IR (KBr) 3100, 3020, 3000, 2960, 2930, 2860, 2260, 1640, 1435; ^{1}H NMR (CD_3COCD_3) 5.17 and 5.01 (s, 2 × 2 H, H_2C=C (9,10)), 3.98 (s, 2 H, HC(1,8)), 3.67 and 3.36 (d, 17, 2 × 2 H, H_2C(3,6)), 1.60 (s, 6 H, $(CH_3)_2C$=C(11)); ^{13}C NMR (CD_3CN) 147 (m, C(11)), 143.7 (m, C(9,10)), 137.2 (m, C(2.7)), 114.9 (m, C=C(11)), 112.5 (m, CN), 112.0 (m, CN), 102.6 (t, 159, CH_2=C(9,10)), 55.1 (dm, 152, C(1,8)), 40.2 (m, C(4,5)), 32.5 (t, 140, C(3,6)), 19.7 (qq, 126, $^3J_{C,H}$ = 4.5, $(CH_3)_2C$=C(11)); MS, 313 (20), 312 (12, M^+), 298 (34), 297 (100), 169 (98), 156 (30), 153 (30), 141 (28), 132 (94). Anal. Calcd for $C_{20}H_{16}N_4$ (mol wt 312.375): C, 76.90; H, 5.16; N, 17.94. Found: C, 77.37; H, 5.16; N, 17.88.

15-Isopropylidenetetracyclo[6.6.1.0^{2,7}.0^{9,14}]pentadeca-2(7),9(14)-diene-4,4,5,5,11,11,12,12-octacarbonitrile (13). A mixture of **7** (50 mg, 0.27 mmol) and TCNE (70 mg, 0.54 mmol) in acetone (2 mL) was stirred at 20 °C for 12 h. The bisadduct **13** was precipitated by addition of a few drops of pentane and cooling to −10 °C: yield 80 mg (67%); colorless crystals; mp 268–269 °C dec; UV (EtOH, 95%) final absorption (ϵ_{230} 5200); IR (KBr) 3030, 2990, 2950, 2930, 2880, 2860, 2260, 1615, 1440; ^{1}H NMR (CD_3COCD_3) 4.3 (s, 2 H, HC(1,8)), 3.75 (br s, 8 H, H_2C(3,6,10,13)), 1.50 (s, 6 H, $(CH_3)_2C$=C:15)); ^{13}C NMR (CD_3CN) 160 (m, C(15)), 143.1 (m, C(2,7,9,14)), 112.5 (m, CN), 112.1 (m, CN), 100.5 (m, C=C(15)), 55.8 (d, 152, C(1,8)), 40.1 (m, C-(4,5,11,12)), 33.8 (t, 140, C(3,6,10,13), 22.6 (qq, 126, $^3J_{C,H}$ = 4, $(CH_3)_2C$=C(15)); MS, 441 (14), 440 (28, M^+), 398 (6), 375 (49), 297 (66), 169 (47), 107 (42), 105 (56), 91 (47), 67 (100). Anal. Calcd for $C_{26}H_{16}N_8$ (mol wt 440.468): C, 70.90; N, 3.66; N, 25.44. Found: C, 70.63; H, 3.84; N, 25.28.

Dimethyl 11-Isopropylidene-9,10-dimethylenetricyclo-[6.2.1.0^{2,7}]undeca-2(7),4-diene-4,5-dicarboxylate (14). A mixture of **7** (0.22 g, 1.2 mmol), dimethyl acetylenedicarboxylate (0.171 g, 1.2 mmol), and toluene (5 mL) was heated in a Pyrex tube sealed under vacuum to 60 °C for 2 h. After solvent evaporation, the crude adduct **14** was purified on a silica gel column (hexane/EtOAc, 3:1) and recrystallized from hexane/EtOAc, yielding 0.305 g (78%) of colorless crystals: mp 112–113 °C; UV (dioxane) 238 (14 030), 244 (13 700), 255 (sh, 10 680); UV (CH_3CN) 237 (13 300), 244 (13 050), 253 (sh, 9850); IR (KBr) 3010, 2990, 2980, 1740, 1725, 1640, 1430, 1300, 1270, 1250, 1245, 1150, 890; ^{1}H NMR ($CDCl_3$) 5.05 and 4.88 (s, 2 × 2 H, H_2C=C(9,10)), 3.75 (s, 6 H), 3.6 (s, 2 H, HC(1,8)), 3.1 (m, 4 H, H_2C(3,6)), 1.6 (s, 6 H, $(CH_3)_2C$=C(11)); ^{13}C NMR (CD_3CN) 169.3 (m, CO), 149.1 (m, C(11)), 145.5 (m, C(9,10)), 138.3 (m, C(2,7)), 134.3 (m , C(4,5)), 112.3 (m, C=C(11)), 100.8 (t, 158, H_2C=C(9,10)), 54.8 (dm, 150, C(1,8)), 52.9 (q, 146, CH_3OOC), 27.5 (t, 130, C(3,6)), 19.7 (qq, 126, $^3J_{C,H}$ = 4, $(CH_3)_2C$=C(11)); MS, 327 (13), 326 (59, M^+), 309 (28), 294 (100), 279 (85), 267 (24), 251 (23), 242 (14), 235 (32), 227 (26), 208 (45), 193 (47), 178 (29), 165 (32), 156 (31), 149 (41), 141 (27), 115 (25). Anal. Calcd for $C_{20}H_{22}O_4$ (mol wt 326.39): C, 73.60; H, 6.79. Found: C, 73,67; H, 6.74.

