liquid (16.4 g, 81%), consisting of a 60:17:10:10 mixture of **9c**, **10c**, **9b**, and **10b**: ^{1}H NMR (CCl_4) (Scheme V) δ 4.28 (1, d, J = 7.6 Hz, OCHO), 4.06 (1, m, H_E), 3.40 (1, dd, J = 8.4, 4.8 Hz, H_A), 3.27, 3.20 (6, 2 s, 2 OCH_3), 2.36 (1, m, H_B), 2.10 (1, ddd, J = -12.6, 7.0, 3.6 Hz, H_D), 1.73 (1, m, isopropyl CH), 1.42 (dt, J = -12.6, 7.5 Hz, H_C), 1.12 (3, d, J = 6.1 Hz, CH_3), 0.91, 0.86 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 85.18 (C_2), 43.62 (C_3), 36.12 (C_4), 72.53 (C_5), 102.36 (C_6), 53.33, 50.20 (2 OCH_3), 28.93 (C_7), 20.45, 20.20 (C_8, C_9), 22.64 (C_{10}).

General Procedure for the Formation of Acetals 10 with 2,3-Trans Relationship. 8 (0.1 mol), prepared by the general method for epimerization of aldehydes 7 to 8, was dissolved in 100 mL of CH_3OH. Then 0.3 mol of trimethyl orthoformate and 0.3 g of *p*-toluenesulfonic acid were added, and the mixture was refluxed for 5 h. After being cooled to room temperature, the solution was washed twice with saturated K_2CO_3 solution and dried (K_2CO_3). After filtration and evaporation of the solvent and excess trimethyl orthoformate the crude products were purified by distillation.

(2*S,3*R**)-2-Isopropyltetrahydrofuran-3-carbaldehyde dimethyl acetal (10a)** was obtained as a colorless liquid (17.1 g, 91%): bp 84-86 °C/16 Torr; IR 2960, 2940, 2880, 2830, 1465, 1450, 1390, 1365, 1260, 1215, 1190, 1120, 1075, 1060, 990, 900 cm^{-1}; ^{1}H NMR (CS_2) (Scheme V) δ 4.10 (1, d, J = 7.2 Hz, OCHO), 3.60 (2, m, H_E, H_F), 3.38 (1, t, J = 5.0 Hz, H_A), 3.25, 3.22 (6, 2 s, 2 OCH_3), 2.17 (1, m, H_B), 1.81 (2, t, J = 6.6 Hz, H_C, H_D), 1.64 (1, m, isopropyl CH), 0.88, 0.84 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (C_6D_6) (Scheme V) δ 85.75 (C_2), 44.53 (C_3), 28.71 (C_4), 67.16 (C_5), 106.66 (C_6) 54.23, 52.14 (2 OCH_3), 32.24 (C_7), 20.09, 17.60 (C_8, C_9). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71. Found: C, 63.74; H, 10.77.

(2*S,3*R**,5*S**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde dimethyl acetal (10b)** was obtained as a colorless liquid (16.6 g, 82%): bp 96-98 °C/16 Torr; IR 2960, 2930, 2880, 2830, 1465, 1450, 1390, 1385, 1365, 1190, 1120, 1105, 1080, 1065, 980, 910 cm^{-1}; ^{1}H NMR (CCl_4) (Scheme V) δ 4.15 (1, d, J = 7.2 Hz, OCHO), 3.82 (1, ddq, J = 9.6, 5.4, 6.0 Hz, H_E), 3.43 (1, dd, J = 5.0, 4.6 Hz, H_A), 3.27, 3.23 (6, 2s, 2 OCH_3), 2.18 (1, dddd, J = 9.6, 7.2, 5.0, 2.5 Hz, H_B), 1.90 (1, ddd, J = -12.5, 5.4, 2.5 Hz, H_C), 1.68 (1, m, isopropyl CH), 1.32 (1, ddd, J = -12.5, 9.6Hz, H_D), 1.14 (3, d, J = 6.0 Hz, CH_3), 0.90, 0.86 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 85.38 (C_2), 44.46 (C_3), 36.08 (C_4), 73.82 (C_5), 106.07 (C_6), 54.12, 51.77 (2 OCH_3), 32.25 (C_7), 19.77, 17.17 (C_8, C_9), 20.77 (C_{10}). Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.25; H, 10.92.

