Cueto-Felgueroso, University of Oviedo, for anatomical dissection of *T. fimbria*. We also thank Miss C. Minardi, Mr. A. Trabucco, and Mr. G. Villani for technical assistance and Mr. R. Turco for artwork. The NMR spectra and the mass spectra were, respectively, obtained from the ICMIB-NMR Service and from the "Servizio di Spettrometria di Massa del CNR e dell'Università di Napoli"; both staffs are gratefully acknowledged.

Registry No. 4, 62410-96-2; 5, 132541-84-5; 6, 132618-68-9; 7, 55314-49-3; 8, 132564-12-6; 9, 132541-85-6; 10, 132541-86-7; 9-acyl-$PGF_{3\alpha}$ $C_{20:5}$ fatty acid ester, 132564-41-1; 9-acyl-$PGF_{3\alpha}$ $C_{14:0}$ fatty acid ester, 132541-87-8; 11-acyl-$PGF_{3\alpha}$ $C_{22:6}$ fatty acid ester, 132541-88-9; 11-acyl-$PGF_{2\alpha}$ $C_{20:4}$ fatty acid ester, 132541-89-0; 9-acyl-$PGF_{2\alpha}$ $C_{22:6}$ fatty acid ester, 132541-90-3; 9-acyl-$PGF_{3\alpha}$ $C_{16:0}$ fatty acid ester, 132564-13-7; 11-acyl-$PGF_{3\alpha}$ $C_{a3:0}$ fatty acid ester, 132541-91-4; 11-acyl-$PGF_{2\alpha}$ $C_{18:1}$ fatty acid ester, 132541-92-5; 9-acyl-$PGF_{2\alpha}$ $C_{16:0}$ fatty acid ester, 132541-93-6; 11-acyl-$PGF_{3\alpha}$ $C_{18:1}$ fatty acid ester, 132541-94-7; 11-acyl-$PGF_{2\alpha}$ $C_{18:0}$ fatty acid ester, 132541-95-8; 9-acyl-$PGF_{3\alpha}$ $C_{16:1}$ fatty acid ester, 132541-96-9; 9-acyl-$PGF_{2\alpha}$ $C_{16:1}$ fatty acid ester, 132541-97-0; 3, 123314-21-6; 11-acyl-$PGF_{3\alpha}$ $C_{20:4}$ fatty acid ester, 132564-42-2; 11-acyl-$PGF_{2\alpha}$ $C_{22:6}$ fatty acid ester, 132541-98-1.

Use of *N,N'*-Dimethoxy-*N,N'*-dimethylurea as a Carbonyl Dication Equivalent in Organometallic Addition Reactions. Synthesis of Unsymmetrical Ketones

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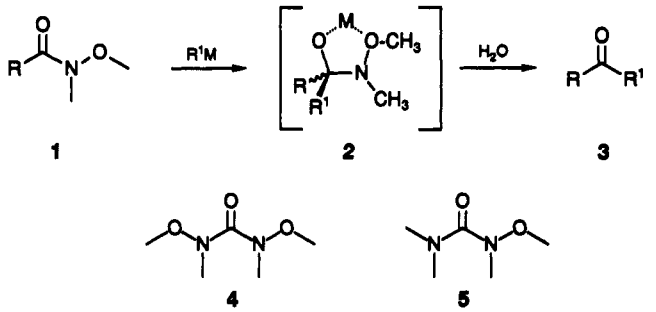
Many methods for the formation of ketones by the addition of organometallic reagents to CO_2 equivalents appear in the literature.[2] These include the addition of the organometallic reagent to carboxylic acid derivatives,[3-8] direct addition to CO_2, and reactions employing a transition-metal catalyst.[4] Even though many of these approaches produced the desired ketones, yields were often low and the reaction conditions were specific and not broadly applicable. A common complicating factor is the concomitant addition of the organometallic reagent to the ketone to produce a tertiary alcohol.

Several research groups have introduced ester or amide derivatives in which the formation of tertiary alcohols is not a problem.[5-8] These derivatives (e.g., 1) contain a ligand that stabilizes by chelation the tetrahedral intermediate 2 formed by addition of the organometallic reagent. The most effective of these appear to be amides



(1)[7] or ureas (4, 5),[9] which use the *N*-methoxy-*N*-methyl ligand. Nahm and Weinreb discovered that several *N*-methoxy-*N*-methylamides reacted cleanly with Grignard and organolithium reagents to produce ketones.[7] For these compounds, the intermediate adduct (2, M = Li, Mg) is stable up to room temperature. The ketone 3 is formed only during the hydrolysis, and the intermediate 2 can actually be submitted to additional chemical manipulation (e.g., deprotonation and alkylation of a remote *N,N*-dimethylhydrazone present in the molecule[10]).

