroform. The combined rinsings and filtrate were evaporated from a water bath at 50 °C with a water aspirator, yielding an oily solid, which was recrystallized from pentane to give 1.5 g (65%) of 1,1-dichloroethanesulfonyl chloride (**6**), mp 37–38.5 °C. The sulfonyl chloride was identified by comparison of IR and NMR spectral data and a mixture melting point with an authentic sample prepared by the oxidation of 1,1-dichloroethanesulfenyl chloride (**7**).

1,1-Dichloroethanesulfenyl Chloride (7). A solution of 19.5 g (0.167 mol) of ethyl dithioacetate[15] dissolved in 100 mL of pentane was cooled to −40 °C. Anhydrous Cl_2, evaporated from 35.5 g (0.50 mol) of precondensed chlorine, was flashed over the surface of the stirred solution. The solid ethanesulfur trichloride was filtered through a plug of glass wool set in a chilled (−30 °C) funnel. The pentane was evaporated from the filtrate by means of a water aspirator and the residual yellow liquid was distilled to give 27.4 g (70%) of the sulfenyl chloride: bp 45 °C (28mm) (lit.[16] bp 46 °C (28 mm)); NMR ($CDCl_3$) δ 2.54 (s, CH_3).

1,1-Dichloroethanesulfonyl Chloride (6). An ethereal solution of perphthalic acid[14] (488 mL, 0.47 M, 0.230 mol) was added to a solution of 20.79 g (0.115 mol) of 1,1-dichloroethanesulfenyl chloride in 100 mL of anhydrous ether at 0 °C. The mixture was stored overnight in a refrigerator at −5 °C. The phthalic acid formed was removed by filtration and the solid was washed with three 50-mL portions of anhydrous ether. The ether was removed from the combined filtrate and washings by rotary evaporation with a water aspirator to yield a yellow oily solid. Recrystallization from pentane yielded 9.0 g (38%) of the sulfonyl chloride: mp 36–38 °C; IR ($CHCl_3$) 1390 cm^{-1}, 1175 (SO_2); NMR ($CDCl_3$) δ 2.57 (s, CH_3). An analytical sample was prepared by two further recrystallizations from pentane followed by vacuum sublimation, mp 37.0–38.5 °C.

Anal. Calcd for $C_2H_3Cl_3O_2S$: C, 12.17; H, 1.54; S, 16.25. Found: C, 12.27; H, 1.54; S, 16.47.

Treatment of Oxythiobenzoyl Chloride with Phenyldiazomethane. *cis*-Oxythiobenzoyl chloride (2.1 g) was prepared according to the procedure of King and Durst[1] from 9.6 g (0.05 mol) of phenylmethanesulfonyl chloride and 8 mL (0.057 mol) of triethylamine in 750 mL of cyclohexane (freshly distilled from CaH_2). A solution of phenyldiazomethane (ca 0.0121 mol) in ether was prepared according to the method of Yates and Shapiro[17] from 5.8 g of sodium hydroxide, 11 mL of water, 72 mL of methanol, and a solution of 4 g of azibenzil in 90 mL of ether. To a solution of 2.1 g (0.0121 mol) of oxythiobenzoyl chloride in 20 mL of anhydrous ether was added dropwise an ethereal solution of phenyldiazomethane (ca. 0.0121 mol) at room temperature. Gas evolution was noted and after complete addition the mixture was refluxed for 30 min, 2 mL (0.014 mol) of triethylamine was added, and the mixture was refluxed for 2 h. The precipitated triethylamine hydrochloride was filtered and washed with 15 mL of cold (5–10 °C) ether. The filtrate was washed with three 20-mL portions of 3 N hydrochloric acid and two 15-mL portions of water, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to afford a solid admixed with an orange oil. Addition of 5 mL of a 1:1 mixture of ether–ligroin (bp 67–71 °C) to the mixture followed by filtration afforded 0.9 g of white plates, mp 141–143 °C. Recrystallization from ligroin (bp 67–71 °C) yielded 0.8 g (33.6%) of 2,5-diphenyl-1,3,4-thiadiazole, mp 142.5–144 °C (lit.[8] mp 141–142 °C), which was identified by mixture melting point and comparison of its infrared spectrum with that of an authentic sample.

Acknowledgment. The authors thank the National Science Foundation for generous support of this work.

