5a (R = Me), 2388-68-3; **5a** (R = *n*-Bu), 53663-38-0; **5a** (R = *t*-Bu), 25752-95-8; **5b** (R = Me), 2388-69-4; **5b** (R = *n*-Bu), 21128-54-1; **5b** (R = *t*-Bu), 25752-96-9; **5c** (R = Me), 699-20-7; **5c** (R = *n*-Bu), 73732-39-5; $Cr(Co)_6$, 13007-92-6; MeSH, 74-93-1; *n*-BuSH, 109-79-5; Me_3CSH, 75-66-1; 1-(butylthio)-3-(methylthio)benzene, 86393-31-9; di-*n*-butyl disulfide, 629-45-8.

Direct One-Pot Synthesis of Terminal Olefins and Deuterio Olefins from Carboxylic Acid Chlorides

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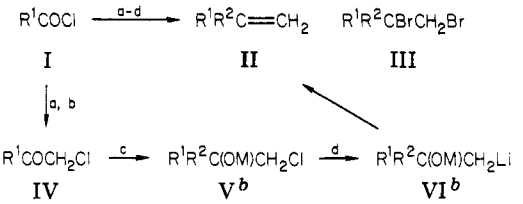
Recently we have reported a regioselective method to obtain olefins and deuterio olefins from α-chloro carbonyl compounds, Grignard reagents or lithium aluminum hydride or deuteride, and lithium.[1] These results prompted us to use the Nierenstein chloromethylation reaction[2] in a one-pot tandem process with the above-described method to obtain terminal olefins and deuterio olefins using carboxylic acid chlorides as starting materials.

The reaction of a carboxylic acid chloride (I) with diazomethane in ether (1:2 molar ratio) at −20 °C and further addition of an ethereal solution of hydrogen chloride (1:1.5 molar ratio) leads to an α-chloromethyl ketone (**IV**);[2] after removal of the excess of hydrogen chloride the chloro ketone was successively treated in situ with a mixture of a Grignard reagent/magnesium bromide at −40 °C and lithium powder (1:3 molar ratio) at −40 to +20 °C. After hydrolysis with aqueous hydrochloric acid the corresponding disubstituted terminal olefin (II1–II30) was obtained (see Scheme I and Table I, entries 1–30). Reaction of the initially generated chloro ketone IV[2] with a Grignard reagent leads to a chlorinated alkoxide, V (M = MgBr),[1,3] which by further lithiation yields a β-substituted organolithium compound, VI (M = MgBr);[4] the spontaneous β elimination of this intermediate VI affords the corresponding olefin II.

In order to improve the reaction yield, we studied different reaction conditions. (a) While the best results were obtained when the addition of the Grignard reagent was carried out in ether, in the lithiation step tetrahydrofuran had to be added to the reaction mixture; otherwise, the reaction times were longer. When the lithiation was carried out in diglyme (Table I, entries 35 and 41), the yields do not vary substantially. (b) When anhydrous magnesium bromide was added with the Grignard reagent (1:1 molar ratio) the yield was highly increased; without this salt yields were lower than 10%. (c) Best yields were obtained when an excess of the organomagnesium (1:2 molar ratio) was used. (d) A stoichiometric amount of lithium (1:2 molar ratio) was used when R^2 = Ph (Table I, entries 6, 11, 17, and 23) in order to avoid the reduction of the resulting conjugated double bond by excess metal.[1]

Scheme I[a]



[a] (a) CH_2N_2, Et_2O; (b) HCl, Et_2O; (c) $R^2MgBr/MgBr_2$ or $LiAlH_4/AlCl_3$ or $LiAlD_4/AlCl_3$; (d) Li. [b] M = MgBr or $Al(OR)_2$.

