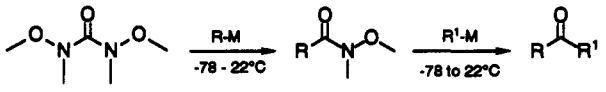
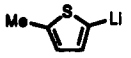
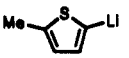
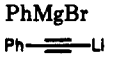
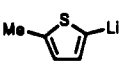
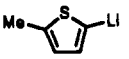
Table I. Preparation of Weinreb Reagents (1) and Unsymmetrical Ketones (3) Using *N,N'*-Dimethoxy-*N,N'*-dimethylurea (4)



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.

Acknowledgment. We thank the National Science Foundation and the Wisconsin Alumni Research Foundation (WARF) for support of this research.

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.

(11) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

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

(1) Rotem, M.; Shvo, Y. *Organometallics* **1983**, *2*, 1689. Rotem, M.; Goldberg, I.; Shvo, Y. *Organometallics* **1984**, *3*, 1758. Rotem, M.; Goldberg, I.; Shmueli, U.; Shvo, Y. *J. Organomet. Chem.* **1986**, *314*, 183.

0022-3263/91/1956-2912$02.50/0

Table I. Reactions of Alkynes with Formic Acid

alkyne	time (h)	yield[a] (%)	product
phenyacetylene	0.5	96	acetophenone
diphenylacetylene	10	94	deoxybenzoin
1-octyne	6	92	2-octanone
4-octyne	10	83	4-octanone
1-phenyl-1-heptyne	5	89	heptanophenone

[a] Determined by GC analyses using an internal standard.

takes place by simply heating the alkyne in formic acid at 100 °C.

$$RC{\equiv}CR + HCOOH \rightarrow RCOCH_2R + CO \quad (1)$$

The scope of this process was examined with a variety of representative simple alkynes (Table I). Diaryl, dialkyl, arylalkyl, and terminal alkynes are reactive and gave excellent yields of ketones, while dimethyl acetylenedicarboxylate was found to be unreactive. The most reactive alkyne studied is phenyl acetylene, which in fact slowly reacts with formic acid even at room temperature, liberating CO and generating acetophenone. The regioselectivity of the process was demonstrated in experiments with phenylacetylene and 1-phenyl-1-heptyne. The only compounds produced with these two alkynes were acetophenone and heptanophenone, respectively.

The reaction presented in eq 1 amounts to the formal hydration of a triple bond, a well-known reaction which is catalyzed by Hg salts,[2] its Nafion modification,[3] or strong acids,[4] in the presence of water. In our case formic acid serves as a formal water donor. We took care to use formic acid which was dried with boric anhydride and then freeze–thawed twice. The stoichiometric formation of carbon monoxide in every reaction (measured quantitatively and identified by mass spectrometry) rules out the possible addition of water to the triple bond. Furthermore, no significant rate difference could be detected using dried and nondried (98%) formic acid. It must therefore be concluded that formic acid is the source of the elements of water for the above hydration reaction of alkynes.

Thermodynamically the reaction is highly favored (alkynes have positive heat of formation). Thus, the heat of reaction for propyne and formic acid to give acetone and CO is −31.7 kcal/mol. Experimental evidence (vide infra) indicates that the reaction is a two-stage process proceeding via the enol formate, as described in the following equation:

$$RC{\equiv}CR + HCOOH \rightarrow RC(OCHO){=}CHR \xrightarrow{HCOOH} RCOCH_2R + HCOOH + CO \quad (2)$$

