limited by charge repulsion. As the solution becomes basic, the concentrations of radicals such as **1c** increase and the nitrogen to nitrogen couplings predominate over disproportionations. At moderate acidities cross-disproportionation between the cation radical and the neutral radical leads to the imino methine **6**, which can add either water or methanol to give intermediates **7** and **8**. These species can couple after oxidation with more mesidine radicals to give **9** and **10**. To achieve aromaticity, formaldehyde can be eliminated from **9**. The methoxymethyl group of **10**, however, cannot be eliminated. Migration ensues in a manner similar to the dieneone–phenol rearrangement. Protonation of the imino nitrogen facilitates the migratory process. The resulting arylamines can be oxidized and hydrolyzed to anils **3** and **4**. Migration is suggested prior to hydrolysis because the corresponding keto forms of **9** and **10** would be expected to cleave in acidic media to a phenol and aniline on the basis of Miller's studies of quinamines.[8]

Intermediate **8**, 2,6-dimethyl-4-methoxymethylaniline, was prepared by an alkaline zinc reduction of the corresponding nitro compound, bp 96–98° (0.65 mm), which was the product of a methoxide displacement of bromide from 2,6-dimethyl-4-bromoethylnitrobenzene. The latter was obtained from the phosphorus tribromide treatment of the benzyl alcohol, mp 39–40°, derived from a diborane reduction of 3,5-dimethyl-4-nitrobenzoic acid. Intermediate **8** was an oil: nmr ($CDCl_3$) δ 6.86 (s, 2), 4.24 (s, 2) 3.45 (m, 2), 3.25 (s, 3), 2.02 ppm (s, 6); benzamide mp 55.6°; mol wt 165 (mass spectrum, 70 eV).

An equimolar mixture of intermediate **8** and mesidine was oxidized under the original conditions that give product **4**. The anil **4** was formed in 61% yield; no anil **3** was detected. The control run without **8** afforded a 23% yield of anil **4** and a 51% yield of anil **3**. When methanol was replaced by tetrahydrofuran in the reaction mixture containing **8**, product **4** was obtained in 35% yield and the anil **3** in 13% yield. In the control reaction containing mesidine alone, no **4** was formed and the principal product was the anil **3** (61%). Intermediate **7**[9] and mesidine were also oxidized together to give 59% anil **3** and 22% anil **4** under the original conditions. Without methanol in the reaction mixture, the yield of anil **3** was 75%. In all of these cases azo compounds were formed in <5% yields. These experiments with intermediates support the proposed reaction path.

Oxidation reactions involving migrations have been extended to 2,4,6-triethylaniline with a dichromate system[10] and to 2,6-dimethyl-4-benzylaniline with the ferricyanide system. A fuller report of these reactions as well as other mesidine oxidation results will be given subsequently. The scope of oxidative migrations of anilines is broadened by these findings. Heretofore the other authenticated migrations have been the NIH shifts of deuterium or tritium in the oxygenations of amides of aniline and, to a lesser degree, aniline, by microsomal hydroxylases[11] or peroxytrifluoroacetic acid.[12]

Acknowledgment.—We are grateful to the National Science Foundation for partial financial support through an institutional grant program.

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[8] B. Miller, *J. Amer. Chem. Soc.*, **86**, 1135 (1964). Quinamines substituted in the ortho and para positions undergo neither a quinamine rearrangement nor a dienone–phenol rearrangement.

[9] B. C. Saunders and J. Wodak, *Tetrahedron*, **23**, 473 (1967).

[10] This system for the oxidation of 10 mmol of amine consists of 10 mmol of $K_2Cr_2O_7$, 10 ml of acetic acid, 20 ml of methanol, and 100 ml of water. The pH range is 1.8–2.1.

[11] S. Udenfriend, P. Zaltzman-Nirenberg, J. Daly, G. Guroff, C. Chidsey, and B. Witkop, *Arch. Biochem. Biophys.*, **120**, 413 (1967).

[12] (a) D. Jerina, J. Daly, W. Landis, B. Witkop, and S. Udenfriend, *J. Amer. Chem. Soc.*, **89**, 3347 (1967); (b) D. Jerina, J. Daly, and B. Witkop, *Biochemistry*, **10**, 366 (1971).