The method was extended to the preparation of monosubstituted olefins and deuterio olefins (II with R^2 = H or D) by using $LiAlH_4/AlCl_3$ or $LiAlD_4/AlCl_3$[1] as the nucleophile instead of the Grignard reagent R^2MgBr in the addition to the α-chloro ketone IV. The procedure was carried out under reaction conditions similar to those described above, and the reaction involves the same former intermediates V and VI with M = Al $(OR)_2$ (see Scheme I). The low molecular weight olefins were isolated and identified as the *vic*-dibromo derivatives III which were obtained by addition of bromine to the olefin at the end of the reaction sequence (Table I, entries 31–34 and 38–40).

The procedure described herein is, in our opinion, a method of choice for the preparation of terminal olefins and deuterio olefins.[7]

Experimental Section

General Methods. For general experimental information see ref 1. Diazomethane[25] and anhydrous magnesium bromide[26] were prepared by literature methods. The ether solution of hydrogen chloride was prepared by passing HCl gas through anhydrous ether and was used as a ca. 4 N solution. The products previously described (see notes in Table I) were identified by comparison of NMR and IR spectra with those of authentic samples. All new compounds exhibited satisfactory spectral and analytical data (see supplementary material).

Synthesis of Terminal Olefins and Deuterio Olefins II from Carboxylic Acid Chlorides I. Isolation as *vic*-Dibromo Derivatives III. General Procedure. To a previosly evacuated 250-mL two-necked flask containing a solution of diazomethane (40 mmol) in ether was added a solution of the carboxylic acid

(1) Barluenga, J.; Yus, M.; Concellón, J. M.; Bernad, P. *J. Org. Chem.* **1981**, *46*, 2721 and references therein.
(2) Clibbens, D. A.; Nierenstein, M. J. *J. Chem. Soc.* **1915**, *107*, 1491.
(3) Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.
(4) Intermediates of this type have recently been obtained by direct metalation of the corresponding chlorinated compound[5] or indirectly by mercury–metal transmetalation from organomercurials.[6]
(5) Barluenga, J.; Yus, M.; Flórez, J. *J. Chem. Soc., Chem. Commun.*, in press.
(6) Barluenga, J.; Fañanás, F. J.; Villamaña, J.; Yus, M. *J. Org. Chem.* **1982**, *47*, 1560 and references therein.
(7) For a review on the obtention of terminal olefins and the Wittig reaction, see, for instance: Sekiguchi, A.; Ando, W. *J. Org. Chem.* **1979**, *44*, 413.
(8) Bunnet, J. F.; Davis, G. T.; Tanida, H. *J. Am. Chem. Soc.* **1962**, *84*, 1606.
(9) *Beilstein, 4th ed.* **1938**, *1* (3) 830.
(10) Sommers, E. E.; Crowell, T. *J. Am. Chem. Soc.* **1955**, *77*, 5443.
(11) Cram, D. J.; Sahyum, M. R. V. *J. Am. Chem. Soc.* **1963**, *85*, 1257.
(12) Miginiac, L.; Lanoiselle, M. *Bull. Soc. Chim. Fr.* **1971**, *7*, 2716.
(13) *Beilstein, 4th ed.* **1938**, *1* (2), 95.
(14) Johnson, J. D. A.; Kon, G. A. R. *J. Chem. Soc.* **1926**, *128*, 2753.
(15) Barluenga, J.; Yus, M.; Concellón, J. M.; Bernad, P. *J. Org. Chem.* **1983**, *48*, 609.
(16) "Handbook of Tables for Organic Compounds Identification", 5th ed.; CRC Press: Cleveland, OH, 1976.
(17) Bernad, P. Ph.D. Thesis, Oviedo University, Oviedo, Spain, 1981.
(18) Baumgardner, C. L.; Iwerks, H. *J. Am. Chem. Soc.* **1966**, *88*, 5518.
(19) *Beilstein, 4th ed.* **1938**, *1* (3), 246.
(20) *Beilstein, 4th ed.* **1938**, *1* (3), 295.
(21) Wilkinson, R. *J. Chem. Soc.* **1931**, 3058.
(22) *Beilstein, 4th ed.* **1938**, *1* (2), 49.
(23) Schmidt, C. G.; Boord, C. E. *J. Am. Chem. Soc.* **1932**, *54*, 751.
(24) Benkeser, R. A.; Hazdra, J. J. *J. Am. Chem. Soc.* **1959**, *81*, 228.
(25) Arndt, F. "Organic Syntheses"; Wiley: New York, 1948; Collect. Vol II, p 165.
(26) Swain, C. G.; Boyles, H. B. *J. Am. Chem. Soc.* **1951**, *73*, 870.