It is unusual that carboxylic acids add to alkynes in the absence of strong protic acid,[5] Lewis acids,[6] Hg salts and strong acid,[7] Ag salts,[8] or transition-metal catalysts.[9] Thus, this addition reaction requires significant acid activation. Indeed, we have found that under our experimental conditions, acetic acid and phenylacetylene are totally inert. However, it was found[10] that carboxylic acids having pK_a <4.5 do add to the triple bond of phenylacetylene in the absence of strong acid catalyst to give enol esters. In fact, it was noted that ketones are byproducts of this reaction.[10] Thus, the feasibility of the first step of eq 2 is due to the acidity of formic acid which has a pK_a of 3.77. That enol esters are intermediates that are formed under our reaction conditions was experimentally demonstrated by reacting 1-phenyl-1-heptyne with a quantity of formic acid that does not dissolve all the alkyne. This leads to a two-phase system that reacted slowly. Consequently, after 4 h at 100 °C, GC analysis of the reaction solution showed four signals of which one was identified as the starting material and another as heptanophenone. After removal of excess formic acid (see the Experimental Section), the product mixture was analyzed by GC/MS and ^1H NMR. Three out of the four GC signals gave identical MS peaks, m/z 190 $(C_{13}H_{18}O)^+$, assigned to heptanophenone and to fragments of the two isomeric enol formates of heptanophenone, m/z 190 $(C_{14}H_{18}O_2 - CO)^+$. The fourth GC peak was assigned to the starting alkyne, 1-phenyl-1-heptyne, m/z 172 (M^+).

The ^1H NMR spectrum was most informative in identifying the enol formates, giving two singlets, δ 8.23, 8.14 (HCOO), and two triplets, δ 5.28, 5.50 [$CH_2CH{=}C(Ph)$-OOCH]. These results clearly establish the presence in the reaction solution of the *E* and *Z* isomers of 1-(formyloxy)-1-phenyl-1-heptene. Upon subjecting the above four-component mixture to the original reaction conditions with formic acid, it was quantitatively converted into a single product: heptanophenone. The conversion of enol esters to the corresponding ketones (second step) in the presence of carboxylic acids has been previously documented[10] and may, in the present case, proceed via the unstable formic anhydride: HCOOOCH → HCOOH + CO.

In conclusion, the above simple one-pot reaction may be a useful and practical tool in organic synthesis. Presently we are trying to extend this reaction to various functionalized alkynes.

Experimental Section

General. Formic acid (98%) was dried and purified according to a published procedure.[11] All of the alkynes were distilled before use. All the products listed in Table I were identified by comparison with commercial authentic materials.[12] Quantitative GC analyses were carried out on a column packed with SE-30 on acid-washed Chromosorb-W, l = 150 cm, Φ = 0.6 cm, column temperature 140–170 °C, using 1-methylnaphthalene as internal standard. NMR spectra were measured in $CDCl_3$ solutions with TMS as internal standard.

General Procedure. 1-Octyne (7.5 g) and formic acid (100 mL) were heated in an oil bath at 100 °C until all starting material was consumed. The progress of the reaction was monitored by GC analysis of the reaction solution. Quantitative GC analysis at the end of the reaction (6 h) indicated 92% yield of 2-octanone. The cooled reaction mixture was taken up with methylene chloride (170 mL), and the solution was washed with water, sodium carbonate solution, and water, dried over $MgSO_4$, and evaporated in vacuum. The residue was distilled, bp 171–3 °C (lit.[13] bp 173 °C), 7.42 g (85%), of 2-octanone identified by GC (mixed injection with an authentic sample), MS, m/z 128 (M^+). Other alkynes (Table I) were treated and identified similarly.

Determination of CO. Phenylacetylene (1.10 g, 10.8 mmol) and formic acid (5.0 mL) were placed in a 10-mL round-bottom flask equipped with reflux condenser that was properly connected

(2) March, J. *Advanced Organic Chemistry*; Wiley: New York, 1985; p 683.
(3) Olah, G. A.; Meidar, D. *Synthesis* **1978**, 671.
(4) Noyce, D. S.; Matesich, A. M.; Peterson, E. *J. Am. Chem. Soc.* **1967**, *89*, 6225.
(5) Fahey, R. C.; Lee, D. J. *J. Am. Chem. Soc.* **1966**, *88*, 5555.
(6) Hudrlik, P. F.; Hudrlik, A. M. *J. Org. Chem.* **1973**, *38*, 4254 and references cited therein.
(7) Lemaire, H.; Lucas, H. J. *J. Am. Chem. Soc.* **1955**, *77*, 939.
(8) Ishino, I.; Hirashima, T. *Nippon Kagaku Kaishi* **1985**, *2*, 198.
(9) Sasaki, Y.; Dixneuf, T. B. *J. Chem. Soc., Chem. Commun.* **1986**, 790 and ref 1.
(10) Montheard, J.-P.; Camps, M.; Benzaid, A. *Synth. Commun.* **1983**, *13*, 663.
(11) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1988.
(12) 4-Octanone, commercially unavailable, was prepared by oxidation of the available 4-octanol with Jones reagent.
(13) *Handbook of Chemistry and Physics*, 62nd ed.; CRC Press: Boca Raton, FL, 1981–2; p C-406.

