1,3-Dipolar Cycloadditions to Difluoroallene. The Regiochemistry of Diazoalkane Additions

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The regiochemistry of 1,3-dipolar diazoalkane cycloadditions to 1,1-difluoroallene (DFA) and fluoroallene was investigated. While simple frontier orbital HOMO–LUMO interactions seem to control the π-bond specificity with which DFA cycloadds to diazoalkanes, the orientation with which these dipoles add to DFA's C_2–C_3 bond varies and is determined by a balance of two factors. One is a frontier orbital interaction which in the case of allene dipolarophiles is apparently dominated by a novel secondary orbital interaction. Steric effects, however, become increasingly important as the carbon terminus of the diazoalkane becomes increasingly bulky.

1,1-Difluoroallene (DFA) is a remarkably reactive dienophile which has been shown to undergo Diels–Alder reactions exclusively with its non-fluorine-substituted C_2–C_3 double bond, this in dramatic contrast to its lack of such regiospecificity in [2 + 2] reactions.[1] Knowing that DFA's LUMO is the C_2–C_3 π^* orbital,[2] we hypothesized that all concerted cycloadditions in which the DFA LUMO interaction is dominant should take place regiospecifically at its C_2–C_3 π bond.

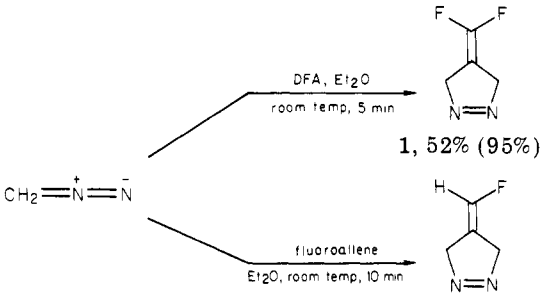
While the orientation of diene addition to DFA's C_2–C_3 bond showed a general lack of regioselectivity, it was believed that significant insight into those factors giving rise to DFA's regiochemical behavior would be provided by a study of additions of 1,3-dipoles, which are generally more regioselective in their cycloadditions.

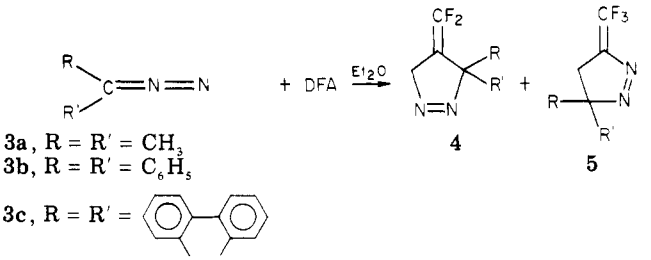
In this report we would like to present our results on the cycloadditions of a number of diazoalkanes to DFA and fluoroallene, results which reinforce our hypothesis that the regiochemical aspects of DFA cycloadditions are unusually mechanistically diagnostic. Diazoalkanes were chosen for our initial study in view of the considerable amount of theoretical[3] and experimental[4] data that is available relative to their behavior as 1,3-dipoles. Moreover the expected pyrazoline adducts were of great interest to us as potential precursors to fluorinated trimethylenemethanes.

Results

Diazomethane indeed was found to undergo totally regiospecific cycloaddition to both DFA[5] and fluoroallene[5,6] to form pyrazolines **1** and **2**. ^{19}F NMR analysis of the product mixtures indicated only one product to have formed in each case. Adducts **1** and **2** were extremely labile compounds but could be purified by careful distillation at reduced pressure, and they were characterized spectroscopically.

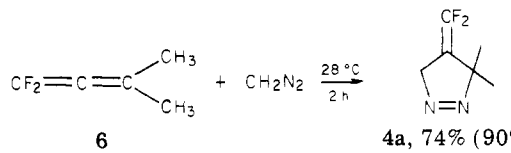
In contrast, the cycloadditions of dimethyldiazomethane, diphenyldiazomethane, and diazofluorene (**3a–c**) with DFA





were not as regiospecific as those of diazomethane. Each led to *two* adducts, **4** and **5**. While exclusive reaction with the C_2–C_3 π bond of DFA was retained, the orientation of dipole addition lost regiospecificity (Table I).