0022-3263/83/1948-3116$01.50/0

Table I. Obtention of Olefins and Deuterio Olefins II or Their *vic*-Dibromo Derivatives III from Carboxylic Acid Chlorides I

entry	product	R^1 [a]	R^2	bp,[b] °C (torr)	yield,[c] %
1	II1	Me	*n*-Bu	91-93 (760)[d]	72
2	II2	Me	$PhCH_2$	69-70 (20)[e]	28
3[f]	II3	Et	*n*-Pr	41-42 (100)[g]	84
4[f]	II4	Et	allyl	37-38 (100)	67
5	II5	Et	*n*-Bu	65-66 (100)[h]	89
6[i]	II6	Et	Ph	66-68 (10)[j]	46
7	II7	Et	$PhCH_2$	80-82 (10)	72
8	II8	*n*-Pr	*n*-Pr	60-61 (100)	74
9	II9	*n*-Pr	allyl	37-38 (40)[k]	65
10	II10	*n*-Pr	*n*-Bu	47-48 (20)[l]	70
11[i]	II11	*n*-Pr	Ph	77-78 (10)[m]	55
12	II12	*n*-Pr	$PhCH_2$	87-89 (10)[n]	83
13[f]	II13	*i*-Pr	Et	89-90 (760)[o]	75
14	II14	*i*-Pr	*n*-Pr	57-58 (100)[p]	63
15	II15	*i*-Pr	allyl	51-52 (100)	61
16	II16	*i*-Pr	*n*-Bu	77-79 (100)	53
17[f,i]	II17	*i*-Pr	Ph	71-72 (10)[q]	63
18	II18	*i*-Pr	$PhCH_2$	88-89 (10)	85
19	II19	*i*-Bu	Et	55-56 (100)[r]	75
20	II20	*i*-Bu	*n*-Pr	39-40 (20)[s]	63
21	II21	*i*-Bu	allyl	51-52 (40)[t]	61
22	II22	*i*-Bu	*n*-Bu	57-58 (20)	53
23[i]	II23	*i*-Bu	Ph	83-84 (10)	63
24	II24	*i*-Bu	$PhCH_2$	52-53 (1)	85
25	II25	Cy	Et	74-75 (20)	98
26	II26	Cy	*n*-Pr	75-76 (10)	79
27	II27	Cy	allyl	56-57 (4)	99
28	II28	Cy	*n*-Bu	87-89 (10)	71
29	II29	Cy	$PhCH_2$	94-96 (1)	76
30	II30	$PhCH_2$	$PhCH_2$	78-80 (0.1)[u]	93
31	III31	Me	H	45-46 (20)[v]	60
32	III32	Et	H	68-69 (20)[w]	72
33	III33	*n*-Pr	H	71-72 (10)[x]	60
34	III34	*i*-Pr	H	63-64 (12)[y]	60
35[z]	II35	*i*-Bu	H	53-54 (760)[aa]	72
36	II36	Cy	H	70-71 (100)[ab]	95
37	II37	$PhCH_2$	H	48-49 (13)[ac]	90
38	III38	Et	D	54-55 (10)	68
39[f]	III39	*n*-Pr	D	70-71 (10)	58
40	III40	*i*-Pr	D	59-60 (10)	63
41[z]	II41	*i*-Bu	D	53-54 (760)	75
42[f]	II42	Cy	D	54-55 (50)	90
43	II43	$PhCH_2$	D	58-59 (20)	90

