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A NEW APPLICATION OF THE SOMMELET-HAUSER REARRANGEMENT

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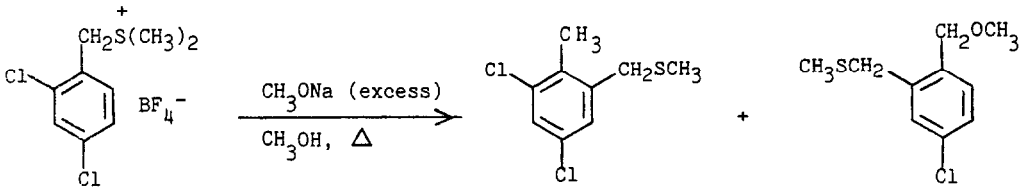
SUMMARY: With appropriate design, the Sommelet-Hauser rearrangement can be used for the introduction of an ortho substituent on an aromatic ring as well as for functionalization of the original ylide side chain in a single operation.

The Sommelet-Hauser rearrangement of sulfonium salts[1] and ammonium salts[2] has been well established as a useful reaction for introducing an ortho substituent in various aromatic systems. In connection with another synthetic project, we prepared sulfide 2[3] from sulfonium salt 1 via the Sommelet-Hauser rearrangement pathway. Interestingly, a minor product, 3,[3] was also isolated from the reaction. The mechanistic implication in the formation of 3 has led us to explore a new synthetic application of the Sommelet-Hauser rearrangement as exemplified in Scheme II.

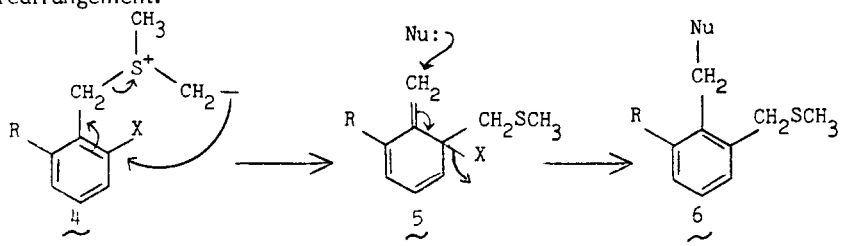
Scheme I



1 2 (58%) 3 (6.6%)

The rearrangement of ylide 4 initially produces the exo-methylenecyclohexadiene intermediate 5. Subsequent nucleophilic attack at the terminus of the exo-methylene group with the concomitant loss of a leaving group X^- affords 6, which possesses two different alkyl substituents amenable to further synthetic elaboration. Predictably, the presence of a good leaving group X^- (e.g., halogen) in the intermediate 5 should facilitate the attack at the exo-methylene group by a variety of soft nucleophiles. In contrast, when an active leaving group is absent, the highly basic n-butyl anion is the only nucleophile that has been reported to add successfully[4,5] to exo-methylenecyclohexadiene intermediates generated in the Sommelet-Hauser rearrangement.

Scheme II

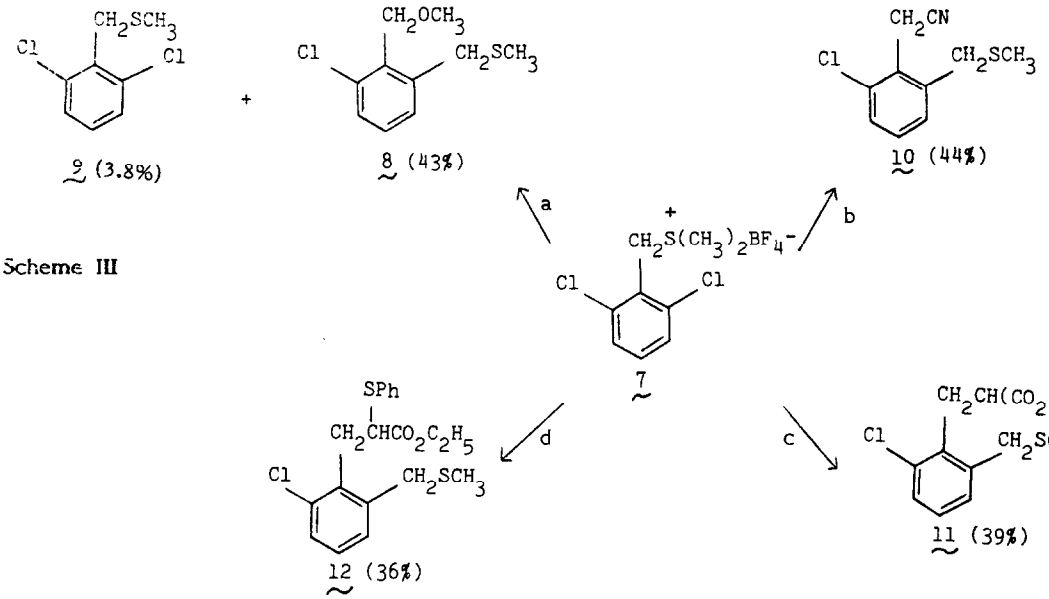


4 5 6

X = halogen, SO_3R' etc.