In the reaction of 2-diazopropane, 39% of the second regioisomer **5a** was observed. While the NMR yield was 99%, pure samples of the products could not be obtained due to their instability to either GLPC or LC conditions. While all NMR and IR spectra of the mixture were consistent with the structural assignments, the structure of **4a** was further confirmed by independent synthesis, via



cycloaddition of diazomethane to 1,1-difluoro-3-methyl-1,2-butadiene (**6**).[5] This cycloaddition proved also to be regiospecific as determined by ^{19}F NMR of the product mixture. Thus the structure of **4a** is confirmed. The structure of **5a**, however, still relies on spectra of the reaction mixture.

The reaction of DFA with diphenyldiazomethane is slower, and the second regioisomer, **5b**, now has become the major product. **5b** was unstable in chloroform solution, but stable in acid-free solvents such as ether. It was unstable to silica gel chromatography but could be purified by rapid recrystallization from hexane. Minor isomer **4b** could be isolated via silica gel chromatography of the mother liquor.

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Table I. Regiochemistry of Diazoalkane Addition to DFA

diazoalkane	conditions	relative yields of regioisomers 4	5	total yield,[a] %
diazomethane	room temp, 5 min	100	0	95
3a	0 °C, 5 min	61	39	99
3b	28 °C, 5 h	14	86	95
3c	room temp, 4 h	28[b]	72	99

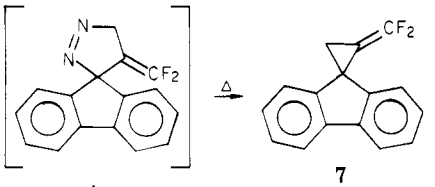
[a] NMR yields. [b] Not isolated (see text).

Table II. ^{1}H NMR Chemical Shifts and Coupling Constants to Fluorine for the Methylene Protons of 4- and 5-(Difluoromethylene)-1-pyrazolines

4-isomer	δ CH_2	J_{HF}, Hz	5-isomer	δ CH_2	J_{HF}, Hz
1	5.1	3.7			
4a	5.2	3.8	5a	2.1	3.7
4b	5.3	3.5	5b	3.0	3.6
4c[a]	5.6	3.5	5c[a]	3.0	3.8

[a] Compound not isolated in pure form.

The reaction of diazofluorene with DFA also yielded regioisomer **5** as the major adduct. While the isolated yield for the crude product mixture was essentially quantitative, the minor isomer **4c** was thermally very unstable, ex-



4c 7

truding nitrogen at room temperature during the course of the reaction to give **7**, which was the product isolated. Pyrazoline **4c** could be observed in the ^{1}H NMR spectrum during the reaction, but by the time reaction was complete, it had all been transformed to **7**. The ^{1}H NMR chemical shift and coupling constant to fluorine in **4c** for the methylene protons are completely consistent with the proposed structure as can be seen by looking at Table II.

Pyrazoline **5c** could not be purified by recrystallization as had been **5b**, and it was just as unstable to silica gel chromatography. However, spectra of the mixture containing 72% pyrazoline **5c** were consistent with the proposed structure as is seen by looking at Table II.

Conjugation of the difluoromethylene group with the azo group appears to lower the $=CF_2$ stretching frequency in the IR spectra of **5a–c** to 1756, 1757, and 1756 cm^{-1}, respectively. More typical $=CF_2$ stretching frequencies are observed for **4a–c**, being 1797, 1780, and 1780 cm^{-1}, respectively.

Discussion

Cycloadditions of diazoalkanes are generally rationalized in terms of their being predominantly HOMO (dipole)–LUMO (dipolarophile) controlled pericyclic reactions.[7] The fact that DFA and fluoroallene cycloadd to diazoalkanes using exclusively their non-fluorine-substituted C_2–C_3 bonds is consistent with this assumption and the

Table III. Solvent Study of Product Ratio for Reaction of Difluoroallene with Diphenyldiazomethane

solvent	dielectric constant	product ratio 4b	5b
Me_2SO-d_6	46.7	14.5	85.5
acetone-d_6	20.7	12.9	87.1
ether	4.3	12.0	88.0
CCl_4	2.2	16.5	83.5
hexane	1.9	14.3	85.7
pentane	1.8	15.6	84.4