(2*S,3*R**,5*R**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde dimethyl acetal (10c)** was obtained as a colorless liquid (16.2 g, 80%), consisting of a 77:17:2 mixture of **10c**, **10b**, and **9b**: bp 96-100 °C/16 Torr; ^{1}H NMR (CCl_4) (Scheme V) δ 4.13 (1, d, J = 7.5 Hz, OCHO), 3.90 (1, m, H_E), 3.46 (1, t, J = 5.4 Hz, H_A), 3.26, 3.23 (6, 2 s, 2 OCH_3), 1.14 (3, d, J = 6.0 Hz, CH_3), 0.89, 0.86 (3, 2 d, J = 6.6 Hz, 2 isopropyl CH_3), other signals superimposed; ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 85.42 (C_2), 45.10 (C_3), 36.58 (C_4), 73.79 (C_5), 106.78 (C_6), 53.70, 51.41 (2 OCH_3), 31.66 (C_7), 20.14, 17.34 (C_8, C_9), 21.32 (C_{10}).

Wolff-Kishner Reduction of Aldehydes 7b and 8b. 7b or **8b**, 7.8 g (0.05 mol), 5 mL of $N_2H_4 \cdot H_2O$, and 5 g of KOH were dissolved in 25 mL of diethylene glycol and heated to 200 °C. When the N_2 evolution was completed, the mixture was cooled to room temperature and poured into cold water. The aqueous phase was extracted three times with ether, and the ethereal solution was washed with dilute HCl and saturated Na_2CO_3 solution and dried ($MgSO_4$). After filtration the solvent was distilled, and the crude products were purified by vacuum distillation.

(2*S,3*R**,5*S**)-2-Isopropyl-3,5-dimethyltetrahydrofuran (11)** was obtained as a colorless liquid (5.8 g, 82%): bp 34-35 °C/10 Torr; ^{1}H NMR ($CDCl_3$) (Scheme V) δ 4.02 (1, sextett, J = 6.0 Hz, H_E), 3.16 (1, t, J = 6.0 Hz, H_A), 2.3-1.5 (3, m, H_B, H_C, H_D), 1.18 (3, d, J = 6.0 Hz, CH_3), 1.02 (3, d, J = 6.0 Hz, CH_3), 0.95 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR ($CDCl_3$) (Scheme V) δ 91.78 (C_2), 35.46 (C_3), 42.50 (C_4), 73.46 (C_5), 32.11 (C_7), 19.07, 18.25 (C_8, C_9), 21.17, 19.85 (C_6, C_{10}). Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.76. Found: C, 75.93; H, 12.71.

$LiAlH_4$ Reduction of Aldehyde 7b. Crude **7b**, 15.6 g (0.1 mol), obtained following the general method for the rearrangement of **6b**, was dissolved in 100 mL of anhydrous ether. Treatment with 0.1 mol of $LiAlH_4$ at -78 °C and usual workup gave the corresponding alcohol. Without isolation the crude product was dissolved in ether and treated with *p*-toluenesulfonic acid chloride in the presence of pyridine. After workup the reaction product was dissolved in ether and treated again with 0.1 mol of $LiAlH_4$. Workup gave **(2*S**,3*S**,5*S**)-2-isopropyl-3,5-dimethyltetrahydrofuran (12,** 9.6 g, 68%): bp 146-148 °C (spinning band column); ^{1}H NMR ($CDCl_3$) (Scheme V) δ 3.9 (1, m, H_E), 3.28 (1, dd, J = 6.0, 7.0 Hz, H_A), 2.3-1.5 (3, m, H_B, H_C, H_D), 1.20 (3, d, J = 6.0 Hz, CH_3), 1.02 (3, d, J = 6.0 Hz, CH_3), 0.95 (6, d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR ($CDCl_3$) (Scheme V) δ 90.51 (C_2), 37.53 (C_3), 44.33 (C_4), 74.35 (C_5), 32.11 (C_7), 18.97, 18.15 (C_8, C_9), 21.33, 19.35 (C_6, C_{10}). Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.76. Found: C, 75.94; H, 12.82.

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Registry No. **2a**, 6117-80-2; **2b**, 6117-82-4; **3**, 41632-89-7; **4a**, 5417-35-6; **4b**, 108008-25-9; **4c**, 108008-26-0; **5**, 108008-24-8; **6a**, 35174-08-4; **6b**, 108008-27-1; **6c**, 108008-28-2; **7a**, 108008-29-3; **7b**, 108034-74-8; **7b** (alcohol), 108008-39-5; **7b** (tosyl ether), 108008-40-8; **7c**, 108008-31-7; **8a**, 77734-06-6; **8b**, 108008-30-6; **8c**, 108008-32-8; **9a**, 108034-75-9; **9b**, 108008-35-1; **9c**, 108008-37-3; **10a**, 108008-34-0; **10b**, 108008-36-2; **10c**, 108008-33-9; **11**, 108008-38-4; **12**, 108034-56-6; $CH(OCH_3)_3$, 149-73-5; 4-$H_3CSO_2C_6H_4COCl$, 98-59-9.