Registry No.—2, 68965-48-0; **3,** 19852-37-0; **4,** 28691-57-8; **5,** 68965-49-1; **6,** 68965-50-4; **7,** 19852-35-8; **8,** 870-73-5; trithioacetaldehyde, 2765-04-0; ethyl disulfide, 110-81-6; *cis*-oxythiobenzoyl chloride, 7214-46-2; phenylmethanesulfonyl chloride, 1939-99-7; phenyldiazomethane, 766-91-6; 2,5-diphenyl-1,3,4-thiadiazole, 1456-21-9.

References and Notes

(1) J. F. King and T. Durst, *Can. J. Chem.*, **44,** 819 (1966).
(2) The simplest halo sulfine which has been isolated is thiophosgene oxide, a compound which undergoes a variety of useful cycloaddition reactions. See (a) B. Zwanenburg, L. Thijs, and J. Strating, *Tetrahedron Lett.*, **4461** (1969); (b) J. Sihanek and M. Zbirovsky, *Chem. Commun.*, 878 (1969); (c) A. Tangerman and B. Zwanenburg, *J. Chem. Soc. Perkin Trans. 2,* **1414** (1979); (d) B. Zwanenburg, L. Thijs, J. Broens, and J. Strating, *Recl. Trav. Chim. Pays-Bas,* **91,** 443 (1972); (e) L. Thijs, J. Strating, and B. Zwanenburg *ibid.,* **91,** 1345 (1972).
(3) Compare L. A. Carpino and H.-W. Chen, *J. Am. Chem. Soc.,* **93,** 785 (1971); **101,** 390 (1979).
(4) Following the completion of the present work it was noted that in the reaction of sulfines with diazoalkanes both episulfoxides and thiadiazoline oxides are formed. The latter appear to be the "normal" products except in the case of reactants bearing bulky substituents. See (a) L. Thijs, A. Wagenaar, E. M. M. van Rens, and B. Zwanenburg, *Tetrahedron Lett.,* 3589 (1973); (b) B. Zwanenburg and A. Wagenaar, *ibid.,* 5009 (1973).
(5) J. Strating, L. Thijs, and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas,* **86,** 641 (1967).
(6) Dimethyl thioketone oxide, generated and similarly, was also too unstable to be isolated. See (a) W. A. Sheppard and J. Diekmann, *J. Am. Chem. Soc.,* **86,** 1891 (1964); (b) B. F. Bonini, G. Maccagnani, A. Wagenaar, L. Thijs, and B. Zwanenburg, *J. Chem. Soc., Perkin Trans. 2,* 2490 (1972).
(7) J. F. King and R. P. Beatson, *Chem. Commun.,* 663 (1970); J. F. King, R. P. Beatson, and J. M. Buchshriber, *Can. J. Chem.,* **55,** 2323 (1977).
(8) R. Stolle and W. Kind, *J. Prakt. Chem.,* [2] **70,** 425 (1904).
(9) Melting points and boiling points are uncorrected. Infrared spectra were obtained on Beckman IR-5 and IR-10 and Perkin-Elmer 237B instruments and NMR spectra on Varian A-60 and Perkin-Elmer R-12 instruments with Me_4Si as internal standard. Elemental analyses were carried out by the University of Massachusetts Microanalytical Laboratory under the direction of Charles Meade and Greg Dabkowski and associates.
(10) (a) I. B. Douglass, V. G. Simpson, and A. K. Sawyer, *J. Org. Chem.,* **14,** 272 (1949); (b) I. B. Douglass and F. T. Martin, *ibid.,* **15,** 795 (1950).
(11) I. B. Douglass, K. R. Brower, and F. T. Martin, *J. Am. Chem. Soc.,* **74,** 5770 (1952). See also H. Brintzinger and H. Ellwanger, *Ber.,* **87,** 300 (1954).
(12) The method is adapted from a general procedure due to Douglass. See M.-L. Kee and I. B. Douglass, *Org. Prep. Proced.,* **2,** 235 (1970), and references therein.
(13) J. F. King and R. P. Beatson, private communication. See ref 7.
(14) H. Bohme, "Organic Syntheses", Collect. Vol. III, E. C. Horning, Ed., Wiley, New York, 1955, p 619.
(15) C. S. Marvel, P. DeRadzitsky, and J. J. Brader, *J. Am. Chem. Soc.,* **77,** 5997 (1955).
(16) I. B. Douglass and C. E. Osborne, *J. Am. Chem. Soc.,* **75,** 4582 (1953).
(17) P. Yates and B. L. Shapiro, *J. Org. Chem.,* **23,** 759 (1958).