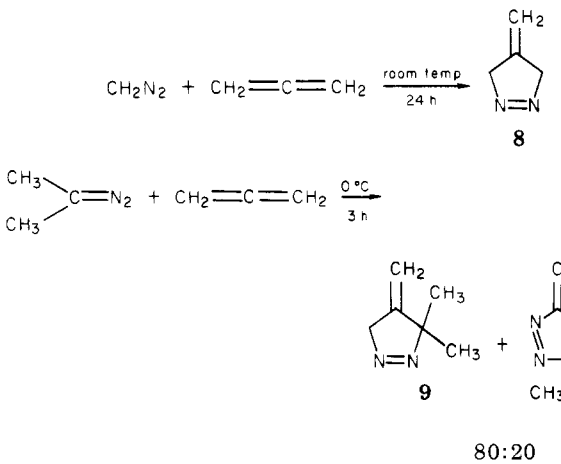
results reinforce our hypothesis of the diagnostic nature of these reactions. The FMO theory however fails to explain the dramatic reversal of regioselectivity with respect to diazoalkane. Calculations indicate that diazomethane, diazopropane, and diphenyldiazomethane all have virtually identical orbital coefficients for their HOMO.[8] This leads to the incorrect prediction that their regiochemistry in cycloadditions should be the same.

One possible explanation could be polar effects in the cycloaddition transition state. The lack of a significant solvent-polarity effect on **4:5** product ratios as seen in Table III diminishes the credibility of this explanation.

It is proposed that the observed regiochemistry for the diazoalkane cycloadditions be rationalized in terms of two opposing effects, one involving frontier orbital interaction and the other a steric effect.

If a preference in terms of frontier orbital interaction is for the carbon end of the 1,3-dipole to interact with the central carbon of difluoroallene, a preference for formation of pyrazoline **4** would be observed. Thus when both ends of the diazoalkane have similar sizes, as with diazomethane, the frontier orbital interaction is dominant and product **4** is exclusively observed. However, as the substituents on the diazoalkane become larger, the sterically more favored product **5** becomes increasingly important in the reaction mixture, actually becoming the major product with bulky aromatic substituents. This reversal of regiochemistry has been observed before for cycloadditions of diazoalkanes with thiete 1,1-dioxide.[8]

A survey of the literature reveals that allene itself reacts with diazomethane[9] and diazopropane,[9,10] though at much slower rates than difluoroallene. The product ratios are similar to the difluoroallene cycloadditions. Thus the same steric reversal of regiochemistry appears to be occurring for allene as with difluoroallene.



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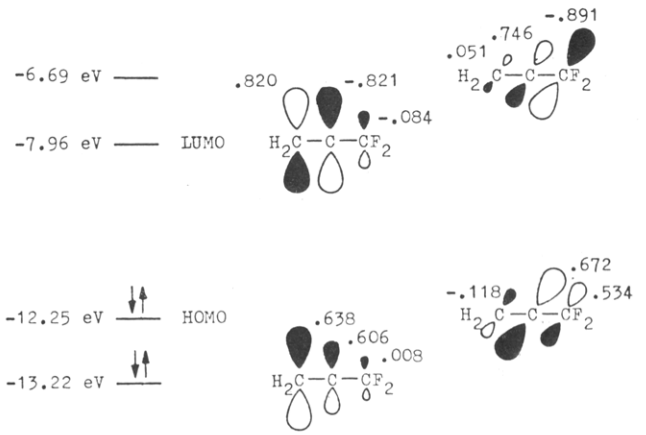

Figure 1. Extended Hückel MO energies and AO coefficients for difloroallene.

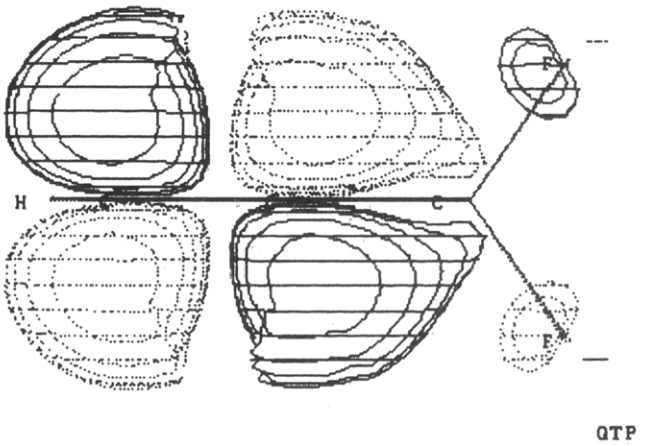

Figure 2. Contour surface for the wave function of the difluoroallene LUMO.

