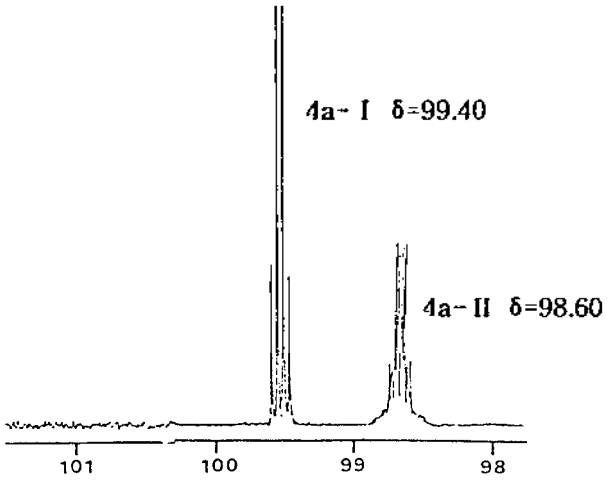

Figure 2. ^{13}C(GD)NMR Signals C1 at C2 of the stereoisomeric ozonides **4a-I** and **4a-II**.

spectra of the previously obtained mixtures of the stereoisomeric ozonides **4a, 4b** and **4c**, as summarized in Table 1. In particular, the ^{13}C NMR spectrum of **4a-I** exhibited a quartet for the signal of C(2) due to coupling with the CH_3 group, whereas the spectrum of the other isomer exhibited a quartet of a doublet due to long range coupling with the proton at C(1) (Figure 2). This prompted us to assign their stereochemical identities, although the isomers were not separated. These assignments derive support from the fact, that the Z-isomer I exhibited the ^{1}H NMR signal for the CH group in the ozonide ring upfield from that of the corresponding E-isomer II.

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Electrophilic Substitution Reaction and A Novel [1,3] Rearrangement of 4-Lithio-5-*p*-toluenesulfonyloxypyrazoles

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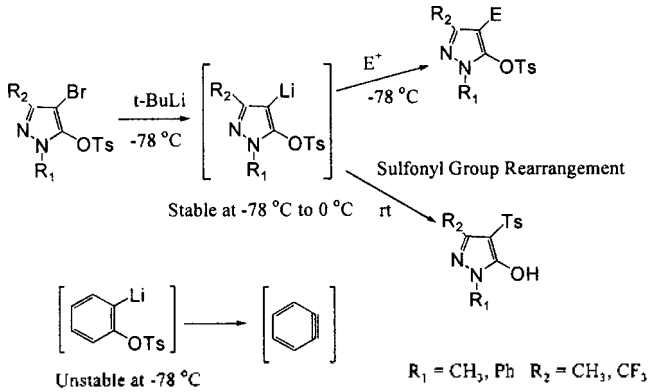
Recently, we have reported a new synthesis of 4-benzoyl-3-trifluoromethyl-5-*p*-toluenesulfonyloxypyrazoles exhibiting herbicidal activities involving [1,3] rearrangement of benzoyl group in 5-benzoyloxy-4-bromo-3-trifluromethylpyrazoles *via* lithium-bromine exchange reaction using *tert*-butyllithium.[1] In connection with this study, we wish to report the electrophilic substitution reaction and a new type of sulfonyl group rearrangement of the 4-lithio-5-*p*-toluenesulfonyloxypyrazoles.

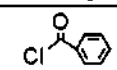
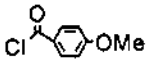
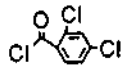
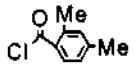
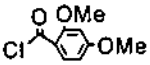
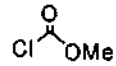
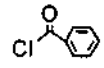
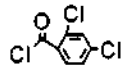
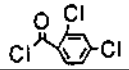
It has been known that *ortho*-lithio-*p*-toluenesulfonyloxybenzene is unstable even at very low temperature leading to benzyne intermediate which results in the multimerized by-products.[2] However, the benzyne equivalents in the five membered aromatic heterocycles have not been known in the literature, and we assumed that 4-lithio-5-*p*-toluenesulfonyloxypyrazoles would be relatively stable and useful for the preparation of new pyrazole derivatives.

