Table I
Preparation of 2-Substituted Benzothiazoles (1) from 2-Aminothiophenol (2) and Carboxylic Acids (3)

Entry	R	Reaction time (temp, °C)	Yield,[a] %
a	CH_3	1 h (25) 10 h (70)	93[b]
b	$CH_3(CH_2)_5$	1 h (25) 10 h (75–80)	96[c]
c	$PhCH_2$	1 h (25) 10 h (75)	89[c]
d	3-Pyridyl-CH_2	1 h (25) 10 h (75–80)	86[d]
e	Cyclohexyl	1 h (25) 10.5 h (80–85)	88[e]
f	$(CH_3)_2CH$	15 h (25) 8 h (70)	74[c]
g	3-$MeOC_6H_4$	1 h (25) 10 h (95)	85[f]
h	4-ClC_6H_4	10 min (25) 17.5 h (90–95)	83[g]
i	2-Furyl	1 h (25) 10 h (75–80)	84[h]
j	PhCH=CH	1 h (25)[i] 10 h (55)	57[j]
k	$(CH_3)_2C=CH$	1 h (25) 10 h (55)	19[k]
l	$(CH_3)_3C$	1 h (25)[l] 10 h (75–80)	<10

[a] Yield after purification by column chromatography (SiO_2). All products exhibited the reported or expected ^{1}H-NMR, IR, mass spectral characteristics and were identical in all respects to authentic material (when available). [b] Identical in all respects to distilled commercial material (Aldrich). [c] For previous characterization see J. Metzger and H. Plank, *Bull. Soc. Chim. Fr.*, 1692 (1956); R. Guglielmetti, E. J. Vincent, J. Metzger, J. Berger, and R. Garnier, *ibid.*, 4195 (1967). [d] For preparation of authentic material see ref 4a. [e] For preparation of authentic material see ref 5. [f] Mp 81–82 °C (lit. mp 82–83 °C): F. A. Babiehev, L. A. Kirpianova, and T. A. Dashevskaya, *Urk. Khim. Zh. (Russ. Ed.)*, **32,** 706 (1966); *Chem. Abstr.*, **65,** 13682a (1966). [g] Mp 115–116 °C (lit.[4c] mp 117–118 °C). [h] Mp 103–104.5 °C (lit. mp 105 °C): M. T. Bogert and A. Stull, *J. Am. Chem. Soc.*, **47,** 3078 (1925). [i] Weight (g) of P_2O_5/CH_3SO_3H (1/10, w/w): mmol substrate was 2:1. [j] Mp 110–111 °C (lit. mp 112 °C): D. M. Brown and G. A. R. Kon, *J. Chem. Soc.*, 2147 (1948). [k] Mp 78–80 °C (lit. mp 81–82 °C): E. B. Knott, *ibid.*, 3793 (1965). [l] Evolution of gas evident, presumably CO and isobutylene.

(**3l**), appears to decarbonylate under the reaction conditions (evolution of gas).

The ease with which the reagent P_2O_5/CH_3SO_3H (1/10, w/w) may be handled, especially on large preparative scales, is particularly noteworthy.[10] This fact coupled with the reagent's ability to promote the direct condensation of a wide range of carboxylic acids (**3**) with 2-aminothiophenol (**2**) in high yields makes this procedure a particularly convenient and attractive method for the direct preparation of 2-substituted benzothiazoles when compared to related direct condensation methods.[2,6,8,9]

Experimental Section[11]

Preparation of 2-Substituted Benzothiazoles. The General Procedure is Illustrated with 2-Methylbenzothiazole (1a). A 4.5-g solution of P_2O_5/CH_3SO_3H (1/10, w/w)[10] was treated sequentially with 2-aminothiophenol (3.0 mmol, 376 mg) and acetic acid (3.0 mmol, 180 mg). The resulting solution was stoppered and magnetically stirred at 25 (1 h) and 70 °C (10 h). After cooling, the solution was slowly added to ca. 50–75 mL of aqueous 5% $NaHCO_3$[12] and the resulting solution was made basic to pH paper by the addition of aqueous 10% NaOH. Extraction of the aqueous phase ($CHCl_3$) followed by drying of the combined organic phases ($MgSO_4$) and evaporation of the solvent in vacuo afforded the crude product as a yellow oil. Chromatography (20 g SiO_2, 20 × 1.5 cm, CH_2Cl_2 to 20% Et_2O:CH_2Cl_2 gradient elution) afforded 415 mg (447 theoretical, 93%) of pure 2-methylbenzothiazole (**1a**), as a colorless liquid identical in all respects with distilled authentic material (Aldrich).