What *is* the origin of the FMO-controlled regiochemical preference in these cycloadditions? To answer this question one needs to know the orbital coefficients and energies for the 1,3-dipoles and for difluoroallene. Calculations for 1,3-dipoles have been reported in the literature.[11,12] Calculations for difluoroallene have also been reported[2] but the orbital coefficients necessary for predicting regiochemistry of cycloadditions have not been presented. Consequently, it was necessary to calculate the shapes of the difluoroallene molecular orbitals.

Extended Hückel calculations[13,14] using the experimental geometry for difluoroallene derived from its microwave spectrum[15] gave the results presented in Figure 1. The energies are the extended Hückel energies and are, of course, not reliable. However, the shapes of the molecular orbitals are accurately represented by the extended Hückel method.

A similar calculation for diazomethane indicated that the larger terminal HOMO coefficient lies on the carbon atom (0.741 vs. −0.641) while for the LUMO, the larger coefficient lies on terminal nitrogen (−0.833 vs. 0.013).

The experimental FMO energies for difluoroallene[2] (HOMO = −10.1 eV, LUMO = −0.8 eV) and diazomethane[11] (HOMO = −8.8 eV, LUMO = +0.2 eV) indicate clearly that the controlling FMO interaction is that of the LUMO of difluoroallene with the HOMO of diazomethane.

It is apparent from Figure 1 that the classical view of an allene as having two orthogonal, noninteracting π bonds is an oversimplification. Looking more closely at the LUMO of difluoroallene, which is the frontier orbital of interest in explaining the regiochemistry of its concerted cycloadditions, one can see the significance of including all of the atomic orbital contributions. Figure 2 is a graph of the LUMO for difluoroallene, which includes the contributions from atomic orbitals of all the atoms. The contributions to the wavefunction from the carbon and fluorine atomic orbitals of the CF_2 obviously have a significant effect on shape of the LUMO. Specifically, the bonding interaction of the C_1 p-orbital with the C_2 p-orbital results in *reinforcement* of the wave function at C_2. What this means is that even though the AO coefficients for C_3 and C_2 are virtually identical (0.820 and 0.821), the value of the wave function is larger at C_2 for the LUMO.

The kind of orbital contribution we see here is generally called a "secondary interaction" and is usually ignored when predicting regiochemistry of cycloadditions. Interactions of a similar nature have been proposed to explain regiochemical aspects of nitrone and diazomethane cycloadditions to cyanoacetylenes[16] and acetylenecarboxylic esters,[17] respectively. To our knowledge such interactions have not been previously invoked as a factor in allene cycloadditions.

It appears moreover that the enhancement of the apparent coefficient at C_2 of difluoroallene is to a significant effect due to the presence of the fluorine substituents. A similar calculation of the LUMO orbital coefficients for allene (C_2H_4) shows coefficients of +0.610 and −0.652 at C_1 and C_2, respectively, with only a relatively small (−0.01) contribution from C_3.

In an effort to demonstrate more conclusively the regiochemical significance of this "secondary orbital interaction" a perturbation calculation was performed for the two modes of cycloaddition of diazomethane to difluoroallene. Such a calculation involves an estimation of the change in energy which accompanies the interaction of the two species, diazomethane and DFA, which are involved in the cycloaddition.[18-20] For our model, only the frontier orbital interaction of the HOMO of the diazomethane and the LUMO of difluoroallene were considered, and perturbation calculations for the two regioisomeric transition states (i.e., for formation of **4** and **5**) were performed by the extended Hückel method. For this model, diazomethane is still linear and it is positioned exactly between C_2 and C_3 of difluoroallene at a distance of 2.7 Å. The values obtained for the numerator of the equation are −0.0620 for formation of regioisomer **4** and −0.0456 for formation of regioisomer **5**. These results predict product **4** to be favored and are in agreement with the experimental fact that **4** is preferred in the absence of steric interactions.

Conclusions

The observations that fluoroallene and difluoroallene

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cycloadd to diazoalkanes using exclusively their nonfluorine-substituted C_2–C_3 bonds is consistent with the assumption that these reactions are HOMO (dipole)–LUMO (dipolarophile) controlled pericyclic processes.

With regard to the orientation of addition of the diazoalkane moieties, two factors seem to be involved. First, dipolar cycloadditions to fluoroallenes should inately favor a regiochemistry which binds the dipole terminus of the larger HOMO coefficient to the central carbon of the allene. This is not simply due to the magnitude of the AO coefficient at the central carbon, but is due to a secondary orbital interaction in which a contribution from the "orthogonal" allenic carbon (in our cases the fluorine-substituted carbon) *reinforces* the wave function at the central carbon.