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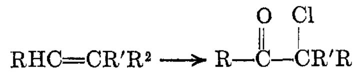
Chromyl Chloride in Acetone. α-Chloro Ketones or Ketones Directly from Olefins

Summary: Oxidation of olefins with chromyl chloride in acetone affords the α-chloro ketones in good yield; zinc dust reduction prior to work-up produces the corresponding ketones.

Sir: We have found that reaction of disubstituted (R′ = H) and trisubstituted olefins with chromyl chloride in acetone effects the following unique conversion.



$$\mathrm{RHC{=}CR'R^2} \longrightarrow \mathrm{R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle Cl}{|}}{C}R'R^2}$$

Addition of zinc dust to the crude reaction mixture results in reduction of the α-chloro ketone to the corresponding ketone in high yield. With exception of the recent reports of Freeman and coworkers,[1] the chromyl chloride oxidations of olefins were notorious for producing complex mixtures of little synthetic value.[2] The key to the success of this new procedure appears to be the use of acetone, a relatively polar solvent by comparison with the previously employed halogenated organic solvents.

Two general procedures (A and B), differing only in the temperature during chromyl chloride addition, were employed. The application of these procedures, as described below for the conversion of cyclododecene to α-chlorocyclododecanone, reveals the simplicity of the method.

Procedure A.—A solution of 16.6 g (0.10 mol) of cyclododecene (Chemical Samples Co.; glc analysis revealed 91% trans, 7% cis, and 2% diene) in 500 ml of reagent acetone was cooled in a Dry Ice–acetone bath to −70° and then treated with 33.0 g (0.21 mol) of chromyl chloride (Alfa Ventron Co.) which was added *via* a dropping funnel with vigorous stirring of the solution. Addition was controlled so that a temperature of −65° was not exceeded. After addition was complete (~30 min), the mixture was stirred at −75° for 1 hr, then allowed to warm to room temperature, and stirred at 23–25° for 1 hr. The homogeneous,

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[1] (a) F. Freeman, P. J. Cameran, and R. H. Dubois, *J. Org. Chem.*, **33**, 3970 (1968); (b) F. Freeman, R. H. Dubois, and N. J. Yamachika, *Tetrahedron*, **25**, 3441 (1969).

[2] (a) R. A. Stairs, D. G. M. Diaper, and A. L. Gatzke, *Can. J. Chem.*, **41**, 1059 (1963); (b) S. J. Cristol and K. R. Eilar, *J. Amer. Chem. Soc.*, **72**, 4353 (1950).

dark red-brown mixture was quenched by slowly pouring it into an ice-cold aqueous solution of $NaHSO_3$ [30 g (0.3 mol) of $NaHSO_3$ in 1000 ml of H_2O]. The green mixture was stirred for 30 min in an ice bath and then extracted with 2 × 500 ml of ethyl acetate–hexane (1:1). The organic phases were washed with 500 ml of H_2O and 500 ml of NaCl (saturated, aqueous), then combined, dried over anhydrous sodium sulfate, filtered, and concentrated to yield a greenish yellow oil weighing 24.0 g (100%). The crude product was distilled to afford 17.1 g (79%) of α-chlorocyclododecanone bp 100–102° (0.075 mm) [lit.[3] bp 117–118° (1.5 mm)] as a yellow liquid which solidified on standing to yield white prisms (from hexane), mp 56–57° (lit.[3] mp 59–60°).

Starting with crude cyclododecene (∼65% trans, 25% cis, 6% alkane, 4% diene), lower yields (50–60%) were obtained.

Procedure B.—The reaction was run identically as procedure A except that the chromyl chloride was added to the solution cooled in an ice–salt bath such that a temperature of 3° was not exceeded. After addition, the mixture was stirred at −5° for 1 hr, then allowed to warm to room temperature, and stirred at 23–25° for 1 hr. The quench and work-up were carried out as before to yield 69% α-chlorocyclododecanone.

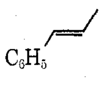
Examination of the table reveals that, although the low temperature procedure (A) gives better yields than B, the yields at the higher temperature (−5 to 3°) are still quite good. The inconvenience of cooling large scale reactions to −70° and the insolubility of many substrates in acetone at such temperatures should make procedure B preferable in certain cases. The improved yields at lower temperatures appear to be due to selective suppression of allylic oxidation which produces α,β-unsaturated ketones, more prominent by-products at higher temperatures. The sensitivity of cyclohexene to allylic attack probably accounts for the below average yield with this olefin.