to a 500-mL graduate cylinder inverted in a breaker of water. The reaction flask was immersed in an oil bath at 100 °C. Gas evolution ceased after 1 h, and the system was left for 1 h to reach ambient temperature (24 °C). Volume of gas: found 250 mL; calcd 263 mL; yield 95%; GC/MS of a sample from the collected gas m/z 28 (M^+).

1-(Formyloxy)-1-phenyl-1-heptene. 1-Phenyl-1-heptyne (2.25 g) and formic acid (6.1 g) were heated at 100 °C for 4 h. Two liquid phases were present throughout the reaction. Workup of the reaction solution as described above for 1-octyne gave a brown liquid which was subjected to GC/MS and ^1H NMR analyses (for results, see text).

A sample of the above mixture (1.0 g) and formic acid (5 g) were heated for 4 h at 100 °C to give quantitatively (GC analysis with 1-methylnaphthalene as an internal standard) a single product identified as heptanophenone by GC (mixed injection with an authentic sample). MS m/z 190 (M^+).

Metal–Halogen Exchange Reactions of 1,5-Diiodonaphthalene. Synthesis of 1,5-Disubstituted Naphthalene Derivatives

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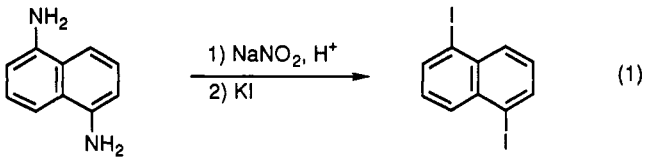
In connection with other investigations, we had need of 1,5-difunctionalized naphthalene derivatives such as carboxylic acids **4** and **6a**. Because these compounds and derivatives thereof were unavailable commercially, our attention turned to synthetic approaches. We felt that 1,5-diiodonaphthalene (**2**)[1] would be ideally suited for our purposes, since it was potentially a precursor both of organometallic reagents and of compounds derived from nucleophilic substitution. Also, **2** could be prepared readily from commercially available 1,5-diaminonaphthalene (**1**) by diazotization/KI.[2] This paper describes our efforts in the preparation of 1,5-disubstituted naphthalenes derived from **2**.

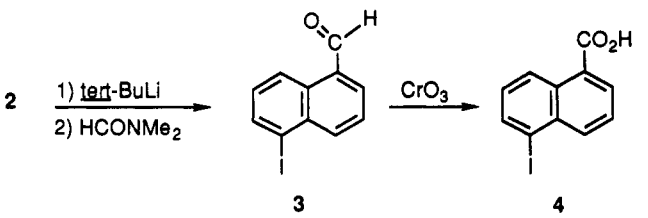


(1)

1 **2**

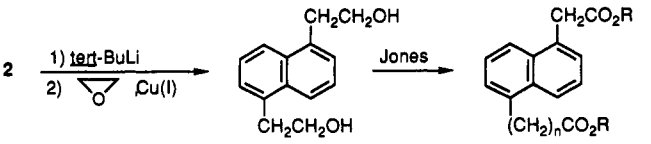
Depending upon reaction conditions, 1,5-diiodonaphthalene could be converted to either a monolithio- or dilithio derivative. A monolithio compound has previously been prepared from 1,8-diiodonaphthalene,[3] but to our knowledge, metal–halogen exchange reactions of **2** have not been reported previously. The difficulties in regioselectively dimetallating naphthalene by hydrogen–metal exchange has been summarized recently.[4] Treatment of **2** with *tert*-butyllithium in a 1:2 molar ratio under equilibrating conditions produced a solution of 1-lithio-5-iodonaphthalene as evidenced by the formation of only monodeuteroiodonaphthalene when the reaction mixture was quenched with methanol-d_4. Treatment of 1-lithio-5-iodonaphthalene with dimethylformamide gave 5-iodonaphthaldehyde **3** in 55% yield. Oxidation of **3** with Jones reagent furnished 5-iodonaphthoic acid **4**[5] (Scheme I).