In the case of diazoalkanes, the carbon atom of the dipole has the larger HOMO coefficient and thus becomes preferentially bound to the central carbon of the allene reagents. However, when substituents other than hydrogen are bound to this carbon, steric interactions create a situation in which the frontier orbital effects apparently become overwhelmed, with the result that the alternative regioisomer becomes increasingly favored.

Experimental Section

Infrared spectra were determined on a Perkin-Elmer 283B spectrophotometer and absorption bands are reported in cm^{-1}. The 60-MHz ^1H NMR spectra were determined on a Varian EM 360L spectrometer; 100-MHz spectra were taken with either a Jeol FX-100 instrument or a Varian XL-100 instrument; 300-MHz spectra were determined on a Nicolet NT-300 spectrometer. Chemical shifts are reported in ppm downfield of internal Me_4Si in $CDCl_3$ solution. The ^{19}F NMR spectra were determined on the Varian XL-100 or the Nicolet NT-300 instruments. Chemical shifts are reported in ppm upfield of internal $CFCl_3$ in $CDCl_3$ solution. The ^{13}C NMR spectra were determined on the Jeol FX-100 or the Nicolet NT-300 instruments. Chemical shifts are reported in ppm downfield of internal Me_4Si in $CDCl_3$ solution. All assignments of ^{13}C NMR resonances are made with the aid of off-resonance spectra or pulse-sequence spectra. Mass spectra were determined on an AEI-MS 30 spectrometer at 70 eV. Exact masses were also determined on an AEI-MS 30. The GLPC analyses and preparative separations were performed on a Varian Aerograph 90-P gas chromatograph with thermal conductivity detector. Elemental analyses were performed by Atlantic Microlabs.

4-(Difluoromethylene)-4,5-dihydro-3*H*-pyrazole (1). An ether solution of diazomethane (75 mL) was prepared from 7.00 g (32.7 mmol) of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide. The solution was vacuum transferred to a glass tube. Into the tube was condensed 2.50 g (32.8 mmol) of difluoroallene. The tube was sealed under vacuum and allowed to warm to room temperature. The yellow solution turned rapidly colorless.

After concentration by rotary evaporation at reduced pressure, the residue was distilled at reduced pressure using a short-path distillation apparatus. The clear, colorless distillate was collected in a flask cooled with a salt–ice bath. The unstable product was stored on dry ice under nitrogen. A total of 2.0 g (52%) of **1** was obtained: bp 41.0–41.5 °C (31 mm), 48.5–49.0 °C (42 mm); UV_{max} 320 nm; IR (film) 2930, 1797 (s), 1554, 1428, 1300, 1275, 1080, 930 cm^{-1}; ^1H NMR (60 MHz) δ 5.1 (t, J_{HF} = 3.7 Hz); ^{19}F NMR (100 MHz) ϕ 84.8 (pentet, J_{HF} = 3.8 Hz); mass spectrum M^+ 118.03375 ± 0.00125 (11 ppm); calcd for $C_4H_4N_2F_2$, 118.03425; deviation −0.00050 (4 ppm).

NMR Yield. Into an NMR tube containing 53.5 mg of benzene (cooled in an ice bath) was added 0.350 mL of diazomethane solution in ether. Into the tube was condensed 0.227 mmol of difluoroallene and the tube was sealed under vacuum. After 15 min at room temperature the ^1H NMR of the yellow solution was integrated. The average of 5 integrations gave an NMR yield of 94.6%.

4-(Difluoromethylene)-4,5-dihydro-3,3-dimethyl-3*H*-pyrazole (4a) and 5-(Difluoromethylene)-4,5-dihydro-3,3-dimethyl-3*H*-pyrazole (5a). An ether solution of diazopropane[21] (20 mL) was prepared from 2.50 g (34.7 mmol) of acetone hydrazone. The solution was vacuum transferred to a 50-mL glass tube and 2.71 g (35.7 mmol) of difluoroallene were condensed into the tube, which was sealed under vacuum. After 3.5 h at −78 °C, the orange diazopropane color was completely gone. The tube was opened and the solution was concentrated by rotary evaporation at reduced pressure to give 0.81 g of clear amber liquid. Analysis by ^1H NMR indicated relative yields of 48.7% for **4a**, 31.4% for **5a**, and 19.9% acetone azine. The unstable products were not able to be isolated from the reaction mixture.