Acknowledgments. The author is especially grateful to Professor E. J. Corey for his helpful advice, suggestions, and valuable discussions throughout this work.

Registry No.—**1a,** 120-75-2; **1b,** 65718-88-9; **1c,** 6265-94-7; **1d,** 33928-36-8; **1e,** 40115-03-5; **1f,** 17626-86-7; **1g,** 10002-44-5; **1h,** 6265-91-4; **1i,** 1569-98-8; **1j,** 1483-30-3; **1k,** 1628-61-1; **1l,** 17626-88-9; **2,** 137-07-5; **3a,** 64-19-7; **3b,** 111-14-8; **3c,** 103-82-2; **3d,** 501-81-5; **3e,** 98-89-5; **3f,** 79-31-2; **3g,** 586-38-9; **3h,** 74-11-3; **3i,** 88-14-2; **3j,** 140-10-3; **3k,** 541-47-9; **3l,** 75-98-9.

References and Notes

(1) This work was assisted financially by a grant from the National Science Foundation.
(2) R. C. Elderfield, "Heterocyclic Compounds", Vol. 5, Wiley, New York, N.Y., 1957, pp 484–722.
(3) (a) F. M. Hamer in "The Chemistry of Heterocyclic Compounds", Vol. 18, A. Weissberger, Ed., Interscience, New York, N.Y., 1964, Chapter 6; (b) T. S. Gore, B. S. Jashi, S. V. Sunthankar, and D. B. Tilak, Ed., "Chemistry of Natural and Synthetic Colouring Matters", Academic Press, New York, N.Y., 1962, pp 573–587 and 615–643; (c) A. Dorlars, C. W. Schellhammer, and J. Schroeder, *Angew. Chem., Int. Ed. Engl.*, **14,** 665 (1975).
(4) For the various examples pertaining to the benzothiazole derivatives prepared herein see (a) H. Iwato, N. Nichimura, and J. Nakano, Japanese Patent 71 31 862; *Chem. Abstr.*, **75,** 140831v (1971); (b) B. Prescott and J. M. Webb, *Antibiot. Chemother. (Washington, D.C.)*, **8,** 33 (1958); (c) W. L. Hubbard, R. E. Grahame, Jr., R. A. Covey, and E. H. Jonis, U.S. Patent 3 876 791; *Chem. Abstr.*, **83,** 92409e (1975); (d) H. Schwartz, Netherlands Appl. 6 607 039; *Chem. Abstr.*, **67,** 100132w (1967); (e) L. W. Wattenberg, M. A. Page, and L. J. Leong, *Cancer Res.*, **28,** 2539 (1968); (f) Gh. Miron and Gh. Ripeanu, *Comun. Acad. Repub. Pop. Rom.*, **11,** 241 (1961); *Chem. Abstr.*, **55,** 17985f (1961).
(5) We have recently employed the benzothiazole nucleus as the center of a wide variety of synthetic operations in which the benzothiazole nucleus serves as a masked carbonyl functionality and have applied this chemistry toward the preparation of various annulation products, cf. E. J. Corey and D. L. Boger, *Tetrahedron Lett.*, 5, 9, 13 (1978).
(6) Generally this direct approach requires rather harsh reaction conditions (e.g., high temperatures, sealed tubes) and affords low to modest yields of the desired 2-substituted benzothiazoles; cf. ref 2 and references cited therein.
(7) B. George and E. P. Papadopoulos, *J. Org. Chem.*, **42,** 441 (1977).
(8) D. W. Hein, R. J. Alheim, and J. J. Leavitt, *J. Am. Chem. Soc.*, **79,** 427 (1957).
(9) Y. Kanaoka, T. Hamada, and O. Yonemitsu, *Chem. Pharm. Bull.*, **18,** 587 (1970).
(10) P. E. Eaton, G. R. Carlson, and J. T. Lee, *J. Org. Chem.*, **38,** 4071 (1973); the reagent was prepared as described with the exception that CH_3SO_3H (98%, Aldrich) was not distilled prior to reagent formation.
(11) Melting points are uncorrected. Infrared spectra (IR) were obtained in $CHCl_3$ for solids or as neat films for liquids and recorded on a Perkin-Elmer 267 spectrophotometer. ^{1}H-NMR spectra were obtained on a Varian A-60 or CFT-20/HFT-80 spectrophotometer in $CDCl_3$ with tetramethylsilane as an internal standard. Mass spectra were recorded on an AEI-MS9 spectrophotometer at 70 eV.
(12) When working on large preparative scales workup is facilitated by pouring directly onto aqueous 10% NaOH.