[a] Cy = cyclohexyl. [b] Distillation interval. [c] Yield of isolated product based on starting carboxylic acid chloride I. [d] Lit.[3] bp 92-93 °C (760 torr). [e] Lit.[8] bp 61 °C (19 torr). [f] Only ether was used as the solvent. [g] Lit.[9] bp 94 °C (760 torr). [h] Lit.[10] bp 120-121 °C (760 torr). [i] The stoichiometric amount of lithium (1:2 molar ratio) was used. [j] Lit.[11] bp 183 °C (760 torr). [k] Lit.[12] bp 113 °C (760 torr). [l] Lit.[13] bp 142-144 °C (768 torr). [m] Lit.[14] bp 86 °C (14 torr). [n] Lit.[15] bp 45-47 °C (1 torr). [o] Lit.[16] bp 89 °C (760 torr). [p] Lit.[16] bp 113 °C (760 torr). [q] Lit.[14] bp 89 °C (15 torr). [r] Lit.[16] bp 109.8 °C (762 torr). [s] Lit.[13] bp 132-133 °C (760 torr). [t] Lit.[17] bp 66-68 °C (100 torr). [u] Lit.[18] bp 97-101 °C (0.3 torr). [v] Lit.[19] bp 140 °C (760 torr). [w] Lit.[20] 78-78.5 °C (45 torr). [x] Lit.[21] bp 85 °C (30 torr). [y] Lit.[22] bp 74-76 °C (20 torr). [z] The lithiation was carried out in diglyme. [aa] Lit.[23] bp 53.6-53.9 °C (760 torr). [ab] Lit.[24] bp 127-128 °C (760 torr). [ac] Lit.[16] bp 156 °C (760 torr).

chloride I (20 mmol) in ether (5 mL) under argon at −20 °C over a period of 5 min. The temperature increased, for a 2-h period of stirring, from −20 to 0 °C, an ether solution of hydrogen chloride (30 mmol) was added at −20 °C, and the mixture was stirred and allowed to warm to room temperature overnight. The resulting solution was carefully distilled (500 torr and 30 °C bath temperature) to remove excess hydrogen chloride and ether until the volume of the reaction mixture was ca. 5 mL. To the residue were added anhydrous magnesium bromide (20 mmol) and the ether solution of the Grignard reagent [40 mmol; or successively aluminum trichloride (20 mmol) in ether (15 mL) and an ether solution of lithium aluminum hydride or deuteride (6 mmol)] at −40 to −60 °C. The reaction mixture was stirred for 8 additional h at ca. −40 °C. THF (10 mL) and lithium powder (60 mmol) were added, and the mixture was stirred and allowed to warm to room temperature overnight. The resulting solution was hydrolyzed successively with water and aqueous hydrochloric acid, and it was extracted with ether. The organic layer was dried over anhydrous sodium sulfate and carefully distilled to afford the corresponding olefin II.

For compounds III, after the addition of lithium powder a bubbler containing a solution of bromine (4.79 g, 60 mmol) in CCl_4 (40 mL) was connected to the reaction flask. The mixture was stirred, allowed to warm to room temperature overnight, and then hydrolyzed with water and aqueous hydrochloric acid. The resulting solution was heated at 50 °C in a water bath, with a stream of argon being passed through the liquid. The CCl_4 solution contained in the bubbler was washed successively with an aqueous solution of potassium carbonate and water and extracted with ether. The organic layer was dried over anhydrous sodium sulfate, and the solvents were removed in vacuo at 15 torr. The residue was distilled to afford the *vic*-dibromo compound III.

Registry No. I (R^1 = Me), 75-36-5; I (R^1 = Et), 79-03-8; I (R^1 = *n*-Pr), 141-75-3; I (R^1 = *i*-Bu), 108-12-3; I (R^1 = Cy), 2719-27-9; I (R^1 = $PhCH_2$), 103-80-0; I (R^1 = *i*-Pr), 79-30-1; II1, 6094-02-6; II2, 3290-53-7; II3, 3404-71-5; II4, 761-75-1; II5, 1632-16-2; II6, 2039-93-2; II7, 3968-89-6; II8, 15918-08-8; II9, 32852-38-3; II10, 62187-09-1; II11, 5676-32-4; II12, 84394-38-7; II13, 7357-93-9; II14, 61847-79-8; II15, 760-75-8; II16, 62187-11-5; II17, 17498-71-4; II18, 86409-69-0; II19, 3404-80-6; II20, 86409-70-3; II21, 42104-34-7; II22, 52763-10-7; II23, 38212-14-5; II24, 86409-71-4; II25, 86409-72-5; II26, 86409-73-6; II27, 86409-74-7; II28, 54248-57-6; II29, 86409-75-8; II30, 14213-80-0; II35, 691-37-2; II36, 695-12-5; II37, 300-57-2;