Analysis of the reaction mixture by IR, ^1H NMR, and ^{19}F NMR gave for **5a**: IR (CCl_4) 1756 cm^{-1} (s); ^1H NMR (60 MHz) δ 2.1 (t, 2 H, J_{HF} = 3.7 Hz), 1.3 (s, 6 H, CH_3); ^{19}F NMR (100 MHz) ϕ 83.2 (d of t, 1 F, J_{FF} = 25, J_{HF} = 3.8 Hz), 94.4 (d of t, 1 F, J_{FF} = 25, J_{HF} = 3.9 Hz).

Spectra of **4a** from the mixture were identical with spectra of the pure material prepared by the alternate route. The relative yields obtained by ^1H NMR integration were 61% for **4a** and 39% for **5a**.

The NMR yield (99%) was determined as for **1**, with DMF the internal standard.

4-(Difluoromethylene)-4,5-dihydro-3,3-dimethyl-3*H*-pyrazole (4a). To an ether solution of diazomethane prepared from 3.5 g (16.3 mmol) of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide in 30 mL of ether was added 858 mg (8.25 mmol) of difluorodimethylallene **6**. After 3 h at room temperature, the pale yellow solution was concentrated at reduced pressure by rotary evaporation and the residue was distilled at reduced pressure using a short-path distillation apparatus. The clear, colorless distillate was collected in a dry ice chilled flask. The unstable liquid was stored on dry ice under nitrogen. A total isolated yield of 0.891 g (74%) of **4a** was obtained: bp 37–38 °C (19 mm), 48–50 °C (36 mm); IR (CCl_4) 2985, 2940, 1780 (s), 1556, 1463, 1285, 1245, 1135, 1050, 920 cm^{-1}; ^1H NMR (60 MHz) δ 5.19 (t, 2 H, J_{HF} = 3.8 Hz), 1.5 (s, 6 H); ^{19}F NMR (100 MHz) ϕ 81.3 (d of t, 1 F, J_{FF} = 59, J_{HF} = 3.6 Hz), 89.7 (d of t, 1 F, J_{FF} = 59, J_{HF} = 3.7 Hz); ^{13}C NMR (100 MHz) δ 149.9 (t, J_{CF} = 284 Hz, $=CF_2$), 89.0 (t, J_{CF} = 22 Hz, C_4), 88.5 (d, J_{CF} = 5 Hz, C_3), 75.9 (d, J_{CF} = 5 Hz, CH_2), 23.9 (CH_3); mass spectrum M^+, 146.0655 ± 0.00134 (9 ppm); calcd for $C_6H_8N_2F_2$, 146.06555; deviation, −0.00005 (0.4 ppm). Anal. Calcd: C, 49.31; H, 5.52; N, 19.17. Found: C, 49.08; H, 5.56; N, 18.99.

The NMR yield (99%) was determined as for **1**, with DMF the internal standard.

5-(Difluoromethylene)-4,5-dihydro-3,3-diphenyl-3*H*-pyrazole (3b) and 4-(Difluoromethylene)-4,5-dihydro-3,3-diphenyl-3*H*-pyrazole (5b). Into a 60-mL glass tube containing 2.4 g (12.4 mmol) of diphenyldiazomethane[22] and 20 mL of ether was condensed 1.03 g (13.6 mmol) of difluoroallene. The tube was sealed under vacuum. After 5 h at room temperature, the deep red color had faded to pale yellow. The tube was opened and the ether was removed by rotary evaporation at reduced pressure to give 3.18 g (95%) of pale yellow solid. Recrystallization from hexane gave a pale yellow solid **4b**: mp 60–65 °C; IR (CCl_4) 3070, 3040, 1757 (s), 1604, 1499, 1452, 1307, 1180, 1096, 699 cm^{-1}; ^1H NMR (60 MHz) δ 7.22 (s, 10 H), 3.02 (t, 2 H, J_{HF} = 3.6 Hz); ^{19}F NMR (100 MHz) ϕ 79.8 (d of t, 1 F, J_{FF} = 17, J_{HF} = 3.6 Hz), 91.5 (d of t, 1 F, J_{FF} = 17, J_{HF} = 3.8 Hz); mass spectrum (12 eV), 242 (M^+ − 28, 100), 241 (69), 222 (85), 204 (10), 191 (16), 165 (12), 127 (26), 109 (15). Anal. Calcd: C, 71.10; H, 4.47; F, 14.06. Found: C, 71.33; H, 4.65; F, 13.84.