Photoreaction of Hexafluorobenzene with Cyclohexane: Evidence for Substitution and Addition Mechanism

Marko Zupan,* Boris Šket, and Barbara Pahor

Department of Chemistry and "Jožef Stefan" Institute, University of Ljubljana, Yugoslavia

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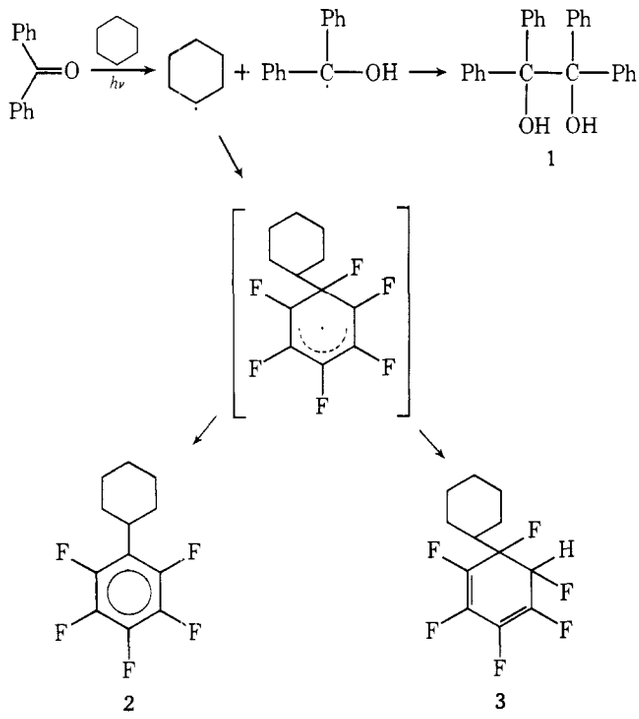
Light-induced substitution reactions of aryl fluorides have been recently reviewed.[1] Bryce-Smith and co-workers[2] have recently observed cine-substitution by nucleophilic substitution of fluorobenzene and difluorobenzenes with primary and secondary amines and found evidence for the addition–elimination mechanism. Irradiation of solutions of hexafluorobenzene in cyclohexane and cyclooctane gives hydrogen fluoride and a complex mixture containing cyclohexylpentafluorobenzene and other radical coupling products.[3]