4-Bromo-5-*p*-toluenesulfonyloxypyrazoles were prepared by bromination of 5-*p*-toluenesulfonyloxypyrazoles or by tosylation of 4-bromo-5-hydroxypyrazoles.[3] 4-Lithio-5-*p*-toluenesulfonyloxypyrazoles as intermediates were prepared by lithium-bromine exchange reaction of 4-bromo-5-*p*-toluenesulfonyloxypyrazoles with *tert*-butyllithium in THF at − 78 °C.

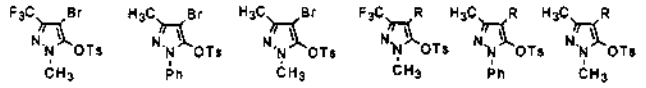


Scheme 1. Use of 4-Litho-5-*p*-toluenesulfonyloxypyrazole Derivatives.

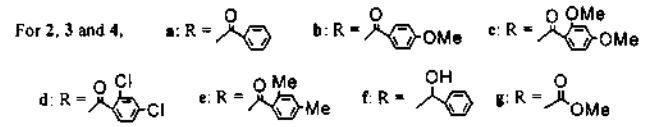
Table 1. Electrophilic substitution Reaction of 4-Bromo-5-*p*-toluenesulfonyloxypyrazoles *via* Lithium-bromine Exchange Using *tert*-Butyllithium

Entry	Substrate	Electrophile	Product	Yield (%)[a]
1	**1a**		**2a**	81
2	**1a**		**2b**	79
3	**1a**		**2c**	78
4	**1a**		**2d**	85
5	**1a**		**2e**	71
6	**1a**		**2f**	91
7	**1a**		**2g**	95
8	**1b**		**3a**	88
9	**1b**		**3c**	82
10	**1b**		**3g**	87
11	**1c**		**4c**[b]	82

[a] isolated yields. [b] *pyrazolate*



1a **1b** **1c** **2** **3** **4**



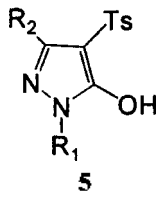
The electrophilic substitution of the intermediates with benzoyl chlorides gave the corresponding 4-benzoyl-5-*p*-toluenesulfonyloxypyrazoles in good yields. This method should offer an efficient preparation of various 4-benzoyl-5-*p*-toluenesulfonyloxypyrazoles including *pyrazolate*, a commercialized herbicide.[4] The reaction of other electrophiles such as benzaldehyde or methyl chloroformate with 4-lithio-5-*p*-toluenesulfonyloxy- pyrazoles also afforded a new type of 4-substituted pyrazole derivatives as shown in Table 1.[5]

We examined a new Fries-type rearrangement of sulfonyl group of 4-lithio-5-*p*-toluenesulfonyloxypyrazoles in order to obtain 5-hydroxy-4-*p*-toluenesulfonylpyrazoles. Sulfonyl Fries-type rearrangements were usually performed in the presence of Lewis acid and not mediated by carbanions,[6] because of the unstability of *ortho*-lithiotoluenesulfonyloxybenzene.[2] When 4-lithio-5-*p*-toluenesulfonyloxypyrazoles formed at −78 °C in THF and warmed up to room temperature, the sulfonyl group was rearranged at 4-position to afford 5-hydroxy-4-*p*-toluenesulfonylpyrazoles **5a-c**. We attempted this rearrangement in various solvents in order to improve the yields, but unsatisfactory results were obtained as shown in Table 2. However, this rearrangement appeared to be novel and useful method for the synthesis of 5-hydroxypyrazoles substituted with sulfone group at 4-position.

Table 2. Fries Rearrangement of Sulfonyl Group of 4-Bromo-5-*p*-toluenesulfonyloxy pyrazoles to 5-Hydroxy-4-*p*-toluenesulfonylpyrazoles *via* Li-Br Exchange Reaction

Entry	Substrate	Solvent	Product	Yield (%)[a]
1	**1a**	THF	**5a**	32
2	**1b**	THF	**5b**	45
3	**1b**	ether	**5b**	35
4	**1b**	THF/HMPA	**5b**	40
5	**1c**	THF	**5c**	48

[a] isolated yields.