Results and Discussion

We report the synthesis of *N,N'*-dimethoxy-*N,N'*-dimethylurea (4) and its use as a carbonyl dication equivalent. This reagent was also independently developed by Hlasta and Court.[9] The urea 4 was formed in 78% yield from the addition of a solution of bis(trichloromethyl) carbonate (triphosgene) in THF to *N*-methoxy-*N*-methylamine. (Trichloromethyl)chloroformate (diphosgene) also works well.

The addition of 4 to solutions of a variety of aryl, alkyl, alkenyl, and alkynyl organometallic reagents in THF readily produced the amide 1. The reactions were clean and occurred in high yield in all cases except where the formation of the organolithium reagent was difficult (1e and 1f, Table I). The reactions proceeded slowly at −78 °C, but rapidly as the reaction mixtures were warmed to 22 °C. A reaction mixture containing 2-lithio-5-methylthiophene and 4 at −78 °C was quenched with a 1 M aqueous/MeOH solution of NH_4Cl after 10 min and gave only 2% of 1a, whereas an analogous reaction mixture that was warmed to room temperature and then quenched gave a near quantitative conversion. The formation of the ketone 3 from the addition of RLi or RMgBr reagents to the amide 1 is well precedented[7] but for completeness is illustrated for compounds 1a, 1d, and 1e.

The urea 4 provides an excellent route to ketones and should prove useful in many synthetic applications. It is easily prepared and purified, is stable for long periods of time, and reacts cleanly with RLi and RMgBr reagents. It should be particularly useful when the intermediate amide 1 cannot be synthesized by traditional methods because of the instability of the parent carboxylic acid.

Experimental Section

General Procedures. Unless otherwise state, all ^1H NMR spectra were measured with reference to $CHCl_3$ (δ 7.24) or TMS (δ 0.0). The $CDCl_3$ triplet (δ 77.0) was used as reference for ^{13}C NMR. Infrared (IR) spectra were taken of neat liquids, unless otherwise stated, between NaCl plates. All elemental analyses were performed by Galbraith Laboratories.

Kugelrohr distillation refers to bulb-to-bulb distillation (bath temperatures are reported). Diethyl ether and tetrahydrofuran (THF) were freshly distilled from sodium benzophenone ketyl.

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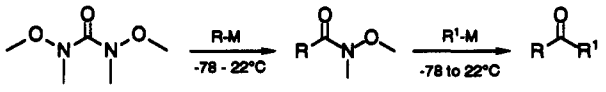
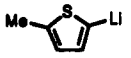
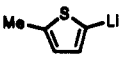
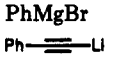
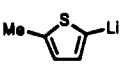
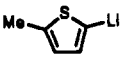
Table I. Preparation of Weinreb Reagents (1) and Unsymmetrical Ketones (3) Using *N,N'*-Dimethoxy-*N,N'*-dimethylurea (4)



4 1 3

RM	product 1	yield, %	R^1M	product 3[a]	yield, %
	a	98	*n*-BuLi	a	99
				b	96
n-BuLi	b	89			
PhLi	c	85			
PhMgBr	c	77			
	d	92		c	91
	e	58		d	60
	f	36			

[a] Compounds **3a**, **3b**, **3c**, and **3d** were prepared from **1a**, **1a**, **1d**, and **1e**, respectively.

Solutions of *n*-BuLi, PhLi, and 2-lithio-5-methylthiophene were titrated with use of 1-propanol with 1,10-phenanthroline as indicator.[11] All reactions involving organometallics were carried out under an atmosphere of dry nitrogen, in glassware that had been dried at 115 °C for at least 2 h.