Polycyclic Amines via Novel [2 + 2] Cycloaddition of Imine[1]

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2,3,4,5,5-Pentachloro-1-azacyclopentadiene (1) has been shown to react differently with enes and dienes to form some unusual [4 + 2] cycloadducts. A [2 + 2] adduct is now isolated from a reaction of 1 with norbornadiene in acetonitrile. In addition to the previously reported azaaldrin (2) and isoazaaldrin (3) as products, a urazole-type adduct was identified by spectroscopic and X-ray diffraction studies to be **2b**. The mechanism of this new adduct formation via a novel [2 + 2] ene-imine reaction is discussed.

The construction of polycyclic compounds containing nitrogen via [4 + 2] cycloaddition of monoazadienes has made great strides in recent years. The 2-aza dienes have proved to be versatile addends in forming tetrahydro-

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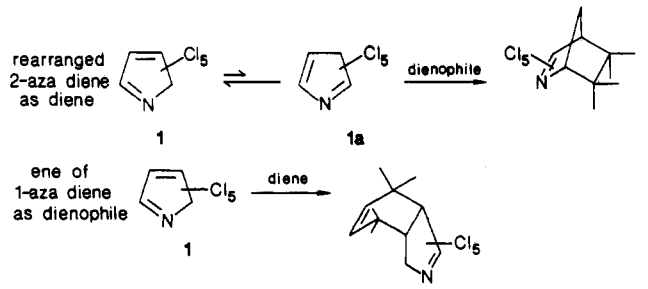
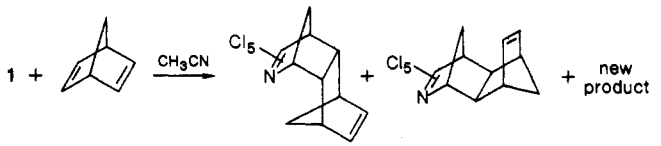
Scheme I



Scheme II



ratio 86:11:3

pyridines and the like.[3] On the other hand, the synthetic use of 1-aza dienes in Diels–Alder reactions have been limited to a few special compounds.[4] Our experience with the behavior of pentachloro-1-azacyclopentadiene (1) has shown striking differences from other 1-aza dienes. Its cycloaddition chemistry is shown in Scheme I. Thus, dienophiles add to 1 only after it has undergone rearrangement to the 2-aza diene **1a**, the products are 2-aza-norbornenes instead of the expected 1-aza compounds.[5] With conjugated dienes such as cyclopentadiene, the ene moiety of 1 reacts as a dienophile to yield [4 + 2] adducts.[6] In addition to these competitive diene and dienophilic properties, we report herein another new reactivity. It involves the imine moiety of 1 participating in a novel [2 + 2] ene–imine cycloaddition.

Results and Discussion

Previously we have reported the Diels–Alder reaction of pentachloro-1-azacyclopentadiene 1 in excess norbornadiene at 90 °C.[7] The major adduct, isolated in about 80% yield, was azaaldrin (**2**), an adduct of the 2-aza diene **1a**. A minor product was identified as isoazaaldrin (**2a**), a stereoisomer of **2**, which features an exo-endo skeleton as compared to the endo-exo of **2**. The surprise in this and subsequent cycloadditions of 1 with various dienophiles as well as dienes was the absence of any 1-aza adducts.[5,6] Hence, there is continuing interest to determine if changing reaction variables or detection technique might reveal new reaction products. By carrying out the norbornadiene reaction in acetonitrile, a third product in addition to **2** and **2a** was indeed detected by GLC analysis of the reaction mixture (Scheme II). The new product was isolated by column chromatography on silica gel and recrystallized from 2-propanol. The X-ray crystallographic ORTEP drawing showing structure **2b** is shown in Figure 1 (supplementary material).

