same Brønsted correlation argues strongly for a general base mechanism, since for a prominent nucleophilic pathway one would expect that anionic and neutral nucleophiles would have quite different reactivities.

There is no support for any significant nucleophilic role for the buffer components in the hydrolysis process. This is in contradiction of Humffray and Ryans' claims[5] but does corroborate the study of Pratt et al. although their substrate was a trisiloxane.[6] Quite likely, the source of the discrepancy in the former's work comes from the "rescaling" procedure used to compare data derived from two different buffer systems, *n*-butylamine and Tris.[5]

What is apparently curious is why the 4-nitrophenyl 4-nitrobenzenesulfonate studied by Williams et al.[8] in 10% aqueous dioxane undergoes direct nucleophilic substitution with many of the same oxyanions as used here. The preference between nucleophilic and general base routes for a given substrate undoubtedly depends upon a variety of complex effects such as steric accessibility, transition-state and ground-state solvation, and the electrophilicity of the substrate. We do not believe that the difference between the behavior of the silane and sulfoxide can be attributed to steric encumbrance in the former since Åkerman[4] reported general base catalysis of the hydrolysis of trimethylphenoxysilane, a much less sterically demanding system. More likely, in our opinion the transition state for oxyanion attack of the sulfonate ester is stabilized because the excess electron density is delocalized to the electronegative oxygens. On the other hand, since the silane has no such delocalization of charge possible, a general base pathway is favored, thereby avoiding the formation of large amounts of negative charge on Si in the transition state.

Acknowledgment. We are grateful to the University of Alberta and Natural Sciences and Engineering Research Council of Canada for financial assistance.

Registry No. 1, 98525-64-5; $CF_3CH_2O^-$, 24265-37-0; 2-$OC_6H_4O^{2-}$, 19021-48-8; $Cl_3CCH_2O^-$, 98525-65-6; 2-$C_5H_4NO^-$, 15473-97-9; 4-$OC_6H_4O^{2-}$, 48100-05-6; 2,4-$(CH_3)_2C_6H_3O^-$, 86260-38-0; 4-$CH_3C_6H_4O^-$, 22113-51-5; $C_6H_5O^-$, 3229-70-7; 4-$ClC_6H_4O^-$, 24573-38-4; 4-$CH_3CO_2C_6H_4O^-$, 98525-66-7; 3-$NO_2C_6H_4O^-$, 16554-54-4; 2,4-$Cl_2C_6H_3O^-$, 53678-12-9; 2,6-$Cl_2C_6H_3O^-$, 53330-27-1; $C_6F_5O^-$, 26910-95-2; 4-$N(CH_3)_2C_5H_4N$, 1122-58-3; succinate, 56-14-4; imidazole, 288-32-4.

Cyclopropanations of Alkenes Using Dibromomethane

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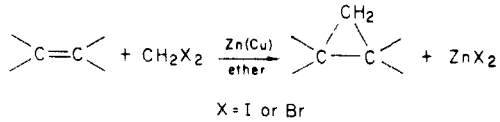
Although the utilization of diiodomethane in Simmons–Smith-type cyclopropanations of alkenes has been well established,[1] employment of the considerably less expensive, easier to purify and store dibromomethane has seldom been reported. This is primarily because the recommended procedure[1,2] for cyclopropanations employing dibromomethane specifies use of a separately prepared 30-mesh granular zinc–copper couple, involves long reaction times, and affords significantly lower isolated yields of cyclopropanation products than from corresponding diiodomethane reactions.



We now report a procedure using dibromomethane for cyclopropanation of alkenes which requires only short reaction times and also gives yields that are competitive with those obtained by using diiodomethane. This procedure utilizes sonocation of the reaction mixture in an ultrasonic cleaning bath to promote the heterogeneous zinc–copper couple reaction with dibromomethane through ultrasonically produced cavitation.[3-5] Also, it makes use of the convenient Rawson and Harrison zinc dust–cuprous chloride method[6] for generating the zinc–copper couple in situ.

Table I summarizes the results of cyclopropanations using dibromomethane and the present procedure on a number of representative alkenes. The data reveal the wide applicability of the procedure as well as its tolerance to various changes in experimental conditions. The yields of cyclopropanes isolated are generally competitive with those obtained with diiodomethane especially if one considers the fact that diiodomethane currently costs almost 20 times per mole greater than does dibromomethane and often requires repurification before use. Thus, for syntheses of cyclopropanes starting with readily available alkenes, the present procedure using dibromomethane is clearly the method of choice if expense is an important factor.