In order to test the validity of the above approach we selected sulfonium salt 7, readily prepared in two steps from commercially available α,2,6-trichlorotoluene, for our model study (Scheme III). When 7 was refluxed in methanol in the presence of excess sodium methoxide (6 equiv), there were produced the desired compound 8[3] (43%) and 9[3] (3.8%). To further study the reactions of the exo-methylene-cyclohexadiene intermediate, generated in situ in the Sommelet-Hauser rearrangement, with other types of nucleophiles, a non-nucleophilic deprotonation reagent was sought. For this purpose, sodium hydride proved to be acceptable. Thus, when a solution of 7 in hexamethylphosphoric triamide (HMPA) was added to a suspension of sodium hydride (2.5 equiv) in HMPA containing sodium cyanide (3 equiv) at room temperature, there was obtained the desired 10[3] in 44% isolated yield. This reaction demonstrates that, with suitable design, the Sommelet-Hauser rearrangement can achieve in one operation the introduction of an ortho substitutent as well as extension of the original ylide side chain. The versatility of this particular approach is further manifested by the synthesis of 11[3] and 12,[3] derived by the treatment of 7 in HMPA with sodium anion of dimethyl malonate and ethyl phenylthioacetate respectively.

In summary, we have shown a new application of the Sommlet-Hauser rearrangement in which both the introduction of an ortho substituent and the functionalization of the original ylide slide chain can be accomplished in one operation. Subsequently, selective manipulation of either adjacent substituent may permit further synthetic elaboration (e.g., $ArCH_2SCH_3 \longrightarrow ArCHO$).[6] Thus, we believe that the approach presented in this report expands the utility of the Sommlet-Hauser rearrangement in organic synthesis.



Scheme III

a = CH_3ONa (excess), CH_3OH; b = NaH, NaCN, HMPA; c = NaH, $NaCH(CO_2CH_3)_2$, HMPA; d = NaH, $NaCH(SPh)CO_2C_2H_5$, HMPA.

Acknowledgement

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References

(1) For review purpose, see (a) B. M. Trost, L. S. Melvin, Jr., "Sulfur Ylides: Emerging Synthetic Intermediates"; Academic Press; New York (1975); (b) E. Block, "Reactions of Organosulfur Compounds"; Academic Press; New York (1978).

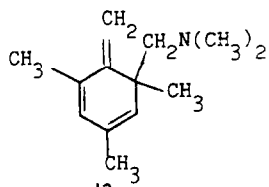
(2) For comprehensive review, see S. H. Pine Org. React., 18, 403 (1970)

(3) All products recorded in this report are liquids and purified by flash column chromatography. Only in one reaction of 7 an isolable side-product was detected. 2: NMR ($CDCl_3$) δ 2.03 (s, 3H), 2.36 (s, 3H), 3.63 (s, 2H), 7.07 (d, H, J = 2Hz), 7.28 (d, H, J = 2Hz). 3: NMR ($CDCl_3$) δ 2.0 (s, 2H), 3.34 (s, 3H), 3.67 (s, 2H), 4.48 (s, 2H), 7.18 (s, 3H). 8: NMR ($CDCl_3$) δ 2.05 (s, 3H), 3.41 (s, 3H), 3.85 (s, 2H), 4.78 (s, 2H), 7.1~7.4 (m, 3H). 9: NMR ($CDCl_3$) δ 2.13 (s, 3H), 4.00 (s, 2H), 7.3 (m, 3H). 10: NMR ($CDCl_3$) δ 2.02 (s, 3H), 3.80 (s, 2H), 4.07 (s, 2H), 7.1~7.5 (m, 3H); IR (neat) 2250 cm^{-1}. 11: NMR ($CDCl_3$) δ 2.02 (s, 3H), 3.51 (d, 2H, J = 7Hz), 3.70 (s, 6H), 3.81 (s, 2H), 4.02 (t, H, J = 7Hz), 7.1 7.4 (m, 3H); IR (neat) 1728 cm^{-1}. 12: NMR ($CDCl_3$) δ 1.02 (t, 3H, J = 7Hz), 2.0 (s, 3H), 3.3~3.5 (m, 2H), 3.7~4.3 (m, 5H), 7.0~7.5 (m, 8H); IR (neat) 1723 cm^{-1}.

(4) (a) C. R. Hauser, D. N. Van Eenam, J. Amer. Chem. Soc., 79, 5512 and 6274 (1957); (b) D. N. Van Eenam, C. R. Hauser, J. Amer. Chem. Soc., 79, 5520 (c) C. R. Hauser, D. N. Van Eenam, J. Org. Chem., 23, 865 (1958); (d) S. H. Pine, B. L. Sanchez, Tet. Letters, 1319 (1969).

(5) Hauser and Van Eenam[4a] reported that both triphenylmethide ion and amide ion failed to react with the exo-methyleneamine 13 at room temperature in ether.

(6) L. A. Paquette, W. D. Klobucar, R. A. Snow, Synth. Comm., 6, 575 (1976).



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