Scheme III

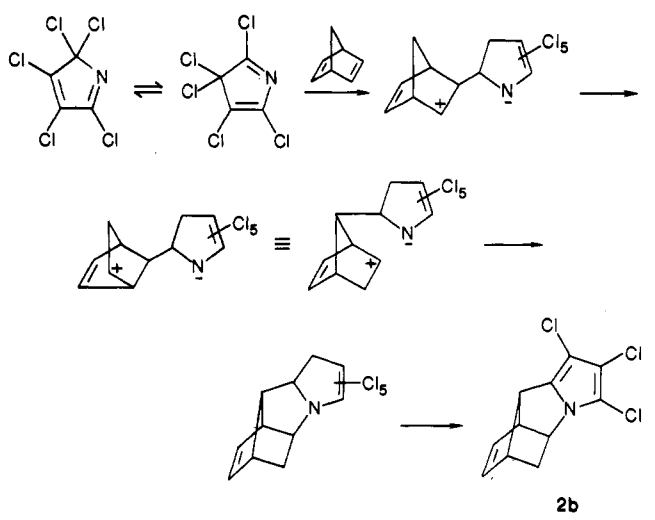


Table I. Crystal Data for $C_{11}NCl_3H_8$

mol formula	$C_{11}H_8NCl_3$
mol wt.	260.55
cell constant[a]	
a, Å	10.628 (7)
b, Å	8.886 (3)
c, Å	11.932 (10)
cell vol, Å^3	1082
linear abs coeff, cm^{-1}	8.12
space group	$P2_1/n$
molecules/unit cell	4
max cryst dimen, mm	1.8 × 0.5 × 0.4
calcd density, g cm^{-3}	1.60

[a] Mo Kα radiation; λ = 0.71069 Å; ambient temperature, 23 ± 1 °C.

The formation of the new adduct **2b** appears to be the first example of a thermal cycloaddition of an olefin to an imine. It is all the more unusual since this [2 + 2] is able to compete, albeit as a minor pathway, with the mainstream [4 + 2] cycloaddition occuring on the same diene. The [2 + 2] reaction probably proceeds via a dipolar intermediate in a multistep mechanism as shown in Scheme III. A significant solvent effect was observed indicating that the formation of the dipolar intermediate may be rate determining. Thus, GLC analysis of reaction mixtures showed that the adduct **2b** accounted for 3% of the cycloadducts in acetonitrile but was reduced to less than 1% in benzene and completely disappeared in cyclohexane. The last step involves aromatization to form the pyrrole nucleus via dechloriantion.

Experimental Section

^{1}H NMR and ^{13}C NMR spectra were obtained with a Varian XL-300 spectrometer. NMR samples were prepared in $CDCl_3$ containing 1% tetramethylsilane (δ_{Me_4Si} = 0). Solid IR spectra were run on a Nicolet 7000 Series FT-IR. GLC analysis was performed on a Varian 2700 chromatograph with dual flame-ionization detector using a 6 ft × 0.125 in. aluminum column packed with 10% SE-30 on Chromosorb WAW DMCS and at 30 mL/min of nitrogen, T_i = 220 °C, T_d = 250 °C, T_c = 190 °C. Combustion analysis was performed by Guelph Chemical Laboratories Ltd. Guelph, Ontario, Canada.

(5α,5aβ,8α,8aβ)-1,2,3-Trichloro-5,5a,8,8a-tetrahydro-5,8-methanocyclopenta[*a*]pyrrolizine (2b). To 6.5 g (27 mmol) of pentachloro-1-azacyclopentadiene (1) in 200 mL of dry acetonitrile was added 9.1 g (108 mmol, 4 equiv) of bicyclo[2.2.1]-hepta-2,5-diene, and the mixture was refluxed for 24 h. The dark

(1) This is part 8 of the Aza Diene Chemistry series.
(2) X-ray diffraction studies were carried out at the Department of Chemistry, College of Arts and Sciences, University of Alabama, Tuscaloosa, Alabama 35486.
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Table II. Some Notable Bond Distances (Å) and Angles (deg) for the New Product $C_{11}H_8NCl_3$

Bond Distances	
C(8)-C(8a)	1.70
C(5)-C(9)	1.68
C(1)-C(8b)	1.29
C(N)-C(5)	1.48
C(5)-C(5a)	1.48
C(N)-C(3)	1.30
Bond Angles	
C(5a)-C(6)-C(7)	102
C(6)-C(7)-C(8)	114
C(5)-C(9)-C(8)	98
C(5a)-C(5)-C(9)	105
C(5)-C(5a)-C(6)	114
C(7)-C(8)-C(8a)	95