***N,N'*-Dimethoxy-*N,N'*-dimethylurea (4).** To a suspension of *N*-methoxy-*N*-methylamine hydrochloride (94%, Aldrich; 10.0 g, 96.5 mmol) in THF (350 mL) at 0 °C was added pyridine (15.8 mL, 195 mmol), to which a solution of bis(trichloromethyl) carbonate (triphosgene; Aldrich; 4.90 g, 16.5 mmol) in THF (80 mL) was added dropwise over 1 h. The reaction mixture gradually warmed to 22 °C as the ice melted and was stirred for 18 h. The white solid was removed by filtration through a plug of silica. The solvent from the filtrate was evaporated, giving a yellow liquid, which was partitioned between 200 mL of ether and 50 mL of 0.05 M HCl. The organic layer was washed with a mixture of brine (50 mL) and NaOH (30%, 3 mL) and then brine (100 mL) and was passed through Na_2SO_4. Evaporation of the solvent gave a light yellow liquid (7.01 g). Kugelrohr distillation [bp 48 °C (14 μm)] produced 5.62 g (78%) of the urea 4: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.04 (s, 3 H), 3.63 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 35.88, 60.26, 163.09; IR 2970, 2930, 2801, 1665 cm^{-1}; MS, M$^+$ 148.0837, calcd for $C_5H_{12}N_2O_3$ 148.0848. Anal. Calcd for $C_5H_{12}N_2O_3$: C, 40.53; H, 8.16; N, 18.91. Found: C, 40.56; H, 8.11; N, 18.40.

***N*-Methoxy-*N*-methylphenylacetylenecarboxamide (1d).** To a solution of phenylacetylene (242 μL, 224 mg, 2.2 mmol) in 13 mL of THF at −78 °C was added a solution of *n*-BuLi (2.61 M in hexane, 2.2 mmol, 0.84 mL) dropwise. Urea 4 (300 μL, 324 mg, 2.2 mmol) was added, and the reaction mixture was warmed to 22 °C. After 10 min the mixture was partitioned between 60 mL of ether and 60 mL of 7% $NaHCO_3$. The ether layer was washed with 60 mL of brine and passed through Na_2SO_4. Evaporation of the solvent gave a yellow liquid. Kugelrohr distillation [bp 80–130 °C (7 μm)] gave 321 mg (77%) of **1d** as a white solid (mp 39.0–39.5 °C) in the neck of the collection bulb. Evaporation of the volatile impurities from the remaining liquid in the collection bulb (8 h, 22 °C, 22 μm) gave an additional 61 mg (15%) of **1d**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.29 (s, 3 H), 3.83 (s, 3 H), 7.35 (m, 3 H), 7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 32.48, 62.14, 80.75, 90.26, 120.36, 128.45, 130.15, 132.52, 154.55; IR ($CDCl_3$) 2975, 2937, 2222, 1634 cm^{-1}; MS, M$^+$ 189.0790, calcd for $C_{11}H_{11}NO_2$ 189.0790.

1-(5-Methyl-2-thienyl)-3-phenyl-2-propyn-1-one (3c). To a solution of **1d** (300 mg, 1.58 mmol) in 5 mL of THF at −78 °C was added a solution of 2-lithio-5-methylthiophene (0.65 M in THF, 1.7 mmol, 2.7 mL), prepared by metalation of 2-methylthiophene with *n*-BuLi in THF at 0 °C for 10 min. After 30 min at −78 °C, the mixture was quenched with 0.5 mL of a 1 M NH_4Cl solution in MeOH–H_2O (1:1). The mixture was partitioned between 30 mL of 1:1 ether–hexane and 30 mL of 7% $NaHCO_3$. The organic layer was washed with 30 mL of brine and passed through a cone of Na_2SO_4. Evaporation of the solvent gave a yellow crystalline solid. Purification by preparative TLC (1:3 EtOAc–hexane) gave 323 mg (91%) of **3c** (R_f = 0.5) as light yellow crystals: mp 82–84 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.56 (br s, 3 H), 6.85 (dq, J = 3.8, 0.9 Hz, 1 H), 7.43 (m, 3 H), 7.63 (m, 2 H), 7.82 (d, J = 3.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 16.23, 86.31, 91.10, 120.02, 127.08, 128.57, 130.60, 132.88, 135.87, 142.65, 151.74, 169.30; IR 3067, 2927, 2862, 2247, 2200, 1611 cm^{-1}; MS, M$^+$ 226.0456, calcd for $C_{14}H_{10}SO$ 226.0452.

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Supplementary Material Available: Experimental procedures for the preparation of **1a–c,e,f** and **3a,b,d** and ^{1}H and ^{13}C NMR spectra of compounds **1a–f**, **3a–d**, and **4** (14 pages). Ordering information is given on any current masthead page.

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The Reaction of Alkynes and Formic Acid

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Our studies of the addition of carboxylic acids to alkynes, which was found to be catalyzed by organo-ruthenium complexes,[1] have led to the discovery of a simple and synthetically useful process. The reaction is described in eq 1, and *it is not* catalyzed by transition-metal complexes or by any other catalyst. The chemical transformation

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