Tetramethyl 15-Isopropylidenetetracyclo[6.6.1.0^{2,7}.0^{9,14}]-pentadeca-2(7),4,9(14),11-tetraene-4,5,11,12-tetracarboxylate (15). A mixture of **7** (0.21 g, 1.14 mmol), dimethyl acetylenedicarboxylate (0.34 g, 2.4 mmol), and toluene (5 mL) was heated in a Pyrex tube sealed under vacuum to 60 °C for 24 h. After solvent evaporation, crude **15** was recrystallized from hexane/EtOAc (3:1), yielding 0.373 g (70%) of colorless crystals: mp 177–187 °C dec; UV (CH_3CN) final absorption (ϵ_{200} 23 100); IR (KBr) 3000, 2970, 2920, 2860, 2840, 1730, 1680, 1640, 1430, 1290, 1270, 1240, 1230, 1150, 1060; ^{1}H NMR ($CDCl_3$) 3.75 (s, 12 H), 3.65 (s, 2 H) 3.2 (m, 8 H), 1.45 (s, 6 H); ^{13}C NMR (CD_3CN) 169.5 (m, CO), 160.3 (m, C(15)), 143.9 (m, 2,7,9,14)), 134.5 (m, C(4,5,11,12)), 96.0 (m, C=C(15)), 54.6 (dd, 150, $^3J_{C,H}$ = 6, C(1,8)), 52.8 (q, 148, CH_3O), 29.8 (tm, 135, C(3,6,10,13)), 18.7 (qq 126, $^3J_{C,H}$ = 4, $(CH_3)_2C$=C(15)); MS, 469 (6), 468 (10, M^+), 466 (15), 450 (6), 435 (31), 407 (100), 377 (63), 348 (37), 318 (26), 215 (36), 202 (35), 59 (37). Anal. Calcd for $C_{26}H_{28}O_8$ (mol wt 468.505): C, 66.65; H, 6.02. Found: C, 66.76; H, 6.15.

For the kinetic measurements ref 17.

Acknowledgment. We thank Hoffmann-La Roche & Co. (Basel), the Swiss National Science Foundation, and the Fonds Herbette (Lausanne) for generous support. We are grateful to Mr. C. Debonneville for technical assistance.

Registry No. 2, 56677-16-8; **7**, 82614-18-4; **8**, 51510-23-7; **9**, 82614-21-9; **10**, 82614-22-0; **11**, 82614-23-1; **12**, 82614-19-5; **13**, 82614-20-8; **14**, 82614-24-2; **15**, 82614-25-3; TCNE, 670-54-2; CO, 630-08-0; methanol, 67-56-1; dimethyl acetylenecarboxylate, 762-42-5.

(17) Pilet, O.; Chollet, A.; Vogel, P. *Helv. Chim. Acta* **1979** *62*, 2341.

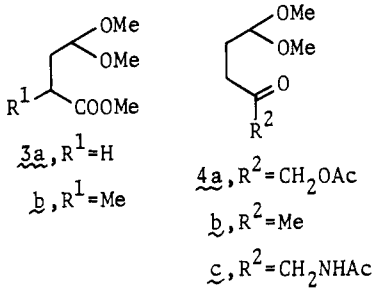
Convenient Syntheses of 4,4-Dimethoxy Esters and Ketones[1]

Tameo Iwasaki,* Takashi Nishitani, Hiroshi Horikawa, and Ichizo Inoue

Department of Synthetic Chemistry, Research Laboratory of Applied Biochemistry, Tanabe Seiyaku Co. Ltd., 3-16-89 Kashima, Yodogawa-ku, Osaka 532, Japan

Received December 3, 1981

We have previously reported[2] a new synthetic method for the formation of unconventional nucleosides having oxacycloalkane substituents wherein [(trimethylsilyl)-oxy]alkanal dimethyl acetals (Me_3Si acetals, **1**) undergo a novel reaction with 2,4-bis[(trimethylsilyl)oxy]pyrimidines under Lewis acid catalyzed conditions (Scheme I). In connection with the above work, we required routes to 1,4-dicarbonyl compounds **3** and **4** which are key inter-



mediates for the preparation of the Me_3Si acetals.