Scheme I



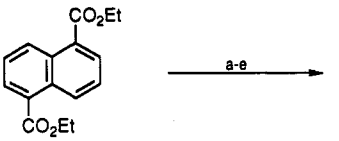
3 **4**

Scheme II



5

6a, n=1, R = H
6b, n=1, R = Et
7a, n=0, R = H
7b, n=0, R = Et



6b

[a] $LiAlH_4$, then H_3O^+.[9,12] [b] $MeSO_2Cl$, Me_3N. [c] KCN.[10] [d] KOH then H_3O^+. [e] EtOH, heat.

Dilithiation of **2** was accomplished by use of 4 equiv of *tert*-butyllithium. Treatment of the dilithio compound with an excess of ethylene oxide under copper catalysis[6] furnished diol **5** (56%). Direct conversion of **5** to 1,5-naphthalenediacetic acid **6a**[7] was complicated by competitive oxidation at the benzylic carbons.[8] Under the best conditions found, a mixture of **6a** and **7a** could be obtained in a 74% yield in a ratio of ca. 5:1, respectively. Diacids **6a** and **7a** were separated and characterized as their ethyl esters **6b** and **7b** (Scheme II). Diester **6b** could also be prepared by homologation of naphthalene-1,5-dicarboxylic acid by standard reactions requiring five steps.

An attempt to prepare diacid **6a** by treatment of **2** with sodiomalonic ester under copper catalysis[11] gave only the monoalkylated product **8** (38 or 50% on the basis of recovered **2**) after hydrolysis and decarboxylation.

Experimental Section

All moisture- or oxygen-sensitive reactions were conducted under a N_2 atmosphere. Melting points were taken on a Thomas

(1) Suzuki, H.; Kondo, A.; Inouye, M.; Ogawa, T. *Synthesis* **1986**, 121.
(2) Hedgson, H. H. *J. Chem. Soc.* **1947**, 80.
(3) Sugihara, Y.; Yamamoto, H.; Mizone, K.; Murata, I. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1247. Katz, H. E. *Organometallics* **1986**, *5*, 2308.
(4) Schlosser, M.; Choi, J. H.; Takagishi, S. *Tetrahedron* **1990**, *46*, 5633.
(5) This acid was prepared previously via the Sandmeyer reaction of 5-aminonaphthoic acid: Seer, C.; Scholl, R. *Ann.* **1913**, *398*, 92.
(6) Huynh, C.; Dergurni-Bonmechal, F.; Linstrumelle, G. *Tetrahedron Lett.* **1979**, 1503.
(7) This acid has previously been reported as a product of the reaction of naphthalene with chloroacetic acid in the presence of ferric oxide–potassium bromide: Ogata, Y.; Ishiguro, J.; Kitamura, Y. *J. Org. Chem.* **1951**, *16*, 239.
(8) Similar problems in the oxidation of β-phenylethanol derivatives have been reported: Plaue, S.; Heissler, D. *Tetrahedron Lett.* **1987**, *28*, 1401.
(9) This diol was previously made from 1,5-(dichloromethyl)-naphthalene via the diacetoxy derivative: Lock, G.; Schneider, R. *Ber. Dtsch. Chem. Ges.* **1951**, *84*, 636.
(10) Muruhashi, S.; Matsukawa, H. *Bull. Inst. Phys. Chem. Research, Tokyo* **1942**, *21*, 509; *Chem. Abstr.* **1952**, *46*, 8072h.
(11) Setsune, J. I.; Matsukawa, K.; Wakemoto, H.; Kitao, T. *Chem. Lett.* **1981**, 367.
(12) Lock, G. *Monatsh. Chem.* **1950**, *81*, 850.

0022-3263/91/1956-2914$02.50/0