at 0°. The hydroboration was done by adding 10 mmol of 1-methylcyclopentene and stirring for 2 hr at 0°. For the oxidation 15 ml of ethanol was added, followed by 5 ml of $\sim 3\ N$ NaOH, and 2 ml of 30% H_2O_2 added dropwise (vigorous reaction). The completion of the oxidation was ensured by maintaining the reaction mixture at 50° for 15 min. The absolute and relative yields of the alcohols were determined by glpc using undecane as the internal standard. (The amount of the internal standard was chosen such that its peak size was closer to that of the minor component. The reliability of the instrument in determining the minor component present in such small quantities was checked by analyzing known synthetic mixtures of the two components in the proportions expected from the reaction.) *trans*-2-Methylcyclopentanol were obtained in 94% yield. There was present <0.2% tertiary alcohol and no cis isomer.

The results are summarized in Table I together with comparable data for hydroboration with BH_3 in THF.

TABLE I

PRODUCTS FROM HYDROBORATION–OXIDATION OF REPRESENTATIVE OLEFINS WITH BH_2Cl IN ETHYL ETHER AND BH_3 IN TETRAHYDROFURAN

		Relative yield of products, %	
Olefin	Products	BH_2Cl–OEt_2[a]	BH_3–THF[b]
1-Hexene	1-Hexanol	>99.5	94
	2-Hexanol	<0.5	6
2-Methyl-1-butene	2-Methyl-1-butanol	>99.9	99
	2-Methyl-2-butanol	<0.1	1
Norbornene	*exo*-2-Norbornanol	>99.8	99
	endo-2-Norbornanol	<0.2	1
2-Methyl-2-butene	3-Methyl-2-butanol	99.7	98
	2-Methyl-2-butanol	0.3	2
1-Methylcyclopentene	*trans*-2-Methylcyclopentanol	>99.8	98.5
	1-Methylcyclopentanol	<0.2	1.5
Styrene	2-Phenylethanol	96	81[c]
	1-Phenylethanol	4	19[c]
α-Methylstyrene	2-Phenyl-1-propanol	100	100
	2-Phenyl-2-propanol	0	0
2-Pentene	2-Pentanol	58[d]	55[d]
	3-Pentanol	41[d]	45[d]
4-Methyl-2-pentene	4-Methyl-2-pentanol	60[d]	57[e]
	2-Methyl-3-pentanol	40[d]	43[e]
4,4-Dimethyl-2-pentene	4,4-Dimethyl-2-pentanol	79[d]	58[e]
	2,2-Dimethyl-3-pentanol	21[d]	42[e]

[a] Total yields were 95 ± 5%. [b] Reference 1a,b. [c] Reference 1c. [d] Cis olefin. [e] Trans olefin.

The results with olefins, such as 2-pentene, 4-methyl-2-pentene, and 4,4-dimethyl-2-pentene, reveal a slightly greater directive effect compared to BH_3, but very minor compared to disiamylborane. Consequently, disiamylborane remains the hydroborating agent of choice when it is desirable to use steric effects to control the direction of addition. The results with the 2-pentenes show that the direction of addition of BH_2Cl is not significantly influenced by steric effects. Therefore, the powerful directive effects observed with the other olefins must be due to electronic (polar) effects.

The question arises as to why the results for the directive effects are so different in ethyl ether from those reported for THF. The reaction in THF is relatively slow. In fact, it may be that only a small part of the reaction in THF proceeds through the monochloroborane–tetrahydrofuranate, but proceeds instead through a small equilibrium concentration of borane (eq 4). ($BHCl_2$ in THF does not hydroborate

$$2ClH_2B\text{–THF} \rightleftharpoons Cl_2HB\text{–THF} + H_3B\text{–THF} \qquad (4)$$

olefins to any significant extent under these conditions[7].) On the other hand, there is little doubt that the hydroboration in ethyl ether must be proceeding through the BH_2Cl entity.