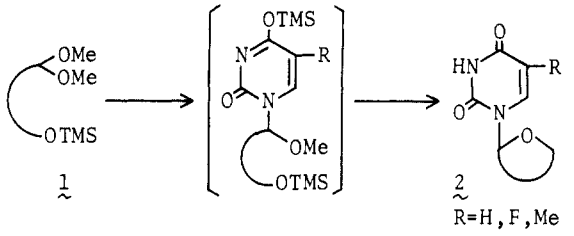
The recent literature is replete with synthetic methods for formation of 1,4-dicarbonyl compounds since they are of extensive value for the syntheses of some natural products consisting of five-membered heterocycles such as pyrroles and furans as well as cyclopentenone ring systems.[3-10] We herein report a convenient synthesis of 4,4-dimethoxy esters **3** and ketones **4** based on electrochemical reactions of 2-substituted furans.

4,4-Dimethoxy Esters. It is well documented that the anodic oxidation of furans gives rise to the methoxylation at the 2- and 5-positions of the furan rings to provide the 2,5-dimethoxy-2,5-dihydrofurans.[11,12] Recently, Torii et al.[13] have developed a highly efficient procedure for either

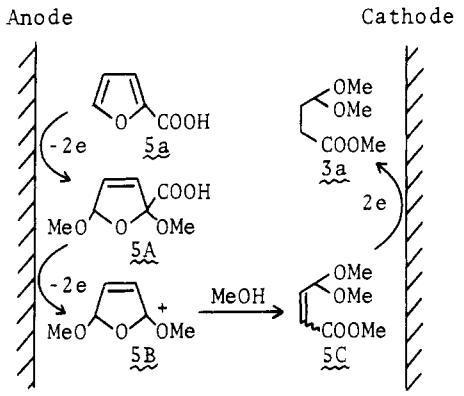
(1) Synthetic Electroorganic Chemistry. 15. Some of the results have already been presented in a preliminary form at the 1st Symposium on Elecroorganic Chemistry, Kyoto, Japan, 1980; p 23.
(2) Iwasaki, T.; Nishitani, T.; Horikawa, H.; Inoue, I. *Tetrahedron Lett.* **1981**, 1029.
(3) Stork, G.; Bork, R. *J. Am. Chem. Soc.* **1964**, *86*, 935.
(4) Ellison, R. A. *Synthesis* **1973**, 397.
(5) Mukaiyama, T.; Araki, M.; Takei, H. *J. Am. Chem. Soc.* **1973**, *95*, 4763.
(6) Stowell, J. C. *J. Org. Chem.* **1976**, *41*, 560 and references cited therein.
(7) Hazen J. R. *J. Org. Chem.* **1970**, *35*, 973.
(8) See, for example: Sherman, E.; Dunlop, A. P. *J. Org. Chem.* **1960**, *25*, 1309.
(9) Miles, D. H.; Loew, P.; Johnson, W. S.; Kluge, A. F.; Meinwald, J. *Tetrahedron Lett.* **1972**, 3019.
(10) Jone, T. H.; Blum, M. S.; Fales, H. M.; Thompson, C. R. *J. Org. Chem.* **1980**, *45*, 4778.
(11) Weinberg, N. L.; Weinberg, H. R. *Chem. Rev.* **1968**, *4*, 449.
(12) Tomilov, A. P.; Mairanovskii, S. G.; Fioshin, M. Y.; Smirnov, V. A. "Electrochemistry of Organic Compounds"; Wiley: New York, **1972**; p 417.

0022-3263/82/1947-3799$01.25/0

Scheme I



Scheme II



(*E*)- or (*Z*)-4,4-dimethoxy-2-butenoate by anodic oxidation of 2-substituted furans using platinum electrodes. We have examined a one-step synthesis of 4,4-dimethoxy alkanoates from 2-furoic acid (**5a**) and the derivative by electrochemical reactions using graphite electrodes.