Experimental Section

General Procedures. Boiling points are uncorrected. ^1H NMR spectra were measured at 90 MHz with a Varian EM-390 spectrometer. Chemical shifts are reported in ppm downfield from Me_4Si and were referenced from Me_4Si and/or $CHCl_3$ internal standards. Zinc dust (Mallinckrodt), cuprous chloride (Mallinckrodt), dibromomethane (Aldrich), and anhydrous ether (Mallinckrodt) were used without further purification. The various alkenes were obtained commercially and redistilled before use.

General Procedure for Cyclopropanations Using CH_2Br_2. A 500-mL three-necked, round-bottomed flask is fitted with a Graham condenser and drying tube over an Allihn condenser and a pressure equalized dropping funnel and equipped for overhead mechanical stirring. Into the flask are added 52 g (0.80 mol) of zinc dust, 8.0 g (0.08 mol) of cuprous chloride, 75 mL of anhydrous ether, and 70 g (0.40 mol) of dibromomethane. To the addition funnel is added 0.20 mol of the alkene in 50 mL of anhydrous ether. The apparatus is positioned in a 125-W Branson ultrasonic bath which is filled to about 3 cm from the top with water preheated to 45–50 °C. Sonocation and stirring are started, and the position of the ultrasonic bath beneath the reaction vessel is varied so as to achieve maximum cavitation. Then the alkene is added dropwise to the reaction mixture over a 5–10-min period. After approximately a 1-h induction period, the reaction of the dibromomethane and zinc–copper couple usually starts. This is evidenced by a change in the color of the reaction mixture from gray to a purple-gray and by the onset of rapid refluxing. The stirring and sonocation are then continued for an additional 3 h.

As an alternative procedure, which results in a shorter induction period but otherwise has no major effect on the reaction, addition of the alkene is postponed until after the reaction of the zinc-

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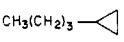
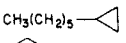
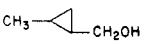
Table I. Cyclopropanations of Various Alkenes Using Dibromomethane and Zinc Dust-Cuprous Chloride in Ether by Stirring and Sonocation in a 125-W Ultrasonic Bath[a]

starting alkene	product	sonocation conditions[b]	total reac time, h	distilled yield, %
		A	4	60
		A	4	72
		B	2.5	64
		B	2.5	40
		B	2	50
$CH_3(CH_2)_3CH{=}CH_2$		A	4	30
$CH_3(CH_2)_5CH{=}CH_2$		B	2	28
		B	3.5	41
$CH_3CH{=}CHCH_2OH$		A	4	57

[a] Reactions were generally carried out by using 0.2 mol of alkene, 0.4 mol of dibromomethane, 0.8 mol of zinc dust, and 0.08 mol of cuprous chloride in 125 mL of ether using a bath temperature of 45 ± 5 °C. [b] (A) All reagents were present initially and sonocation was continued throughout the reaction period. (B) The alkene was added after vigorous reaction of the CH_2Br_2 and Zn dust was under way (ca. 30 min), and sonocation was continued for an additional 30-60 min and stirring without sonocation for a further 30-60 min.

copper couple and dibromomethane starts (ca. 30 min). Sonocation is continued for an additional 60 min and stirring without sonocation for a further 60 min.

After the reaction is complete, the ultrasonic bath is removed, and the reaction mixture is cooled in an ice bath, diluted with 200 mL of *n*-pentane, and, while being stirred, treated by dropwise addition of 150 mL of saturated aqueous ammonium chloride solution. The organic layer is separated, and the aqueous layer is washed with *n*-pentane (1 × 50 mL). The combined organic layer is washed with 10% NaOH (3 × 100 mL) and saturated aqueous NaCl (1 × 100 mL) and dried over anhydrous $MgSO_4$. The solvents are removed by distillation on a stream bath through a Vigreux column, and the remaining oil is fractionally distilled.