Compound **4b** was very unstable in chloroform solution and unstable to silica gel. The mother liquor from recrystallization was concentrated by rotary evaporation at reduced pressure to give an oil which was subjected to silica gel chromatography ($CHCl_3$). A yellow oil was obtained which was **5b**: IR (CCl_4) 3070, 3040, 1780 (s), 1603, 1560, 1497, 1450, 1284, 1105, 1036, 697 (s) cm^{-1}; ^1H NMR (60 MHz) δ 7.3 (m, 10 H), 5.34 (t, 2 H, J_{HF} = 3.5 Hz); ^{19}F NMR (100 MHz) ϕ 78.6 (d of t, 1 F, J_{FF} = 44, J_{HF} = 3.5 Hz), 82.0 (d of t, J_{FF} = 44 and J_{HF} = 3.5 Hz); mass spectrum, 270 (M^+, 3), 242 (96), 221 (100), 213 (67), 193 (60), 165 (66), 105 (91), 77 (94).

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The relative yields of products by ^1H NMR integration were 14% for **4b** and 86% for **5b**.

4′-(Difluoromethylene)-4′,5′-dihydrospiro[9*H*-fluorene-9,3′-[3*H*]pyrazole] (4c), 5′-(Difluoromethylene)-4′,5′-dihydrospiro[9*H*-fluorene-9,3′-[3*H*]pyrazole] (5c), and 2-(Difluoromethylene)spiro[cyclopropane-1,9′-[9*H*]fluorene] (7). Into a 20-mL glass tube containing 0.485 g (2.52 mmol) of diazofluorene[23] and 7 mL of ether was condensed 0.574 g (7.56 mmol) of difluoroallene. The tube was sealed under vacuum. After 3 h at room temperature, the deep red color had faded to pale amber. The tube was opened and the solvent was removed by rotary evaporation at reduced pressure to give 0.655 g (98%) of thick amber oil. Analysis by ^1H NMR indicated relative yields of 72% for **5c** and 28% for **7**. Flash chromatography (silica gel), eluting with 95% hexane/5% EtOAc, gave 132 mg (20%) of yellow solid **7**: R_f 0.54; mp 78–82 °C (from hexane); IR (CCl_4) 3075, 3050, 3020, 2985, 1844 (s), 1453, 1320, 1240 (s), 1175, 680 cm^{-1}; ^1H NMR (100 MHz) δ 7.85 (m, 2 H), 7.6–7.0 (m, 6 H), 2.42 (t, 2 H, J_{HF} = 5.2 Hz); ^{19}F NMR (300 MHz) ϕ 82.3 (d of t, 1 F, J_{FF} = 56.5, J_{HF} = 5.2 Hz), 86.2 (d of t, 1 F, J_{FF} = 56.5, J_{HF} = 4.8 Hz); ^{13}C NMR (100 MHz) δ 149.9 (dd, J_{CF} = 281.4, 283.4 Hz, $=CF_2$), 144.6, 140.4 (substituted aromatic), 127.4, 127.3, 120.2 (aromatic), 78.2 (t, J_{CF} = 36.0 Hz, C_2), 34.4 (d, J_{CF} = 6.1 Hz, C_1), 20.0 (d, J_{CF} = 4.9 Hz, CH_2); mass spectrum M^+, 240.07408 ± 0.00245 (10 ppm); calcd for $C_{16}H_{10}F_2$, 240.07506; deviation, −0.00098 (4 ppm). Anal. Calcd: C, 79.99; H, 4.20. Found: C, 79.89; H, 4.23.

Compound **7** reacted slowly with oxygen in solution, but was indefinitely stable in the absence of oxygen and the purified solid was stored under nitrogen. The major product **5c** was very unstable in $CHCl_3$ solution and did not elute from the silica gel column. Spectroscopic analysis of the product mixture containing **5c** and **7** gave for pyrazoline **5c**: IR (CCl_4) 1756 (s) cm^{-1}; ^1H NMR (60 MHz) δ 2.97 (t, J_{HF} = 3.8 Hz, CH_2); ^{19}F NMR (100 MHz) ϕ 79.2 (d of t, 1 F, J_{FF} = 15.2, J_{HF} = 3.6 Hz), 89.4 (d of t, 1 F, J_{FF} = 15.2, J_{HF} = 3.8 Hz).