Electrolysis of **5a** in methanol containing ammonium bromide–triethylamine under a constant current (62.5 mA/cm^2) with graphite electrodes in an undivided cell afforded the desired 4,4-dimethoxy ester **3a** in 77% yield. An 8-F/mol amount of electricity, twice the theoretical amount, is required to force the reaction to completion.

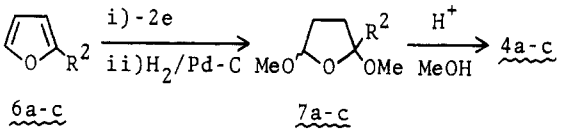
Scheme II depicts the electron-transfer reactions occurring at the electrodes. Both the anodic and cathodic processes are involved in this reaction. The anodic process[13] consists of the methoxylation of **5a** via a two-electron transfer to yield the dimethoxylated compound **5A**, followed by a two-electron transfer from **5A** to the anode to form the carbonium ion **5B**. Methyl 4,4-dimethoxy-2-butenoate (**5C**) formed by the nucleophilic attack of methanol on **5B** would be transferred to the cathode and then reduced to the product **3a**. In this reaction, the current density is one of the critical factors for the efficient formation of **3a**. Indeed, when the intermediate **5A**, which was prepared by saponification of methyl 2,5-dimethoxy-2,5-dihydrofuran-2-carboxylate,[14] was electrolyzed in methanol in the presence of triethylamine under a constant current of 62.5 mA/cm^2, **3a** was obtained in 52% yield. On the other hand, on electrolysis of **5A** under a constant current of 6 mA/cm^2, only the formation of methyl (*Z*)-4,4-dimethoxy-2-butenoate[13] was observed. The cathodic potential in the course of the electrolysis of **5a** under a constant current of 62.5 mA/cm^2 shifted from −1.58 to −1.99 V vs. SCE which is enough to reduce the olefin (**5C**).[16]

Table I. Effect of Electrolytes on Electrochemical Formation of 3a[a]

run	NH_4Br,[b] molar equiv	Et_3N,[b] molar equiv	yield,[c] %
1	0.10	1.50	34
2	0.10	1.12	31
3	0.10	0.56	60
4	0.10	0.28	70
5	0.05	0.28	78
6	0.20	0.28	73
7	0.50	0.28	28

[a] **5a** (0.2 mol) was electrolyzed in 350 mL of methanol. Details are given in the Experimental Section. [b] The values are based on the amount of **5a** used. [c] Isolation yields.

Scheme III



The use of the other electrolysis systems such as tetraethylammonium perchlorate (or tosylate)–triethylamine or ammonium bromide–sodium methoxide did not allow the reaction to proceed in good yields. In these cases, the amount of byproducts with higher boiling points than **3a** became significantly larger than that obtained in the ammonium bromide–triethylamine system; the byproducts are presumably formed by hydrodimerization and/or oligomerization of the activated olefin (**5C**).[17] The relative amount of ammonium bromide and triethylamine also have an influence on the product yields. The best yield was obtained with the use o 0.05 molar equiv. of ammonium bromide and 0.25 molar equiv. of triethylamine. The results are shown in tabular form in Table I.

The above procedure was also applied to the preparation of the substituted 4,4-dimethoxy esters. 3-Methyl-2-furoic acid (**5b**), for example, was electrolyzed under the best conditions to yield the corresponding ester (**3b**) in 65% yield.

Elecrochemical reactions involving both anodic and cathodic processes as described above show promise of wide application as a new tool in synthetic organic chemistry.

4,4-Dimethoxy Ketones. Several authors have demonstrated that 1,4-dicarbonyl compounds are prepared in situ from 2-substituted furans by utilizing anodic oxidation[19] or chemical oxidation[20] as a key step. We have examined the electrochemical transformation of the 2-substituted furans **6a–c** into the 4,4-dimethoxy ketones **4a–c** (Scheme III).