Cyclopropanation of Cyclohexene. The reaction of 21 g (0.26 mol) of cyclohexene, 88 g (0.50 mol) of CH_2Br_2, 66 g (1.0 mol) of zinc dust, and 9.9 g (0.10 mol) of CuCl in 100 mL of ether for 4 h gave 15 g (60%) of distilled bicyclo[4.1.0]heptane: bp 114–117 °C; n^{25}_D 1.4550 (lit.[8] bp 116–117 °C; n^{25}_D 1.4546); NMR (CCl_4) δ 0.0 (q, 1 H, cyclopropyl), 0.2–1.0 (m, 3 H, cyclopropyl), 1.0–2.0 (m, 8 H). The distillation pot residue weighed about 3 g.

Cyclopropanation of Cyclooctene. The reaction of 21 g (0.19 mol) of cyclooctene, 72 g (0.41 mol) of CH_2Br_2, 52 g (0.80 mol) of zinc dust, and 7.6 g (0.08 mol) of CuCl in 125 mL of ether for 4 h gave 17 g (72%) of distilled bicyclo[6.1.0]nonane: bp 69–71 °C (30 torr); n^{25}_D 1.4673 [lit.[8] bp 89 °C (66 torr); $n^{25.5}_D$ 1.4668]; NMR (CCl_4) δ −0.3 (m, 1 H, cyclopropyl), 0.4–2.3 (m, 15 H). The distillation pot residue weighed about 4 g.

Cyclopropanation of α-Pinene. The reaction of 27 g (0.20 mol) of α-pinene, 70 g (0.40 mol) of CH_2Br_2, 52 g (0.80 mol) of zinc dust, and 8.0 g (0.08 mol) of CuCl in 125 mL of ether for 2.5 h gave 9.1 g of unreacted α-pinene and 8.0 g (40% based on reacted α-pinene) of pure 2,7,7-trimethyltricyclo[4.1.1.$0^{2,4}$]octane: bp 82–84 °C (35 torr); $n^{21.5}_D$ 1.4760 [lit.[10] bp 78 °C (36 torr); n^{20}_D 1.4782]; NMR (CCl_4) δ 0.2 (m, 1 H, cyclopropyl), 0.4–2.5 (m, 17 H, with CH_3's at 1.10, 1.15, and 1.25). The distillation pot residue weighed about 5 g.

Cyclopropanation of β-Pinene. The reaction of 27 g (0.20 mol) of β-pinene, 70 g (0.40 mol) of CH_2Br_2, 52 g (0.80 mol) of zinc dust, and 8.0 g (0.08 mol) of CuCl in 125 mL of ether for 2 h gave 15 g (50%) of distilled 6′,6′-dimethylspiro[cyclopropane-1,2′-norpinane]: bp 71–73 °C (18 torr); n^{25}_D 1.4765 [lit.[10,11] bp 80 °C (25 torr); n^{20}_D 1.4762]; NMR (CCl_4) δ 0.0–0.7 (m, 4 H, cyclopropyl), 1.0 (s, 3 H, endo-CH_3), 1.2 (s, 3 H, exo-CH_3), 1.1–2.3 (m, 8 H). The distillation pot residue weighed about 15 g.

Cyclopropanation of 1-Hexene. The reaction of 15 g (0.18 mol) of 1-hexene, 69 g (0.40 mol) of CH_2Br_2, 52 g (0.80 mol) of zinc dust, and 7.8 g (0.079 mol) of CuCl in 125 mL of ether for 4 h gave 5.3 g (30%) of distilled *n*-butylcyclopropane: bp 94–96 °C; n^{31}_D 1.4010 [lit.[12] bp 99.5 °C; n^{20}_D 1.4042]; NMR (CCl_4) δ −0.1 (m, 2 H, cyclopropyl), 0.2–0.8 (m, 3 H, cyclopropyl), 0.8–1.6 (m, 9 H). The distillation pot residue weighed 9 g.

Cyclopropanation of 1-Octene. The reaction of 22 g (0.20 mol) of 1-octene, 70 g (0.40 mol) of CH_2Br_2, 52 g (0.80 mol) of zinc dust, and 8.0 g (0.08 mol) of CuCl in 125 mL of ether for 2 h gave 7.3 g (28% based on reacted 1-octene) of distilled *n*-hexylcyclopropane: bp 90–100 °C (47 torr); n^{22}_D 1.4176 [lit.[13] bp 148 °C (760 torr); n^{25}_D 1.4160]; NMR (CCl_4) δ 0.2 (m, 2 H, cyclopropyl), 0.1–0.8 (m, 3 H, cyclopropyl), 0.8–1.7 (m, 13 H). The distillation forerun contained 1.3 g of unreacted 1-octene. The pot residue weighed 8 g.