0022-3263/78/1943-2297$01.00/0

Scheme I



We now report that 24-h irradiation of a solution of hexafluorobenzene in cyclohexane in the presence of benzophenone with λ 300–350 nm at T = 25 °C leads to the formation of three products. A white crystalline product, which precipitated from solution and was filtered off, was easily recognized as 1,1,2,2-tetraphenyl-1,2-dihydroxyethane (1). The filtrate was evaporated in vacuo and the crude reaction mixture was analyzed by ^{19}F-NMR spectroscopy and separated by preparative TLC. The main product formed (**2**, 61%, mp 43–44 °C) shows in its ^{19}F spectrum three signals: δ_F −148.5 (2 F, dd), −165.0 (1 F, t), −169.5 (2 F, td), with the coupling constants 24 and 9 Hz; in its mass spectrum it shows the following fragments m/e 250 (M^+, 53, calcd for $C_{12}F_5H_{11}$ m/e 250.0781, found m/e 250.0780), 208 (9), 195 (9), 194 (100), 181 (31). From the spectroscopic data we established that cyclohexylpentafluorobenzene was formed. The minor product (**3**, 23%, oil product) formed shows in its ^{19}F-NMR spectrum six multiplets: δ_F −146.25 (dm), 146.85 (dd), −152.25 (dm), −153.75 (dm), −164.25 (dm), and −170.25 (ddm) with the following coupling constants $^2J_{F2,H}$ = 60 Hz, $^3J_{F1,F2}$ = 21 Hz and $^3J_{F3,F4}$ = $^3J_{F5,F6}$ = 24 Hz. Product **3** was converted by heating to product **2**. Product **3** shows in its mass spectrum the following fragments: m/e 250 (M^+ − HF, 52%, calcd for $C_{12}H_{11}F_5$ m/e 250.0781, found m/e 250.0785), 194 (100), 183 (90), 182 (60), 121 (44), 82 (36). On the basis of the spectroscopic data and chemical transformations, we established the structure of the product **3** as 1-cyclohexyl-1,2,3,4,5,6-hexafluoro-3,5-cyclohexadiene.

Reduction of the irradiation time from 24 to 6 h or prolongation to 60 h affected only the overall yield of the products but not the ratio of the substitution and addition products (**2**/**3** = 3:2, determined by ^{19}F NMR), which reduced the possibility of the formation of substitution product (**2**) by photoelimination of **3**, as was suggested by photonucleophilic substitution reactions of fluorobenzene and difluorobenzenes.[2] On the basis of the above mentioned observations, the mechanism presented in Scheme I is suggested. In the presence of benzophenone a cyclohexyl radical is formed, which then reacts with hexafluorobenzene forming radical species A, transforming by two different paths to **2** and **3**.

Being interested in the effect of ring magnitude of the cycloalkene on photosubstitution and addition reactions, we also studied the reactions with cyclopentane and cycloheptane. The reaction with cyclopentane resulted in the formation of 1-cyclopentylpentafluorobenzene in very low yield (2%) and greater amounts of 1,1,2,2-tetraphenyl-1,2-dihydroxyethane and cyclopentylcyclopentane, while the reaction with cycloheptane under the conditions mentioned above failed. Photosubstitution reactions with some n-alkanes, i.e., n-hexane and n-heptane, also did not occur.

It is known that free-radical substitutions with fluorosubstituted aromatic molecules occur readily using aryl radicals, and extensive studies have been made using diaryl peroxides as the source of these radicals.[4] Arylation of pentafluorobenzene does indeed occur using dibenzoyl peroxide, but $(C_6F_5COO)_2$ gives only tar.[5] The thermal reaction (T = 70 °C) of hexafluorobenzene in cyclohexane solution in the presence of dibenzoyl peroxide did not result in the formation of cyclohexylpentafluorobenzene (**2**) or 1-cyclohexyl-1,2,3,4,5,6-hexafluoro-3,5-cyclohexadiene (**3**) as in the case of the photoinitiated reaction but only polymeric material was isolated.

Experimental Section

Irradiation was carried out in a Rayonet Photochemical Chamber, Reactor Model RPR-100, with RPR 253.7 nm, RPR 300 nm, and RPR 350 nm lamps. IR spectra were recorded by using a Perkin-Elmer 257 spectrometer, ^{1}H- and ^{19}F-NMR spectra were determined by a Jeol JNM-PS-100 from CCl_4 solution with Me_4Si and CCl_3F as internal standards, and mass spectra were recorded on a CEC 21-110 spectrometer. Melting points were determined on a Kofler apparatus and are uncorrected. Gas liquid partition chromatography was carried out on a Varian Aerograph Model 1800 and preparative TLC on Merck-PSC-Fertigplatten Kieselgel F 254.

Materials. The hexafluorobenzene and benzophenone were obtained from commercial sources and purified to conform with published physical and spectral data. Solvents were purified by literature methods[6] and stored over molecular sieves.