Anodic oxidation of 2-(acetoxymethyl)furan (**6a**) in methanol containing ammonium bromide at 10–20 °C with graphite electrodes in an undivided cell gave a mixture of *cis*- and *trans*-2,5-dimethoxy-2-(acetoxymethyl)-2,5-dihydrofuran in 80% yield. The hydrogenation of the dimethoxy compound was readily achieved in methanol over palladium on charcoal. The reduced dimethoxy compound (**7a**) was treated with a catalytic amount of a strongly acidic cation-exchange resin (SK-1B, H^+ form) in methanol for 1.5 h to afford the corresponding 4,4-dimethoxy ketone

(13) Tanaka, H.; Kobayashi, Y.; Torii, S. *J. Org. Chem.* **1976**, *41*, 3482.
(14) The saponification of methyl 2,5-dimethoxy-2,5-dihydrofuran-2-carboxylate[15] was carried out in 95% methanol containing 1 molar equiv of potassium hydroxide to afford the carboxylic acid **5A** in 52% yield as a syrup.
(15) Clauson-Kaas, N.; Limborg, F. *Acta Chem. Scand.* **1952**, *6*, 551.
(16) The Epc value (−2.08 V vs. SCE) was obtained in a dimethylformamide–0.2 M tetraethylammonium chloride system with a platinum cathode.
(17) Biazer, M. M.; Petrowitsch, J. P. *Prog. Phys. Org. Chem.* **1970**, *7*, 189.
(18) Beck, F. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 760.
(19) Shono, T.; Matsumura, Y.; Hamaguchi, H.; Nakamura, K. *Chem. Lett.* **1976**, 1249.
(20) Floyd, M. B. *J. Org. Chem.* **1978**, *43*, 1641.

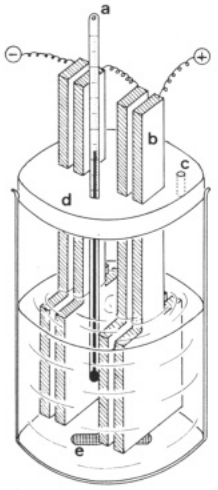


Figure 1. Electrolysis apparatus: a, thermometer; b, graphite electrode; c, gas outlet; d, rubber; e, stirrer bar.

(**4a**) in 76% yield; 10% of the starting material was recovered. In this reaction, the byproduct, 4-oxo-5-acetoxypentanal, was isolated in 4% yield. This is presumably formed by the action of a small amount of water included in the methanol.

The other 2-substituted 2,5-dimethoxytetrahydrofurans (**7b,c**) were also treated under the same conditions as above to give the corresponding 4,4-dimethoxy ketones (**4b,c**) in 57–71% yields.

Experimental Section

Equipment. All the boiling points were uncorrected. NMR spectra were measured by using a Hitachi Perkin-Elmer R-20 high-resolution NMR spectrometer with tetramethylsilane as an internal standard. Mass spectra were obtained on a Hitachi M-60 mass spectrometer. The electrolyses were carried out by using Hokuto PGS 2500 (2.5 A, 60 V) and PGS 2000 (2A-120V) potentiogalvanostats attached to a Hokuto HA-108A coulometer.

Reagents. Commercial reagent grade ammonium bromide and triethylamine were used without further purification. 2-Furoic acid was recrystallized from ethyl acetate. 2-Methylfuran was used without purification. 3-Methyl-2-furoic acid,[21] 2-(acetoxymethyl)furan,[22] and 2-(acetamidomethyl)furan[23] were prepared according to the methods described in the literature. The dried strongly acidic cation-exchange resin (SK-1B, H^+ form) was prepared by washing the resin (H^+ form) with methanol, followed by drying in vacuo over phosphorous pentoxide.

Methyl 4,4-Dimethoxybutanoate (3a). 2-Furoic acid (**5a**) (22.4 g, 0.2 mol) was dissolved in 350 mL of methanol containing 5.6 g of triethylamine and 1.12 g of ammonium bromide. The solution was put in an ordinary 500-mL beaker in which two pairs of graphite elecrodes 40 cm^2 in area were fixed, the electrode-to-electrode distances being 2–4 mm (see Figure 1). A constant current of 2.5 A (current density 62.5 mA/cm^2) was passed through the solution of 18–20 °C. The applied voltage between both the terminal electrodes changed from 14 V in the initial stage to 40 V in the final stage of the reaction. After twice the theoretical amount of electricity (8 F/mol) was passed, the solution was evaporated to dryness in vacuo. The residue was dissolved in 300 mL of ethyl acetate, washed with brine, dried over magnesium sulfate, and evaporated to dryness in vacuo. The residue was distilled by using a short-path distillation apparatus to afford 25.0 g (77% yield) of compound **3a**: bp 61–64 °C (4 mmHg) [lit.[7] bp 84 °C (12 mmHg)]. The electrolyses under the conditions shown in the Table I were carried out in a manner similar to that described above.