The reaction is remarkably clean with trans-disubstituted olefins; only trace by-products are visible by glc. However, cis-disubstituted olefins react more slowly and afford poorer yields;[4] the unsaturated ketone is the major by-product. With the trisubstituted olefin 2-methyl-2-heptene a chlorohydrin is the only significant product in addition to the expected chloro ketone.

With a simple change in the work-up, this oxidation process becomes a one-step ketone synthesis.[5]

Preparation of Cyclododecanone.—Procedure A was followed with these modifications. After reaction, the mixture was treated with 50 ml of glacial acetic acid, and excess zinc dust while cooling in an ice bath, and then stirred at 23–25° for 3 hr or until the chloro ketone had been completely converted to ketone as determined by glc analysis of aliquots withdrawn. The mixture was then poured into 500 ml of cold H_2O and extracted with 2 × 500 ml of ethyl acetate. After the normal work-up, 18.2 g (95%) of crude cyclododecanone was isolated. Distillation afforded 14.0 g (75%) of pure cyclododecanone, bp 119–121° (9 mm), mp 58–59° [lit.[6] bp 120–125° (12 mm), mp 59–61°].

Unlike Freeman's aldehyde and ketone syntheses[1a,b] this route clearly involves reduction of an intermediate α-chloro carbonyl compound. Following Freeman's procedure for oxidation of *trans*-propenylbenzene (**1**), and using a bisulfite work-up, the chlorohydrin **2**, but none of the chloro ketones **3** and **4**, was obtained.



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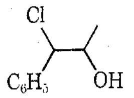

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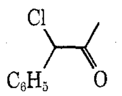

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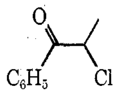

4

On standing at room temperature chlorohydrin **2** rearranged spontaneously to benzyl methyl ketone, the product which Freeman reports.[1b] Oxidation of olefin **1** in acetone, following procedure B, gave the chloro ketones **3** and **4** (3:1) as the major products.

While studying the effect of solvent polarity on these oxidations, we made several novel observations pertaining to the mechanism of oxidation of olefins by chromyl chloride (Table I);[7] we will report these results shortly.

TABLE I

OXIDATION OF OLEFINS BY CrO_2Cl_2 IN ACETONE[a]

Olefin	Yield, % (chloro ketone)[b]	Procedure
trans-cyclododecene	70	B
trans-cyclododecene	79(90)	A
trans-5-decene	(90)	A
trans-5-decene	(81)	B
cis-5-decene	(65)	B
cis-5-decene	(68)	A
trans-2-octene	70[c]	A
4,4-dimethyl-*trans*-2-pentene	60[d]	A
2-methyl-2-heptene	45[e]	A
cyclohexene	38	A
norbornene	58	A

[a] Generally run using 10 mmol (glc) or 0.1 mol (prep) of the olefin. [b] Yields were determined by isolation or by glc (parentheses). [c] 1:1 mixture of the two possible chloro ketones. [d] 10:1 mixture of 4,4-dimethyl-3-chloro-2-pentanone and 4,4-dimethyl-2-chloro-3-pentanone. [e] 2-Chloro-2-methyl-3-heptanone plus 32% of an unidentified chlorohydrin.

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[3] L. I. Zakarin and V. V. Korneva, *Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk.*, 1817 (1962) [*Chem. Abstr.*, **68**, 7841*d* (1963)].

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[5] Other one-step procedures for oxidation of an olefin to a carbonyl compound: (a) H. C. Brown and C. P. Gary, *ibid.*, **83**, 2951 (1961); (b) A. Aguilo, *Advan. Organometal. Chem.*, **5**, 321 (1967); (c) G. T. Rodeheaver and D. F. Hunt, *Chem. Commun.*, **818** (1971).

[6] L. Ruzicka, M. Stoll, and H. Schinz, *Helv. Chim. Acta*, **9**, 256 (1916).

[7] K. B. Sharpless and A. Y. Teranishi, manuscript in preparation.

[8] National Institute of Health Predoctoral Fellow, 1969–1972.