N-(α-Chloroalkyl)phthalimides

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The reaction of formaldehyde with amides and imides to give *N*-(hydroxymethyl)amides and -imides **1,** followed by conversion of **1** into the *N*-halomethyl derivatives **2,** consti-

tutes an important entry into numerous classes of organic compounds.[1] Unfortunately, higher aldehydes generally result in no reaction or in formation of the less synthetically useful *N,N'*-alkylenebis(amides) **3**. Phthalimide, for example, reacts readily with formaldehyde but fails to react with benzaldehyde. *N*-(α-Chloroethyl)phthalimide has been obtained by the alternative procedure of addition of dry HCl to *N*-vinylphthalimide,[2] but compounds such as *N*-(α-chlorobenzyl)-phthalimide obviously are not available from this method.

$$\mathrm{RCONHR' + CH_2O \rightarrow RCONR'CH_2OH}$$

1

$$\rightarrow \mathrm{RCONR'CH_2X}$$

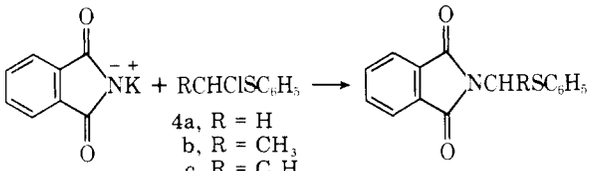
2

$$\mathrm{(RCONH)_2CHR''}$$

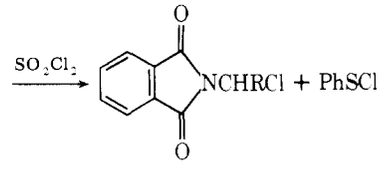
3

We now report a new method for preparation of *N*-(α-chloroalkyl)phthalimides which complements the hydroxymethylation and HCl addition routes.

Reaction of potassium phthalimide in dimethylformamide with an equimolar amount of an α-chloroalkyl phenyl sulfide **4**, an aldehyde equivalent, gives the corresponding *N*-[α-



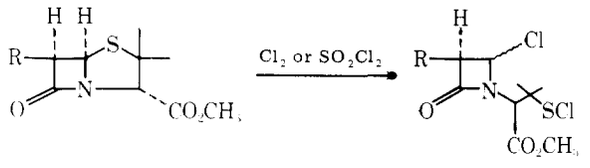
5a, R = H
b, R = CH_3
c, R = C_6H_5



6a, R = H
b, R = CH_3
c, R = C_6H_5

(phenylthio)alkyl]phthalimide **5** in fair to good yields. Treatment of **5** in methylene chloride with an equivalent of sulfuryl chloride produces the *N*-(α-chloroalkyl)phthalimides **6** in excellent yields. The accompanying product phenylsulfenyl chloride is removed readily from the reaction mixture concomitant with removal of solvent by rotary evaporation.

α-Amidoalkyl sulfides have been prepared previously from reaction of **1** or **2** with mercaptans,[1a,3] from heating of amides or imides with excess dimethyl sulfoxide,[4] and, more recently, from treatment of amides with chloromethyl methyl sulfide in strong acid,[5] a process related to the procedure reported here. Additionally, nongeneral routes are available for the special case of 2-azetidinones.[6] The conversion of α-amidoalkyl sulfides to *N*-(chloroalkyl)amides appears to have been reported previously only for the specific example of a penicillin derivative.[7] Both steps of the present procedure should be applicable to a wide variety of both sulfides and amido and imido compounds.



R = phthalimido

Experimental Section

General. Melting points were determined on a Mel-Temp apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian T-60 or EM-360 spectrometer. Elemental analyses were performed by Atlantic Microlab, Inc.

***N*-[(Phenylthio)methyl]phthalimide (5a).** Chloromethyl phenyl sulfide[8] (31.7 g, 0.20 mol) was added in 15 min to a stirred suspension of 37.0 g (0.20 mol) of potassium phthalimide in 150 mL of dimethylformamide. The mixture was heated on a steam bath for 4.0 h and then was added to 600 mL of ice water. After 10 min, the resulting mixture was filtered to obtain 47.9 g (89%) of crude product, mp 116–120 °C. Recrystallization from 350 mL of carbon tetrachloride gave 20.0 g of material with mp 126–127 °C (lit.[3] mp 127 °C) and 9.0 g of a second crop with mp 120–123 °C.