The preparation of compound **3a** in quantities up to 1 mol can readily be achieved by using a potentiogalvanostat. 2-Furoic acid (112.1 g) was dissolved in 1.5 L of methanol containing 28.3 g of triethylamine and 4.9 g of ammonium bromide. The solution was put in an ordinary 2-L beaker in which six pairs of electrodes 40 cm^2 in area were fixed in the same manner as that shown in Figure 1. After twice the theoretical amount of elecricity (8 F/mol) was passed, the electrolyzed solution was treated under the same conditions as above to afford 103 g (64% yield) of compound **3a**.

Methyl 2-Methyl-4,4-dimethoxybutanoate (3b). 2-Methyl-3-furoic and (12.6 g, 0.1 mol) was dissolved in 350 mL of methanol containing 2.8 mL of triethylamine and 0.9 g of ammonium bromide. The solution was electrolyzed under the same conditions as described above to give 11.5 g (65% yield) of compound **3b**: bp 61–63 °C (2.2 mmHg); IR (film) 1740 cm^{-1}; NMR (CCl_4) δ 1.15 (d, 3 H), 1.2–2.7 (m, 3 H), 3.20 (s, 6 H), 3.60 (s, 3 H), 4.29 (t, 1 H); MS, m/e 176 (M^+), 175, 174, 173, 165, 163, 145, 143, 129, 127, 117, 115, 105, 89, 85. Anal. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.42; H, 9.03.

2-Substituted 2,5-Dimethoxytetrahydrofurans 7a–c. Typical procedure is exemplified by the preparation of 2-(acetoxymethyl)-2,5-dimethoxytetrahydrofuran (**7a**).[24] 2-(Acetoxymethyl)furan (**6a**; 210 g, 1.5 mol) was dissolved in 1.5 L of methanol containing 20.5 g of ammonium bromide. The electrolysis was carried out at 5–10 °C under a constant current of 2.5 A by using the same apparatus as described above. The reaction was discontinued when 2 F/mol of electricity was passed. To the electrolyzed solution was added 100 mL of methanolic sodium methoxide (prepared by using 4.83 g of sodium), and the mixture was evaporated to dryness in vacuo below 30 °C. To the residue was added 1.5 L of ethyl acetate. The mixture was washed with 200 mL of water, dried over magnesium sulfate, and then evaporated to dryness in vacuo. The residue was distilled under reduced pressure to afford 243 g (80% yield) of 2-(acetoxymethyl)-2,5-dimethoxy-2,5-dihydrofuran, bp 80–100 °C (1.8 mmHg) [lit.[24] bp 117–119 °C (17 mmHg)].

The hydrogenation of the dimethoxylated product (107 g, 0.53 mol) obtained above was carried out in the presence of 10% palladium on charcoal (10 g) at atmospheric pressure. The catalyst was filtered off, and the filtrate was evaporated to dryness in vacuo. The residue was distilled under reduced pressure to afford 92 g (85% yield) of 2-acetoxymethyl)-2,5-dimethoxytetrahydrofuran (**7a**), bp 86 °C (1.5 mmHg) [lit.[24] bp 113–115 °C (13 mmHg)].

Compounds **7b** and **7c** were also prepared under the same conditions as above. The overall yields of compounds **7b** and **7c** are as follows. Compound **7b**: 82% yield; bp 76–82 °C (55 mmHg) [lit.[25] bp 147–155 °C (759 mmHg)]. Compound **7c**; 89% yield; mp 57–60 °C (ether) (lit.[23] mp 58–60 °C). The dimethoxylated compounds described above are mixtures of cis and trans isomers.

4,4-Dimethoxy Ketones 4. The typical procedure is exemplified by the preparation of 1-acetoxy-2-oxo-5,5-dimethoxypentane (**4a**). Compound **7a** (2.04 g, 10 mmol) was dissolved in 6 mL of methanol. To this was added 0.1 g of dried SK-1B (H^+ form), and the mixture was stirred for 2 h. In the reaction mixture, two spots (R_f 0.67 and 0.46) other than the starting material (R_f 0.77) were observed on TLC (Merck, silica gel 60 F-254) by using chloroform–tetrahydrofuran (10:1) as a developing solvent. The resin was filtered off, and the filtrate was evaporated to dryness in vacuo. The products were separated by silica gel chromatography with chloroform–tetrahydrofuran (10:1) as an eluent to afford 1.51 g (74%) of compound **4a**: colorless syrup; bp 107–109 °C (2 mmHg); NMR (CCl_4) δ 1.5–2.6 (m, 4 H), 2.05 (s, 3 H), 3.27 (s, 3 H), 4.28 (t, 1 H), 4.58 (s, 2 H); MS, m/e 205 ($M^+ + 1$), 204 (M^+), 203, 173, 145, 131, 113, 99, 86, 84, 81, 75, 71, 58, 47, 43. Anal. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.65; H, 7.72. Chromatography also afforded 0.20 g of starting material and 0.06 g of 4-oxo-5-acetoxypentanal.[26]

Compounds **4b** and **4c** were also prepared under the same conditions as above. Compound **4b**: colorless syrup; 71% yield; bp 108–114 °C (60 mmHg) [lit.[27] bp 85–87 °C (15 mmHg)].