In any case, it is quite clear that hydoboration with monochloroborane–ethyl etherate not only provides a convenient route to dialkylchloroboranes and the corresponding borinic acids and esters, but also provides the anti-Markovnikov alkylborane moiety in far higher isomeric purity than hydroboration with borane itself. This development greatly extends the utility of the hydroboration reaction for the synthesis of regiospecifically and stereochemically pure derivatives.

[7] H. C. Brown and N. Ravindran, unpublished results.

[8] Postdoctoral research associate on National Science Foundation Grant No. 27742X.

RICHARD B. WETHERILL LABORATORY
PURDUE UNIVERSITY
LAFAYETTE, INDIANA 47907

HERBERT C. BROWN*
N. RAVINDRAN[8]

RECEIVED OCTOBER 11, 1972

Migrations in Oxidations of Trisubstituted Anilines

Summary: Homogeneous oxidations of mesidine in moderately acidic mixtures containing methanol afford the expected azo compound and two anils, one of which, 2,6-dimethyl-3-methoxymethyl-*p*-benzoquinone 4-(2′,4′,6′-trimethyl)anil, is formed by an alkyl shift.

Sir: The peroxidase-catalyzed oxidative dealkylation of mesidine (**1**) to the quinone anil **3**, was disclosed by Chapman and Saunders in 1941.[1] Subsequently the reaction was repeated with a variety of chemical oxidants.[2] We wish to report that mesidine can be transformed by several oxidizing systems into an anil, **4**, containing a shifted alkyl group. We consider this finding to be the first case of an alkyl shift in a nonenzymatic oxidation of a substituted aniline. Saunders and colleagues[3] have invoked an alkyl shift in the peroxidase oxidation of 2,4-dimethylaniline[4] to explain the formation of a minor product.

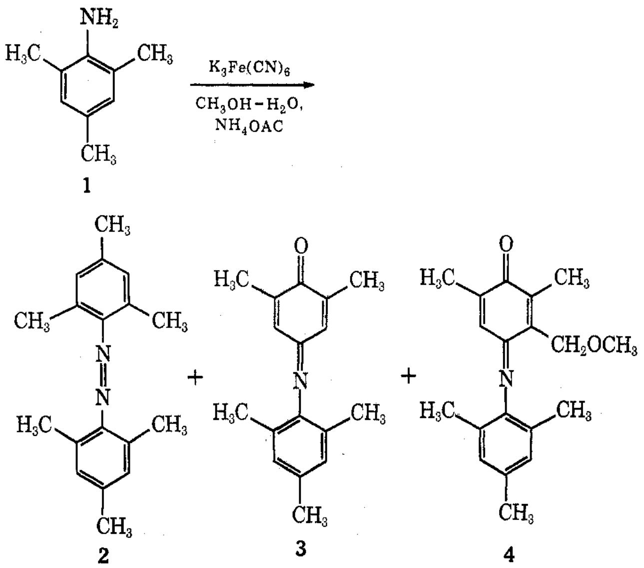
Mesidine, **1**, was oxidized by ferricyanide in a methanol–water mixture to give azo **2**, anil **3**, and a new anil **4** [2,6-dimethyl-3-methoxymethyl-*p*-benzoquinone-4-(2′,4′,6′-trimethyl)anil]. The respective yields were 1.5, 54, and 17%, when a reaction mixture of 0.010 mol of mesidine and 0.076 mol of potassium

[1] N. B. Chapman and B. C. Saunders, *J. Chem. Soc.*, 496 (1941).

[2] A. G. Holmes-Siedle and B. C. Saunders, *Chem. Ind.* (*London*), 164 (1959).