II41, 86409-78-1; II42, 86409-79-2; II43, 60468-24-8; III31, 78-75-1; III32, 533-98-2; III33, 3234-49-9; III34, 10288-13-8; III38, 86409-76-9; III39, 84394-61-6; III40, 86409-77-0.

Supplementary Material Available: Spectral and analytical data for all new compounds (6 pages). Ordering information is given on any current masthead page.

Studies on the Oxidation of Imino Ethers

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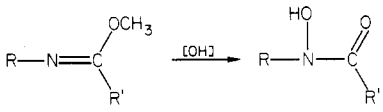
We have investigated the reactivity of imino ethers **1** toward several oxidizing agents with the hope of developing an efficient synthesis of hydroxamic acids **2** (eq 1), a family



(1)

1

3, R = *tert*-butyl; R′ = H
4, R = R′ = *tert*-butyl
5, R = *n*-C_7H_{15}; R′ = CH_3

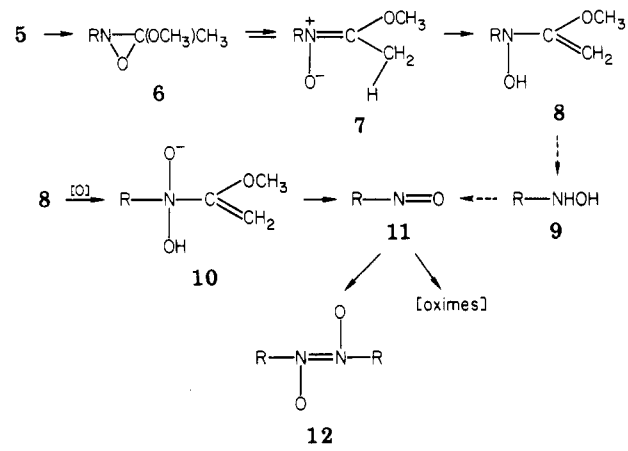
2

of naturally occurring substances with powerful iron-chelating properties.[2] Our unexpected findings constitute the subject of this paper.

The well-precedented epoxidation of imines[3] and imino ethers[4] to oxaziranes suggested that appropriately designed 3-alkoxyoxaziranes might produce hydroxamates upon acid hydrolysis. Indeed, it was first reported in 1971 that treatment of *O*-methylcaprolactim with peracid spontaneously furnished *N*-hydroxycaprolactam in ca. 3% yield.[5,6] Aue and Thomas[4] later showed that acyclic imino ethers such as **3** and **4** formed relatively stable alkoxyoxaziranes with peracetic acid and that in aqueous HCl, **3** decomposed to methyl formate and *N*-*tert*-butylhydroxylamine. Since the condensation of hydroxylamines with active esters furnishes hydroxamic acids, we were encouraged to explore further the chemistry of oxidized imino ethers.

When **5** was reacted with 1 equiv of buffered peracetic acid at −78 °C, only the nitroso dimer **12** could be isolated in 49% yield. No trace of alkoxyoxazirane was detected, even when the oxidation was terminated prematurely. However, NMR spectroscopy after brief reaction times clearly indicated the presence of *n*-heptanal (syn and anti) oximes. When 2 equiv of peracid was used, the yield of **12** rose to 70%. These unexpected results, which are wholly inconsistent with the behavior of **3** and **4**,[4] are best

Scheme I[a]



[a] R = *n*-C_7H_{15}.