***N*-[α-(Phenylthio)ethyl]phthalimide (5b).** Heating a stirred mixture of 19.1 g (0.11 mol) of α-chloroethyl phenyl sulfide[9] and 20.6 g (0.11 mol) of potassium phthalimide in 85 mL of dimethylformamide for 7.0 h on a steam bath and workup as above gave a golden brown solid. This material was treated with 600 mL of boiling chloroform, and the mixture was treated with charcoal and subsequently concentrated to ~400 mL, diluted with 250 mL of petroleum ether, and filtered. Concentration of the filtrate gave 17.1 g (54%) of white product, mp 113–114 °C. Recrystallization from 200 mL of ethanol gave 11.3 g: mp 116–117 °C; NMR ($CDCl_3$) δ 7.90–7.13 (complex, 9), 5.76 (q, 1, J = 7 Hz), and 1.93 (d, 3, J = 7 Hz).

Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; S, 11.32. Found: C, 67.86; H, 4.65; S, 11.27.

***N*-[α-(Phenylthio)benzyl]phthalimide (5c).** Similar treatment of 23.5 g (0.10 mol) of α-chlorobenzyl phenyl sulfide[10] and 18.5 g (0.10 mol) of potassium phthalimide in 100 mL of dimethylformamide gave a brown oil. This oil was dissolved in chloroform and dried ($MgSO_4$), and the solution was concentrated. The residue crystallized upon standing for 2 days. The solid was dissolved in 100 mL of methylene chloride; the solution was extracted with two 100-mL portions of 5% sodium hydroxide solution, dried ($MgSO_4$), and concentrated. The residue crystallized upon trituration with petroleum ether to give 18.5 g (54%) of light tan solid: mp 94–95 °C; NMR ($CDCl_3$) δ 7.85–7.12 (complex, 14) and 6.80 (s, 1).

Anal. Calcd for $C_{21}H_{15}NO_2S$: C, 73.02; H, 4.38; S, 9.78. Found: C, 72.99; H, 4.43; S, 9.18.

***N*-(Chloromethyl)phthalimide (6a).** A solution of 2.7 g (0.020 mol) of sulfuryl chloride in 10 mL of methylene chloride was added dropwise in 15 min to a stirred solution of 5.3 g (0.020 mol) of **5a** in 40 mL of methylene chloride. The solution was stirred for 2.0 h more and then concentrated on a rotary evaporator. The solid residue was collected with the aid of petroleum ether to obtain 3.5 g (90%) of white product whose NMR spectrum and melting point agreed with those of an authentic sample.

***N*-(α-Chloroethyl)phthalimide (6b).** Similar treatment of 5.7 g (0.020 mol) of **5b** gave 3.4 g (81%) of white product: mp 99–101 °C (lit.[2] mp 110–111 °C); NMR ($CDCl_3$) δ 8.03 (complex, 4), 6.33 (q, 1, J = 7 Hz), and 2.18 (d, 3, J = 7 Hz). Recrystallization from 90 mL of benzene–petroleum ether (1:5) gave 2.1 g of an analytical sample, mp 100–102 °C.

Anal. Calcd for $C_{10}H_8ClNO_2$: C, 57.30; H, 3.85; Cl, 16.91. Found: C, 57.49; H, 3.89; Cl, 16.76.

***N*-(α-Chlorobenzyl)phthalimide (6c).** Similar treatment of 4.2 g (0.013 mol) of **5c** gave 2.7 g (80%) of white product: mp 90–91 °C; NMR ($CDCl_3$) δ 7.93–7.26 (complex). This material gave a good elemental analysis. Recrystallization resulted in material of a lower melting point and inferior analysis.

Anal. Calcd for $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71; Cl, 13.05. Found: C, 66.37; H, 3.75; Cl, 12.99.

Registry No.—**4a**, 7205-91-6; **4b**, 13557-24-9; **4c**, 7693-31-4; **5a**, 32637-30-2; **5b**, 69177-58-8; **5c**, 69177-59-9; **6a**, 17564-64-6; **6b**, 2017-95-0; **6c**, 69177-60-2; potassium phthalimide, 1074-82-4; sulfuryl chloride, 7791-25-5.

References and Notes

(1) (a) H. E. Zaugg, *Synthesis*, 49 (1970); (b) H. E. Zaugg and W. B. Martin, *Org. React.*, **14**, 52 (1965); (c) K. W. Ratts and J. P. Chupp, *J. Org. Chem.*, **39**, 3745 (1974); (d) D. Seyferth, R. S. Marmor, and P. Hilbert, *ibid.*, **36**, 1379 (1971); (e) B. S. Drach, E. P. Sviridov, and A. V. Kirsanov, *Zh. Obshch. Khim.*, **42**, 953 (1972).