brown reaction mixture containing the products: **2** (GLC, t_r = 12.5 min), **2a** (GLC, t_r = 14.5 min), and **2b** (GLC t_r = 11.5 min), was evaporated and the residue chromatographed on 100 g of silica gel with hexane as the eluent. Fractions 4-6 containing compound **2b** were evaporated, and the residue were recrystallized from 2-propanol to give 0.21 g (3%) of white crystal: mp 45 °C; mass spectrum, m/z 260 ($M^{\cdot+}$), 225 ($M^{\cdot+}$ - Cl), 190 ($M^{\cdot+}$ - 2Cl), 155 ($M^{\cdot+}$ - 3Cl), 182 (trichloropyridine), 78 (benzene); ^{1}H NMR (δ) H5 4.33, H5a 3.30, H6 5.84, H7 6.47, H8 2.76, H8a 3.46, $H9_{endo}$ 1.27, $H9_{exo}$ 0.79, (J, Hz) 5,5a 2.0, 5a,8a 1.0, 5a,6 3.2, 6,7 5.8, 7,8 3.1, 8,8a 1.0, $8,9_{exo}$ 4.5, $9_{endo},9_{exo}$ 12.0, $5,9_{endo}$ 4.0; ^{13}C NMR (δ) C5 58, C5a 59.5, C6 127, C7 142, C8 49, C8a 61.4, C8b 132, C9 36.5, C1 104, C2 108, C3 110, (J, Hz) 5 163, 5a 147, 6 172, 7 172, 8 153, 8a 151, 9 137.

Anal. Calcd for $C_{11}H_8NCl_3$: C, 50.69; H, 3.09; N, 5.38. Found: C, 50.22; H, 3.12; N, 5.51.

X-ray Crystallography of 2b. Single crystals of the compound were sealed in thin-walled glass capillaries prior to examination. Final lattice parameters as determined from a least-squares refinement of the angular settings of 15 reflections (θ > 20°) accurately centered on an Enraf-Nonius CAD-4 diffractometer are given in Table I. Data were collected on the diffractometer by using procedures which have been previously described.[5] Three standard reflections were used during data collection; none of the intensities decayed by more than 8%. One independent quadrant was measured out to 2θ = 44° and a slow scan was performed on a total of 1546 unique reflections. The final value of R = 0.098 was achieved. The bond lengths and angles of **2b** are shown in Table II; the positional and thermal parameters in Table III (supplementary material).

Supplementary Material Available: Figure 1 (ORTEP drawing of **2b**) and Table III (positional and thermal parameters for **2b**) (2 pages). Ordering information is given on any current masthead page.

Synthesis of 4(5)-Acyl-, 1-Substituted 5-Acyl-, and 1-Substituted 4-Acyl-1*H*-imidazoles from 4-Aminoisoxazoles

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4-Aminoisoxazoles can be acylated with a wide variety of activated carboxylic acids. Hydrogenation of the resulting amides gives α-(acylamino)enaminones, which cyclize to 4(5)-acylimidazoles upon treatment with base. This method allows for the synthesis of acylimidazoles with a wide range of substituents at C-2. Utilization of N-substituted 4-aminoisoxazoles in the same sequence of reactions yields 1-substituted 5-acylimidazoles, a substitution pattern not otherwise easily prepared. Treatment of α-(acylamino)enaminones, derived from N-unsubstituted isoxazoles, with primary amines leads to incorporation of the amine at the β-position with concomitant expulsion of ammonia. This sequence efficiently yields 1-substituted and 1,2-disubstituted 4-acylimidazoles but does not give satisfactory yields of 5-substituted 4-acylimidazoles due to steric inhibition of the amine exchange.

Friedel-Crafts acylation of imidazoles is not possible because of the deactivation that occurs upon complexation of the basic imidazole with the Lewis acid.[1] As a result, other strategies must be employed to synthesize *C*-acylimidazoles. 2-Acylated derivatives can be synthesized indirectly through manipulation of the corresponding hydroxymethyl derivatives, obtained by hydroxymethylation,[2] or directly through carbanions derived from suitably N-protected imidazoles[3,4] and through the photochemical rearrangement of *N*-acylimidazoles.[5] Depending on the substituent pattern, the latter method can also provide 4-acylated imidazoles.[6] As in the 2-acyl series, 4(5)-acylimidazoles can be indirectly prepared through manipulation of the hydroxymethyl compounds obtained by either hydroxymethylation[2,7] or ring synthesis.[8] Metalation chemistry has also been applied to the synthesis of 4(5)-acylimidazoles; however, in addition to N-protection, this generally requires that the 2-position be suitably blocked by a protecting group or an unreactive substituent.[3,9] Our specific interest in 4(5)-acetylimidazoles as pharmaceutical intermediates led us to pursue efficient syntheses of these compounds that proceeded through ring-forming reactions. The first such synthesis developed utilized 3-bromo-4-ethoxy-3-buten-2-

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