Cyclopropanation of 2,3-Dihydropyran. The reaction of 17 g (0.20 mol) of 2,3-dihydropyran, 70 g (0.40 mol) of CH_2Br_2, 52 g (0.80 mol) of zinc dust, and 8.0 g (0.08 mol) of CuCl in 125 mL of ether for 3.5 h gave 8.1 g (41%) of distilled 2-oxabicyclo-[4.1.0]heptane: bp 119–121 °C; n^{22}_D 1.4491 [lit.[13] bp 121 °C; n^{25}_D 1.4488]; NMR (CCl_4) δ 0.2–0.6 (m, 2 H, cyclopropyl), 0.6–1.0 (m, 1 H, cyclopropyl), 1.0–2.0 (m, 4 H, ring residue), 2.9–3.7 (m, 3 H, CHO). The distillation pot residue weighed about 6 g.

Cyclopropanation of Crotyl Alcohol. The reaction of 16 g (0.22 mol) of *trans*-crotyl alcohol, 76 g (0.44 mol) of CH_2Br_2, 53 g (0.82 mol) of zinc dust, and 7.9 g (0.08 mol) of CuCl in 200 mL of ether for 4 h gave 11 g (57%) of distilled *trans*-3-methylcyclopropylcarbinol: bp 50–54 °C (23 torr); n^{25}_D 1.4271 [lit.[14] bp 134–135 °C (760 torr); n^{25}_D 1.4291]; NMR (CCl_4) δ 0.1–1.0 (m, 4 H, cyclopropyl), 1.1 (d, J = 6 Hz, 3 H, CH_3), 3.3 (d, J = 6 Hz, 2 H, CH_2OH), 4.9 (s, 1 H, OH). The distillation pot residue weighed about 2 g.

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Registry No. CH_2Br_2, 74-95-3; cyclohexene, 110-83-8; bicyclo[4.1.0]heptane, 286-08-8; cyclooctene, 931-88-4; bicyclo[6.1.0]nonane, 286-60-2; α-pinene, 80-56-8; 2,7,7-trimethyltricyclo[4.1.1.$0^{2,4}$]octane, 32549-17-0; β-pinene, 127-91-3; 6′,6′-dimethylspiro[cyclopropane-1,2′-norpinane], 35117-81-8; 1-hexene, 592-41-6; butylcyclopropane, 930-57-4; 1-octene, 111-66-0; hexylcyclopropane, 4468-61-5; 3,4-dihydropyran, 110-87-2; 2-oxabicyclo[4.1.0]heptane, 286-16-8; *trans*-crotyl alcohol, 504-61-0; *trans*-2-methylcyclopropylcarbinol, 21003-36-1.

Condensation with Trifluoroacetonitrile: A Simple One Step Synthesis of 5-Cyano-6-(trifluoromethyl)uracil

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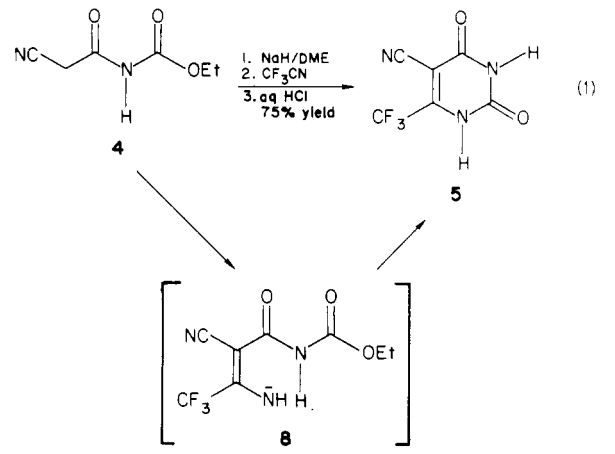
A number of fluorine-substituted uracil derivatives show interesting biological activity. For example, 5-fluorouracil derivatives are useful as antitumor agents, and 5-(trifluoromethyl)deoxyuridine shows marked antiviral activity.[1,2] The binding of 6-substituted uracil to thymidine phosphorylase has been studied. The 6-trifluoromethyl derivative has been reported to bind to this enzyme sevenfold better than the 6-methyl analogue. Presumably the increased activity was due to the increased acidity of the uracil.[3] The 3-substituted-6-(trifluoromethyl)uracils have also been reported as herbicides.[4]