(21) Burness, D. M. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV, pp 628, 649.
(22) The Miner Laboratories "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, p 285.
(23) Clauson-Kaas, N.; Tyle, Z. *Acta Chem. Scand.* **1952**, *6*, 667.
(24) Clauson-Kaas, N.; Dietrich, P.; Nielsen, J. T. *Acta Chem. Scand.* **1953**, *7*, 845.
(25) Elming, N.; Clauson-Kaas, N. *Acta Chem. Scand.* **1952**, *6*, 867.
(26) Miyamoto, F.; Naoki, H.; Takemoto, T.; Naya, Y. *Tetrahedron* **1979**, *35*, 1913.

Compound **4c**: syrup; 57% yield; NMR (CCl_4 δ 1.95 (s, 3 H), 1.6–2.2 (m, 2 H), 2.42 (t, 2 H), 3.25 (s, 6 H), 4.00 (d, 2 H), 4.30 (t, 1 H), 7.10 (br t, 1 H); MS, *m/e* 173, 172 (M – MeO), 171, 158, 157, 156, 142, 141, 140, 131, 129, 116, 115, 114, 103, 102, 101, 100, 99, 98. Anal. Calcd for $C_9H_{17}NO_4$: C, 53.19; H, 8.43; N, 6.89. Found: C, 53.11; H, 8.19; N, 6.92.

The preparation of compounds **4a** and **4b** in quantities up to 0.5 mol can readily be achieved by using the same procedure as described above except that the products are purified by distillation with a short-path distillation apparatus. The yields (50–60%) are slightly lower than those obtained as described above.

(27) Eftax, D. S. P.; Dunlop, A. P. *J. Org. Chem.* **1965**, *30*, 1317.

Acknowledgment. We thank Dr. Muneji Miyoshi, subdirector, and Dr. Ichiro Chibata, director of our laboratory, for their encouragement.

Registry No. 3a, 4220-66-0; **3b**, 25252-24-8; **4a**, 82614-43-5; **4b**, 3209-78-7; **4c**, 82614-44-6; **5a**, 88-14-2; **6a**, 623-17-6; **6b**, 534-22-5; **6c**, 5663-62-7; *cis*-**7a**, 82614-40-2; *trans*-**7a**, 82614-45-7; *cis*-**7b**, 82614-41-3; *trans*-**7b**, 82614-46-8; *cis*-**7c**, 82614-42-4; *trans*-**7c**, 82614-47-9; 2-methyl-3-furoic acid, 6947-94-0; *cis*-2-(acetoxymethyl)-2,5-dimethoxy-2,5-dihydrofuran, 38588-84-0; *trans*-2-(acetoxymethyl)-2,5-dimethoxy-2,5-dihydrofuran, 38588-85-1.

Communications

S_N2 Reactions of Carbanions with Primary and Secondary Alkyl Bromides in Dimethyl Sulfoxide Solution

Summary: 9-Methylfluorenyl carbanions undergo S_N2 reactions with cyclohexyl, isopropyl, isobutyl, and *n*-butyl bromides in high yields in Me_2SO solution with the relative rates of (1.0), 6.4, 8.6, and 56 respectively.

Sir: Although the S_N2 reaction has probably received more attention from organic chemists than any other reaction type, very little quantitative information is available concerning carbanions as nucleophiles. Rate studies have been limited largely to weakly basic enolate ions, such as those derived from β-keto esters, where counterion effects complicate interpretations. More strongly basic carbanions can be generated in hydroxylic solvents only in small and unknown concentrations. For synthetic purposes, high concentrations of strongly basic carbanions are routinely generated in weakly acidic solvents that have a low dielectric constant, such as tetrahydrofuran, but here counterion effects become very strong. The establishment of acidity scales in the strongly dipolar nonhydroxylic ("aprotic") solvents, dimethyl sulfoxide[1] and *N*-methylpyrrolidin-2-one,[2] has provided a groundwork for the generation of carbanions of a wide range of basicity in known concentrations, free of counterion effects. In earlier papers we have reported the results of S_N2 reactions for several families of carbanions reacting with $PhCH_2Cl$;[3] other primary alkyl halides have also been studied.[4] In this communication we report the extension of these studies to cyclohexyl bromide, c-$C_6H_{11}Br$, and isopropyl bromide.