Irradiation of Hexafluorobenzene. Hexafluorobenzene (1 mmol, 186 mg) and 2 mmol (364 mg) of benzophenone were dissolved in 18 mL of cyclohexane. The solution was irradiated at room temperature for 24 h with 300- or 350-nm lamps. 1,1,2,2-Tetraphenyl-1,2-dihydroxyethane was filtered off and the solvent was evaporated in vacuo. The reaction mixture was analyzed by NMR and the products were separated by preparative TLC and 153 mg (61%) of cyclohexylpentafluorobenzene (**2**, mp 43–44 °C) and 63 mg (23%, liquid product) of 1-cyclohexyl-1,2,3,4,5,6-hexafluorocyclo-3,5-hexadiene (**3**) were isolated. Mass spectrum of the product **2**, calcd for $C_{12}F_5H_{11}$ m/e 250.0781, found m/e 250.0780, m/e 250 (M^+, 53), 208 (9), 195 (9), 194 (100), 181 (31); NMR spectrum $\delta_{F_{2,F_6}}$ −148.5 (dd, $J_{F,F}$ = 24, 9 Hz), $\delta_{F_{3,F_5}}$ −169.5 (td, $J_{F,F}$ = 24, 9 Hz), δ_{F_4} −165 (t, $J_{F,F}$ = 24 Hz). Mass spectrum of the product **3**, calcd for $C_{12}F_6H_{12}HF$ m/e 250.0781, found m/e 250.0785, m/e 250 (M^+ − HF, 52), 194 (100), 183 (90), 182 (60), 121 (44), 82 (36); NMR spectrum δ_{F_1} −164.25 (dm, $^3J_{F_1,F_2}$ = 21 Hz), δ_{F_2} = −170.25 (ddm, $^2J_{F,H}$ = 60 Hz, $^3J_{F_1,F_2}$ = 21 Hz), δ_F −152.25 (dm), −153.75 (dm), −146.25 (dm), −146.85 (dd), δ_{CFH} 4.63 (dm, 1 H), δ_{CH} 2.72 (m, 1 H), δ_{CH_2} 1.06–1.94 (m, 10 H).

On heating at T = 150 °C, product **3** was transformed into product **2**. The separation of the crude reaction mixture formed by irradiation by preparative GLC (FFAP 30% on Chromosorb AW at T = 200 °C) gave only cyclohexylpentafluorobenzene.

Irradiation of hexafluorobenzene and benzophenone in cyclopentane gave, after GLC separation (FFAP 30% on Chromosorb AW at T = 170 °C), 2% of cyclopentylpentafluorobenzene (liquid product). Mass spectrum, calcd for $C_{11}F_5H_9$ m/e 236.0624, found m/e 236.0630, m/e 236 (M^+, 4), 139 (30), 123 (39), 85 (39), 84 (47), 69 (30), 67 (62), 41 (100); NMR spectrum $\delta_{F_{2,F_6}}$ −145.5 (dd, $J_{F,F}$ = 24, 9 Hz), $\delta_{F_{3,F_5}}$ −165.75 (td, $J_{F,F}$ = 24, 9 Hz), δ_{F_4} −152.25.

References and Notes

(1) J. Cornelisse and E. Havinga, *Chem. Rev.*, **75**, 353 (1975).
(2) D. Bryce-Smith, A. Gilbert, and S. Krestonosich, *J. Chem. Soc., Chem. Commun.*, 405 (1976).
(3) D. Bryce-Smith, B. E. Connett, A. Golbert, and E. Kendrick, *Chem. Ind. (London)*, 855 (1966).
(4) R. D. Chambers, "Fluorine in Organic Chemistry", Wiley, New York, N.Y., 1973, p 313; W. A. Sheppard and C. M. Sharts, "Organic Fluorine Chemistry", W. A. Benjamin, New York, N.Y., 1969, p 200.
(5) P. A. Claret, G. H. Williams, and J. Coulson, *J. Chem. Soc. C*, 341 (1968);

G. H. Williams, *Intra-Sci. Chem. Rep.*, **3**, 229 (1969); P. H. Oldham, G. H. Williams, and B. A. Wilson, *J. Chem. Soc. B*, 1346 (1970).
(6) A. Weissberger, Ed., "Technique of Organic Chemistry", Vol. VII, Interscience, New York, N.Y., 1955.

Registry No.—**2**, 10304-79-7; **3**, 65915-27-7; hexafluorobenzene, 392-56-3; cyclohexane, 110-82-7.