5

For **5**, **a**: R_1 = -CH_3, R_2 = -CF_3; **b**: R_1 = -Ph, R_2 = -CH_3; **c**: R_1 = -CH_3, R_2 = -CH_3

In conclusion, 4-lithio-5-*p*-toluenesulfonyloxypyrazoles as intermediates were stable, enough to undergo the electrophilic substitution reaction to form 4-substituted-5-*p*-toluenesulfonyloxypyrazoles and also the sulfonyl group rearranged to the 4-position giving the 5-hydroxy-4-*p*-toluenesulfonylpyrazoles under mild conditions.

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3. 4-Bromo-1-methyl-5-*p*-toluenesulfonyloxy-3-trifluoromethylpyrazole was prepared *via* tosylation of 4-bromo-1-methyl-5-hydroxy-3-trifluoromethylpyrazole. 4-Bromo-1-methyl-3-methyl-5-*p*-toluenesulfonyloxypyrazole and 4-bromo-1-phenyl-3-methyl-5-*p*-toluenesulfonyloxypyrazole were prepared by bromination of 1-methyl-3-methyl-5-*p*-toluenesulfonyloxypyrazole and 1-phenyl-3-methyl-5-*p*-toluenesulfonyloxypyrazole, respectively.
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5. The ^{1}H NMR data of the key intermediates and products are as follows; **1a**: (200 MHz, $CDCl_3$) δ 7.86 (2H, d, J=8 Hz, Ar), 7.43 (2H, d, J=8 Hz, Ar), 3.87 (3H, s, N-CH_3), 2.50 (3H, s, -CH_3). **1b**: (60 MHz, $CDCl_3$) δ 7.55 (2H, d, J=8 Hz, Ar), 7.43 (5H, brs, Ar), 7.15 (2H, d, J=8 Hz, Ar), 2.39 (3H, s, -CH_3), 2.28 (3H, s, -CH_3). **1c**: (200 MHz, $CDCl_3$) δ 7.83 (2H, d, J=8 Hz, Ar), 7.38 (2H, d, J= 8 Hz, Ar), 3.70 (3H, s, N-CH_3), 2.48 (3H, s, -CH_3), 2.13 (3H, s, -CH_3). **2d**: (200 MHz, $CDCl_3$) δ 7.39-6.98 (7H, m,

Ar), 3.69 (3H, s, N-CH_3), 2.35 (3H, s, -CH_3), 2.32 (3H, s, -CH_3), 2.29 (3H, s, -CH_3). **2e**: (200 MHz, $CDCl_3$) δ 7.48-7.12 (3H, m, Ar), 3.84 (3H, s, O-CH_3), 3.82 (3H, s, O-CH_3), 3.63 (3H, s, N-CH_3), 2.35 (3H, s, -CH_3). **2f**: (200 MHz, $CDCl_3$) δ 7.70 (2H, d, J=8.5 Hz, Ar), 7.35 (2H, d, J=8.5 Hz, Ar), 7.29-7.26 (5H, m, Ar), 5.81 (1H, s, CH), 3.64 (3H, s, N-CH_3), 2.47 (3H, s, -CH_3). **2g**: (60 MHz, $CDCl_3$) δ 7.92 (2H, d, J=8 Hz, Ar), 7.49 (2H, d, J=8 Hz, Ar), 3.85 (3H, s, O-CH_3), 3.55 (3H, s, N-CH_3), 2.48 (3H, s, -CH_3). **3g**: (200 MHz, $CDCl_3$) δ 7.51-6.93 (14H, m, Ar), 6.05 (1H, s, CH), 2.31 (3H, s, -CH_3), 1.96 (3H, s, -CH_3). **5a**: (200 MHz, MeOH-d_4) δ 7.78 (2H, d, J=7 Hz, Ar), 7.24 (2H, d, J=7 Hz, Ar), 3.31 (3H, s, N-CH_3), 2.37 (3H, s, -CH_3). **5b**: (200 MHz, MeOH-d_4) δ 7.78-7.02 (9H, m, Ar), 2.27 (3H, s, -CH_3), 2.15 (3H, s, Ph-CH_3). **5c**: (200 MHz, MeOH-d_4) δ 7.80 (2H, d, J=8 Hz, Ar), 7.37 (2H, d, J=8 Hz, Ar), 3.47 (3H, s, N-CH_3), 2.48 (3H, s, -CH_3), 2.16 (3H, s, -CH_3).

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