The rates of reactions of these secondary alkyl bromides with carbanions from the 9-methylfluorenyl carbanion family, 9-Me-Fl^-,[3] were found to be first order in each reactant. Substitution was the predominant course of reaction with elimination playing a minor role. Formation of only small amounts of elimination products was at first sight surprising since these carbanions are strongly basic and it has been shown that with strongly basic sodium–enolate ion pairs, elimination may become the major reaction with secondary, and even primary, halides in polyether solvents.[5] Also, c-$C_6H_{11}Br$ has been singled out as being particularly prone to elimination.[6] For example, reactions of c-$C_6H_{11}Br$ with NaOEt/EtOH or *t*-BuOK/*t*-BuOH give exclusively elimination.[7] In acetone or dimethylformamide, most anions (Cl^-, Br^-, AcO^-, ArO^-, CN^-, and HCO_2^-) give more elimination than substitution; azide ion alone gives more S_N2 than E2.[7] (Similar results were obtained with c-$C_6H_{11}I$ and c-$C_6H_{11}OTs$.) As a consequence, it is generally assumed that S_N2 reactions of c-$C_6H_{11}X$ substrates with nucleophiles are subject to some kind of rate retarding steric effect,[8] and that elimination becomes predominant for that reason.

Examination of the literature revealed, however, that reactions of carbanions with c-$C_6H_{11}Br$ often give unusally high yields of substitution products, e.g., 40% for $[Ph_2CC{\equiv}C]^{2-}2M^+$ in NH_3,[9] 76% for $NaCH(CO_2\text{-}t\text{-}Bu)_2$ in *t*-BuOH,[10] 65–77% for PhCH(Na)CN in $PhCH_3$,[11] and 82% for 2-lithio-2*H*-thiopyran in NH_3.[12] Our studies using equimolar amounts of 9-$MeFl^-$ or of 9-$PhCH_2Fl^-$ carbanions with c-$C_6H_{11}Br$ in Me_2SO gave 80% or more of substitution product (Table I).

These synthetic results show that large, delocalized, strongly basic carbanions are remarkably effective in promoting S_N2 reaction in preference to E2 reactions with c-$C_6H_{11}Br$. Their behavior in this respect is in sharp contrast to that of the CN^- ion, which is 9.45 p*K* units less basic than 9-$MeFl^-$ in Me_2SO, but reacts with c-$C_6H_{11}Br$ in acetone at 75 °C to give 92% elimination.[7] The relative insensitivity of 9-$MeFl^-$ ions to increasing steric hindrance

(1) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006–7014.
(2) Bordwell, F. G.; Branca, J. C.; Hughes, D. L.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3305–3313.
(3) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1980**, *45*, 3314–3320; **1981**, *46*, 3570–3571; **1982**, *47*, 169–170.
(4) Hughes, D. L. Ph.D. Dissertation, Northwestern University, Evanston, IL, 1981.
(5) Zook, H. D.; Kelly, W. L.; Posey, I. Y. *J. Org. Chem.* **1968**, *33*, 3477–3480.
(6) House, H. O. "Modern Synthetic Reactions", 2nd ed.; Benjamin: Menlo Park, CA: 1972; p 530.
(7) Beltrame, P.; Biale, G.; Lloyd, D. J.; Parker, A. J.; Ruane, M.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2240–2255.
(8) (a) Bartlett, P. D.; Rosen, L. J. *J. Am. Chem. Soc.* **1942**, *64*, 543–546. (b) Brown, H. C.; Fletcher, R. S.; Johannesen, R. B. *Ibid.* **1951**, *73*, 212–221. (c) Eliel, E. L.; Ro, R. S. *Ibid.* **1957**, *79*, 5995–6000.
(9) Libman, N. M.; Zlobina, V. I.; Kuznetsov, S. G. *J. Org. Chem. USSR (Engl. Transl.)* **1974**, *10*, 2074–2076.
(10) Fonken, G. S.; Johnson, W. S. *J. Am. Chem. Soc* **1952**, *74*, 831–833.
(11) Hancock, E. M.; Cope, A. C. *Org. Synth.* **1945**, *25*, 25–27.
(12) Grafing, R. Verkruijsse, H. D.; Brandsma, L. *J. Chem. Soc., Chem. Commun.* **1978**, 596–597.

0022-3263/82/1947-3802$01.25/0