(2) K. Kato, *Kogyo Kagaku Zasshi*, **59**, 1006 (1956); *Chem. Abstr.*, **52**, 10002b (1958).

(3) H. Bohme and A. Muller, *Arch. Pharm. (Weinheim, Ger.)*, **296**, 54 (1963).

(4) H. H. Otto, *Pharm. Zentralhalle*, **107**, 444 (1968).
(5) L. Bernardi, R. DeCastiglione, and U. Scarponi, *J. Chem. Soc., Chem. Commun.*, 320 (1975).
(6) (a) K. Hirai, H. Matsuda, and Y. Kishida, *Chem. Pharm. Bull.*, **21**, 1305 (1973); (b) A. K. Bose, B. Dayal, J. C. Kapur, B. Lal, and M. S. Manhas, *Tetrahedron Lett.*, 3135 (1974).
(7) S. Kukolja, *J. Am. Chem. Soc.*, **93**, 6267 (1971).
(8) F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, **77**, 572 (1955).
(9) D. L. Tuleen and T. B. Stephens, *Chem. Ind. (London)*, 1555 (1966).
(10) D. L. Tuleen and V. C. Marcum, *J. Org. Chem.*, **32**, 204 (1967).

Regiospecific Synthesis of Isogabaculine

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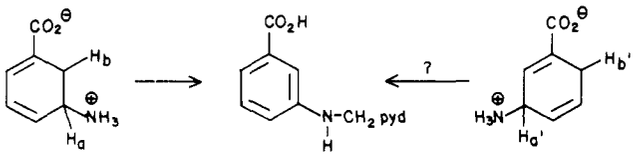
Received September 19, 1978

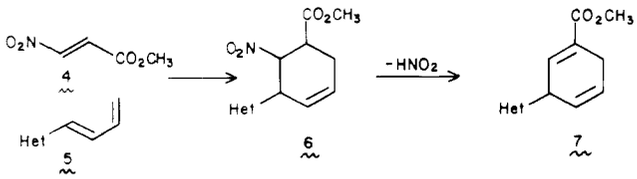
Recently, Mishima and co-workers reported the isolation of the amino acid gabaculine (1) from *Streptomyces toyocaensis*.[2] This curious compound, discovered in the course of studies on enzyme inhibitors, exhibited activity against γ-aminobutyrate aminotransferase (GABA-T).

Rando has set forth an interesting proposal wherein the activity of 1 arises from its competitive reaction with pyridoxal phosphate. It is felt that Schiff base formation is followed by irreversible conversion to *N*-(*m*-carboxyphenyl)pyridoxamine phosphate.[3] Presumably, the generation of **2** involves the usual Schiff base condensation from 1 + pyridoxal phosphate, followed by tautomerizations of H_a and H_b, successively. In the light of these conderations, it would be of interest to examine the behavior of compound **3** with pyridoxal phosphate. It will be recognized that hydrogens a′ and b′ in compound **3** are related in an allylic sense to hydrogens a and b in **1**.

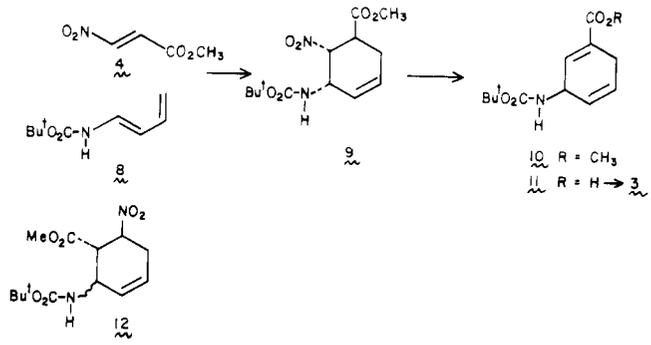


1 2 pyd = pyridoxyl 3

Syntheses of gabaculine have been described by Mishima[2] and subsequently by Sharpless.[4] We have been concerned with developing general routes to dihydrobenzenes containing heteroatoms at one of the sp^3 carbons.[5] Our approach, summarized below, involves Diels–Alder reactions of methyl β-nitroacrylate (**4**),[6] which achieve substitution patterns not accessible via the more precedented use of propiolate esters. It seemed attractive to apply this method to a synthesis of compound **3**, which we have termed "isogabaculine". An efficient regiospecific synthesis of **3** is described below.