It is noteworthy that the existing synthetic routes to the 6-(trifluoromethyl)uracils do not allow a facile derivation at the 5-position,[3-5] which is needed for the synthesis of various analogues for biological evaluations. An acid function such as a cyano group at the 5-position is highly desirable, since it would offer increased opportunities for derivation. However, the 5-cyano derivative was hitherto unknown. It has been reported that an active methylene compound reacted with trifluoroacetonitrile to give the corresponding 2-trifluoromethyl enamine.[6] By employing an active methylene compound with a γ-ester function, such as *N*-(cyanoacetyl)urethane (**4**), one should be able to prepare the corresponding uracil in one step. In fact, treatment of **4** with sodium hydride followed by reaction of the resulting anion with trifluoroacetonitrile gave 5-cyano-6-(trifluoromethyl)uracil (**5**) in 75% yield (eq 1). Presumably the reaction intermediate was enamine **6**, though it was not isolated. The structural assignment of **5** was supported by its spectral properties and combustion analysis. Trifluoroacetonitrile has been condensed with enamines or ynamines to give the corresponding 2,4-bis(trifluoromethyl)pyrimidine.[7] However, trifluoroacetonitrile has not been used for the synthesis of uracils.



(1)

Experimental Section

Melting points are uncorrected. ^{19}F NMR spectra were obtained on a Varian EM-360 spectrometer. ^1H NMR spectra were obtained on a Varian XL-300 spectrometer. ^{13}C NMR spectra were recorded on a JEOL FX-100 spectrometer. Signals are reported in parts per million downfield from tetramethylsilane. Infrared spectra were obtained on a Perkin-Elmer Model 727B infrared spectrophotometer. Mass spectra were obtained on a Finnigan MAT CH7A mass spectrometer. Elemental microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

5-Cyano-6-(trifluoromethyl)uracil (5). To a solution of *N*-(cyanoacetyl)urethane (**4**) (100 g, 0.64 mol, Aldrich Co.) in 700 mL of anhydrous 1,2-dimethoxyethane under an atmosphere of nitrogen was added 34 g (0.7 mol) of sodium hydride (50% oil dispersion). The temperature of the exothermic reaction was kept below 45 °C by a water bath. The resulting muddy gray suspension was stirred for 30 min. After the exothermic reaction subsided, it was warmed to 35 °C by external heating. To this mixture, a stream of trifluroacetonitrile (Fairfield Co.) was added in slowly. At the end of 5.5 h, the uptake of trifluoroacetonitrile became very slow, and an excess amount of trifluoroacetonitrile was used. The resulting brown solution was poured into cold 6 N aqueous hydrochloric acid and extracted with ethyl acetate. The ethyl acetate layer was washed with water, dried ($MgSO_4$), and concentrated to give a solid. It was washed with chloroform/acetonitrile to give 97 g of a cream color solid (75% yield) as **5**: mp 245–253 °C; IR (Nujol) 2250 (m, C≡N), 1703 (s), 1630 (s) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 12.1 (s, N_4H, 1 H), 9.9 (br s, N_1H, 1 H; chemical shift and integration varied with the amount of moisture in Me_2SO-d_6); ^{13}C NMR (Me_2SO-d_6) δ 160.4 (C_4), 149.6 (C_2), 148.9 (C_6, q, J = 35.9 Hz), 118.3 (CF_3, q, J = 278.1 Hz), 111.6 (CN), 86.9 (C_5, q, J = 1.4 Hz); ^{19}F NMR (Me_2SO-d_6, CCl_3F) δ −67.53; mass spectrum, *m/e* (relative intensity) 205 (M^+, 40.3), 162 (40.0), 96 (12.3), 93 (59.9), 28 (100.0).

Anal. Calcd for $C_6H_2F_3N_3O_2$: C, 35.14; H, 0.98; N, 20.49. Found: C, 35.14; H, 0.92; N, 20.48.

Registry No. **4**, 6629-04-5; **5**, 98577-47-0; trifluoroacetonitrile, 353-85-5.

Synthesis and Fluorescence Spectra of Structural Analogues of Potential Benzo[*b*]fluoranthene-DNA Adducts[1,2]

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Benzo[*b*]fluoranthene (**1**), an environmental carcinogen[3-7] interacts in vivo with the DNA of mouse epidermis

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