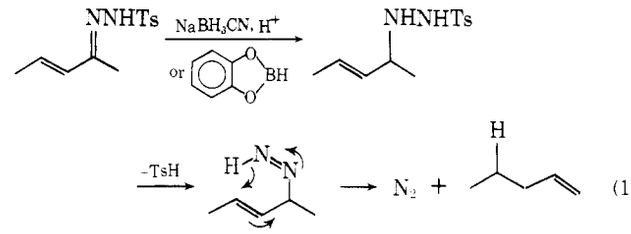
Sodium Borohydride in Acetic Acid. A Convenient System for the Reductive Deoxygenation of Carbonyl Tosylhydrazones

Robert O. Hutchins* and Nicholas R. Natale

Department of Chemistry, Drexel University, Philadelphia, Pennsylvania

Received December 21, 1977

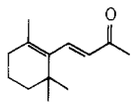
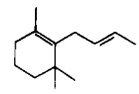
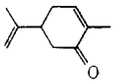
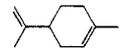
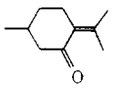
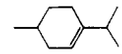
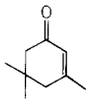
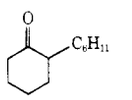
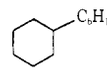
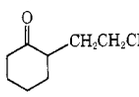
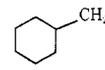
The reductions of carbonyl tosylhydrazones to hydrocarbons with sodium cyanoborohydride in acidic media[1] or with catecholborane[2] provide mild and selective alternatives to standard Wolf–Kishner deoxygenation.[1,2] With α,β-unsaturated derivatives, alkenes are usually furnished in which the double bond migrates to the position formerly occupied by the carbonyl (eq 1) even when such movement produces less thermodynamically stable positional isomers. Thus, alkene linkages may be moved from conjugation with aromatic rings or other π systems and the procedures offer a convenient pathway to exocyclic olefins.[1,2] The mechanism for this intriguing "alkene walk" reaction apparently proceeds through a diazene intermediate which deposits a hydride via a 1,5 migration as illustrated in eq 1.



(1)

The full synthetic potential of the methods are, however, hampered by the relative expense of both hydride reagents,

Table I. Reductive Deoxygenation of Tosylhydrazones with Sodium Borohydride–Acetic Acid

Tosylhydrazone	Registry no.	Method[a]	Time at 70 °C, h	Product	Registry no.	% yield isolated
	21195-61-9	A B C B[b]	2.5 1.0 2.5 3.0		13066-63-2	87 89 52 81
	41780-85-2	A B	2.0 1.0		1003-64-1	72 61
	21195-60-8	A B	2.0 1.5		138-86-3	10 70
	21195-64-2	B	1.5		500-00-5	51
	65226-90-6	B	4.0		1712-47-6	67
	65226-92-8	B	3.0		65226-94-0	57
	21195-62-0	B	5.0		503-44-6	18
$C_6H_5CH{=}CHCHO$	7318-33-4	A B	1.5 1.5	$C_6H_5CH_2CH{=}CH_2$	300-57-2	42 56
$C_6H_5CH{=}CHCOCH_3$	17336-65-1	B	3.0	$C_6H_5CH_2CH{=}CHCH_3$	1560-06-1	54
$CH_3(CH_2)_4CO(CH_2)_4CH_3$	65930-66-7	A B	1.5 1.5	$CH_3(CH_2)_9CH_3$	1120-21-4	81 84
	41780-66-9	A B	2.0 2.0		92-51-3	61 61
	13992-91-1	A B	2.0 2.0		41010-09-7	68 70
$o\text{-}OC_2H_5C_6H_4CHO$	65609-76-9	A B	2.0 3.0	$o\text{-}OC_2H_5C_6H_4CH_3$	614-71-1	44 80
$C_6H_5CO(CH_2)_2CH_3$	41780-81-8	B	4.0	$C_6H_5(CH_2)_3CH_3$	104-51-8	68

[a] Method C involved preparation and utilization of $NaBH(OAc)_3$ in benzene as described in ref 7f; this procedure appears inferior for the present application. [b] The tosylhydrazone prepared in situ in acetic acid from the ketone and tosylhydrazone followed by addition of $NaBH_4$.

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