Cycloaddition of the recently described 1-(*N*-acylamino)-1,3-diene **8**[7] with nitroacrylate **4** provided the Diels–Alder adduct **9**, which crystallized directly from the reaction medium in 68% yield. Examination of the mother liquors of the cycloaddition reaction indicated **9** to be the principal component. Chromatography of the mother liquors on silica gel afforded first, traces of an oily regioisomer of **9** whose NMR spectrum [δ 3.36 ($C\underline{H}CO_2Me$, dd, J = 12 and 6 Hz] indicated it to be structure **12**. In pure form only ca. 0.5% of **12** was obtained, though in fact, there may well have been as much as 1% present in the crude reaction mixture. There was next eluted additional traces of an apparent stereoisomer of **9**, though this was not obtained in pure form. The next fractions contained additional quantities of **9**. However, for preparative ease, the mother liquors were in fact not processed in the synthesis.



The stereochemistry of **9** can not be defined with certainty. It would appear that the *E* relationship of the carbomethoxy and nitro groups of **4** gives rise to a trans relationship of these groups in **9**. Indeed, the coupling constant between the "nitro" and "carbomethoxy" methine protons is 12 Hz. The coupling constant between the "nitro" and "urethane" methine protons is 5 Hz. This would tend to suggest the arrangement shown in **9**, wherein the carbomethoxy and nitro groups are equatorial while the urethane is quasi-axial. However, this assignment is not definitive since the stereoisomer of **9** could not be obtained in sufficiently pure form for meaningful NMR analysis. In any case, in keeping with earlier findings,[5] essentially complete regiochemical control was exerted by the nitro group.

Treatment of **9** with 1 equiv of diazobicycloundecene (DBU) furnished the dihydrobenzene derivative **10** in 70% yield. Conversion of **10** into "isogabaculine" (**3**) was accomplished in two steps. Hydrolysis of the ester with aqueous NaOH followed by acidification and immediate extraction with methylene chloride afforded the intermediate carbamate acid **11** in 73% yield. Treatment of **11** with a 10% aqueous HCl solution and passage of the resultant acidic solution through an ion-retardant ion resin (Bio-Rod AG 11A8), followed by lyophilization of the appropriate fractions, gave *dl*-isogabaculine (**3**) as a white powder in 55% yield. Investigation of the biological properties of **3** is planned.

Experimental Section[8]

Diels–Alder Reaction of Methyl Nitroacrylate (4) with *tert*-Butyl *trans*-1,3-Butadiene-1-carbamate (8). Formation of Methyl 5-(*N*-*tert*-Butoxycarbonylamino)-6-nitro-3-cyclohexene-1-carboxylate (9). A solution of 1.250 g (9.5 mmol) of nitroacrylate[6] **4** in benzene (3.5 mL) was added in dropwise portions over a 5-min period to a stirred solution of carbamate **8**[7] (1.613 g, 9.5 mmol) in benzene (6.5 mL) at room temperature. After stirring for 3 h at room temperature, the reaction mixture was filtered and the solid that was obtained was washed once with benzene (5 mL) to furnish **9** (1.934 g, 68%) as a colorless, analytically pure solid: mp 166–168 °C; λ_{max} ($CHCl_3$) 2.94, 5.77, 5.81, 6.41, 7.32 μm; δ (Me_2SO-d_6, 250 MHz) 1.36 (9 H, s, *tert*-butyl), 2.05–2.13 and 2.44–2.56 (2 H, m, allylic CH_2), 2.50–3.60 (1 H, m, R_2CHCO_2Me), 3.65 (3 H, s, OCH_3), 4.78–4.86 (1 H, m, R_2CHNCO_2), 5.10 (1 H, d of d, J = 12 and 5 Hz, R_2CHNO_2), 5.62–5.67 and 5.77–5.82 (2 H, m, olefinic), 7.25 (1 H, d, J = 9.7 Hz, NH).

Anal. Calcd for $C_{13}H_{20}N_2O_6$: C, 51.99; H, 6.71; N, 9.33. Found: C, 52.31; H, 6.74; N, 9.20.

Methyl 5-(*tert*-Butoxycarbonylamino)-2,5-dihydrobenzoate (10). A cooled (5 °C) solution of **9** (1.503 g, 5.0 mmol) in THF (20 mL) was treated with a solution of DBU (0.767 g, 5.0 mmol) in THF (5 mL) to form a yellow solution. A colorless precipitate began to form after 15 min. The reaction mixture was stirred for 6 h, during which time the temperature was gradually allowed to return to room temperature. The reaction mixture was poured into water (25 mL) and then ex-

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