When the reaction was monitored by ^1H NMR (100 MHz), the CH_2 protons of the unstable intermediate **4c** were observed: ^1H NMR (100 MHz) δ 5.65 (t, J_{HF} = 3.7 Hz). By the time the reaction was complete, **4c** was no longer present.

4,5-Dihydro-4-(fluoromethylene)-3*H*-pyrazole (2). An ether solution of diazomethane (70 mL) was prepared from 7.00 g (32.7 mmol) of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide. The solution was vacuum transferred to a 150-mL glass tube and 1.9 g (32.7 mmol) of fluoroallene were condensed into the tube, which was sealed under vacuum. After 10 min at room temperature, the clear, colorless solution was concentrated by rotary evaporation at 200 mm pressure. The residue was distilled at reduced pressure. The pale yellow distillate was collected in an ice-chilled flask. A total of 2.1 g (64%) of **2** was obtained: bp 59–60 °C (23 mm); IR (CCl_4) 2920, 2822, 1710 (s), 1545, 1420, 1340, 1263, 1183, 1092 (s), 926 cm^{-1}; ^1H NMR (300 MHz) δ 6.67 (d of pentet, 1 H, J_{HF} = 83.9, J_{HH} = 2.7 Hz), 5.16 (t, 2 H, J = 2.8 Hz), 5.06 (t, 2 H, J = 2.8 Hz); ^{19}F NMR (100 MHz) ϕ 121.7 (d of pentet, J_{HF} = 84.0, 3 Hz); mass spectrum M^+, 100.04442 ± 0.00195 (20 ppm); calcd for $C_4H_5N_2F$, 100.04368; deviation, −0.00075 (8 ppm). The unstable product **2** could be stored on dry ice under nitrogen.

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Registry No. 1, 88766-66-9; 2, 86770-87-8; **3a**, 2684-60-8; **3b**, 883-40-9; **3c**, 832-80-4; **4a**, 89210-55-9; **4b**, 89210-57-1; **4c**, 89210-59-3; **5a**, 89210-56-0; **5b**, 89210-58-2; **5c**, 89210-60-6; **6**, 83849-37-0; **7**, 89210-61-7; DFA, 430-64-8; fluoroallene, 51584-22-6; diazomethane, 334-88-3.

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Optically Active Phosphine Oxides. 2.[1] Novel Approach to Enantiomeric Dialkylphenylphosphine Oxides[2]

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New routes to optically active tertiary phosphine oxides of known configuration and of virtually 100% enantiomeric purity have been developed. Alkylation of (−)-(S_P)-ethyl((menthoxycarbonyl)methyl)phenylphosphine oxide (**2**) by treatment with equimolar amounts of sodium hydride and alkyl halide in tetrahydrofuran followed by decarbalkoxylation with LiCl in wet Me_2SO affords (−)-(R_P)-alkylethylphenylphosphine oxides (alkyl: Et-d_3, Pr, *i*-Pr, 4-butenyl, 2-phenylethyl) in satisfactory yields. A considerable degree of asymmetric induction has been observed during the alkylation of **2**. It has also been demonstrated that the enantiomeric phosphine oxide **4b** in which the ligands are isotopically differentiated at the β carbon shows measurable optical activity at 400 nm wavelength. Decarbalkoxylation of **1** gives (−)-(S_P)-methylphenylvinylphosphine oxide (**5**) in 60% yield. The Michael-type reaction of **5** with R_2CuLi provides (−)-(S_P)-(RCH_2CH_2)P(O)MePh (R = Me, Bu) in ca. 65% yield. Sequential treatment of **5** with Bu_2CuLi and allyl bromide gives the addition–alkylation product, i.e., methyl(4-nonen-1-yl)phenylphosphine oxide in 53% yield. In addition reaction of **5** with butadiene is shown to produce cyclohexenylmethylphenylphosphine oxide in 78% yield. Stereochemistry of the latter two conversions is briefly discussed.

Synthesis of chiral phosphines of defined stereochemistry is one of the important objectives of organic chemists during recent years due to the widespread utility of these compounds as ligands in asymmetric catalysis.[3] The possibility of easy, stereoselective interconversion between chiral phosphines and chiral phosphine oxides[4] accords similar importance also to this latter pool of chirality.

A few approaches to optically active phosphine oxides have been developed in the past.[5] However, since the detailed work of Mislow and co-workers in the late sixties

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