explained by the mechanism presented in Scheme I. An initially formed alkoxyoxazirane, **6**, in equilibrium with alkoxynitrone **7**, may unergo a rapid 1,4 hydrogen shift to yield **8**, a migration which cannot occur in the oxidation of **3** and **4**. Intermediate **8** might then decompose directly to *N*-*n*-heptylhydroxylamine **9** in the presence of acetic acid or more probably might be oxidized again to **10**. Several pathways can be envisioned for the decomposition of **10** to nitroso-*n*-heptane **11**, the ultimate progenitor of **12**.[7]

Conversion of **6** to its *N*-oxide followed by direct extrusion of **11** could also in principle give rise to **12**, but the known rate of such oxidations[4] is inconsistent with the present reaction.

Two other epoxidizing agents were also examined. Reaction of **5** with either 2-(hydroperoxy)hexafluoro-2-propanol[8] or with *tert*-butyl hydroperoxide/vanadyl acetylacetonate[9] was extremely sluggish. In each instance only recovered **5** and its hydrolysis product, *N*-*n*-heptylacetamide, were detected.

As an alternative to epoxidation, the direct N-acetoxylation of imino ethers by lead tetraacetate (LTA) was investigated so as to preclude deleterious hydrogen shifts in the first-formed product. Unbuffered LTA promoted the rapid hydrolysis of **5** to *N*-*n*-heptylacetamide. The use of solid buffers such as NaOAc, Na_2HPO_4, or $CaCO_3$ under heterogeneous conditions (CH_2Cl_2 or hexane) afforded complex mixtures of products. With pyridine as the solvent,[10] LTA smoothly transformed **5** into acetoxy imino ether **13**. However, the use of pyridine complicated product isolation; therefore, in subsequent experiments it was replaced with a cross-linked 4-vinylpyridine polymer in hexane as the solvent. Under these conditions, **13** could be isolated in 75% yield (eq 2). The oxidation appears to be general, as lactim ether **14** similarly afforded **15** (79%; eq 3).

This LTA acetoxylation of imino ethers provides a convenient one-step alternative to the conventional NBS oxidation/$Et_4N^+OAc^-$ displacement sequence for preparing 3-acetoxy lactim ethers.[11] Such species are useful reagents

(1) Taken in part from the Ph.D. Dissertion of A.J.B., Cornell Univerity, 1982.
(2) (a) Bapat, J. P.; Black, D. St. C.; Brown, R. F. C. *Adv. Heterocycl. Chem.* **1969**, *10*, 199. (b) J.B. Nielands, *Science (Washington, D.C.)* **1967**, *156*, 1443.
(3) (a) Emmons, W. D. *J. Am. Chem. Soc.* **1956**, *78*, 6208; **1957**, *79*, 5739, 6522. (b) Hawthorne, M. F.; Strahn, R. D. *J. Org. Chem.* **1957**, *22*, 1263.
(4) Aue, D. H.; Thomas, D. *J. Org. Chem.* **1976**, *39*, 3855.
(5) Black, D. St. C.; Brown, R. F. C.; Wade, A. M. *Tetrahedron Lett.* **1971**, 4519.
(6) Aue and Thomas[4] have also reported the formation of *N*-hydroxypyrrolidone in 27% yield from the oxazirane of butyrolactim methyl ether.
(7) Two possibilities are (a) hydroxide elimination from **10** to form an alkenyl nitrosonium species, followed by HO^- attack at the alkene carbon, and (b) N to O alkenyl migration in **10**, followed by elimination of the enol of methyl acetate.
(8) Heggs, R. P.; Ganem, B. *J. Am. Chem. Soc.* **1979**, *101*, 2484.
(9) Tanaka, S.; Yamamoto, H.; Nozaki, H.; Sharpless, K. B.; Michaelson, R. C.; Cutting, J. D. *J. Am. Chem. Soc.* **1974**, *96*, 5254.
(10) Partch, R. E. *Tetrahedron Lett.* **1964**, 3071.
(11) Yamada, Y.; Okada, H. *Agric. Biol. Chem.* **1976**, *40*, 1437.

0022-3263/83/1948-3118$01.50/0