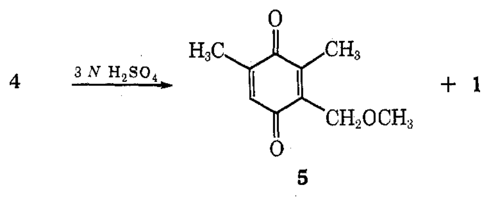
[3] V. R. Holland, B. M. Roberts, and B. C. Saunders, *Tetrahedron*, **25**, 2291 (1969).

[4] The shifted product, 2,5-dimethyl-*p*-benzoquinone bis(2,4-dimethyl)-anil, was formed in 3% yield.



ferricyanide in 100 ml of methanol and 600 ml of water containing 80 g of ammonium acetate was maintained at 45° for 10 days. The pH of the reaction was 6.6. If the reactions were run with 1 to 10 g of potassium hydroxide in place of ammonium acetate, the yields of azo **2** were 91–95% and the yields of anils were 0–3%. Separations were accomplished by the use of dry column chromatography.[5] Reaction times were shortened to 4 hr by the use of dichromate- or persulfate-oxidizing systems. Strongly acidic oxidizing agents such as ferric chloride in hydrochloric acid and ammonium persulfate in acetic acid gave little evidence of reaction.

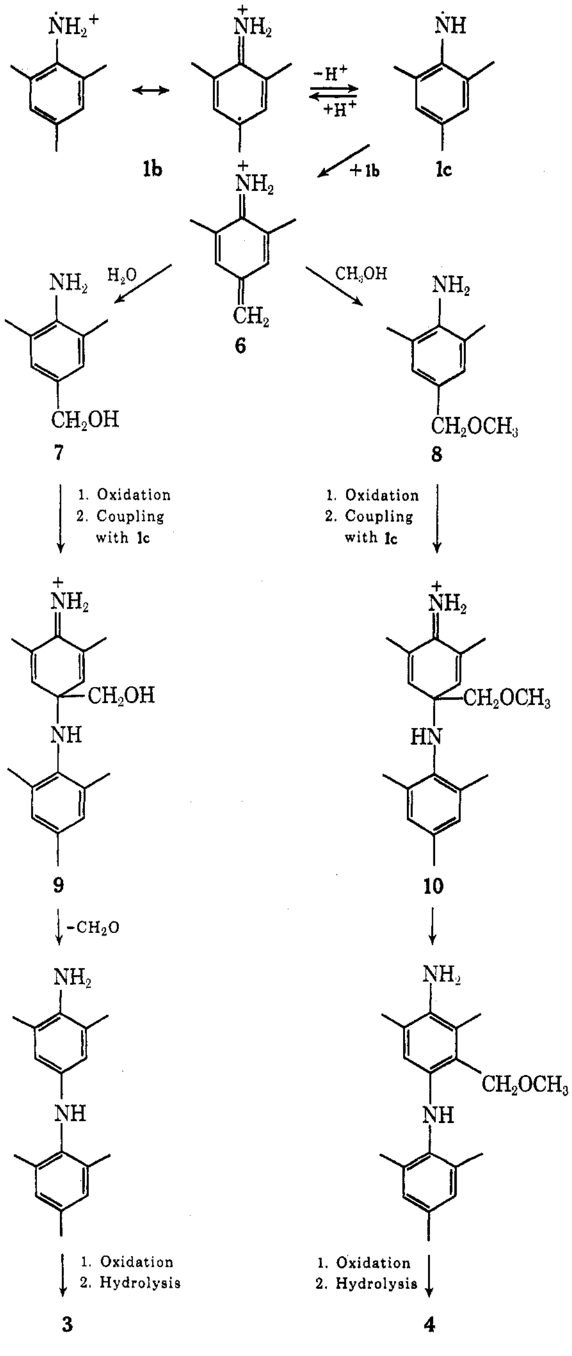
Anil **4** is a purple oil whose ir, uv, and nmr spectra were consistent with the assigned structure: ir (neat) 1639 (C═O), 1109, 1081 cm^{-1} (CH_2OCH_3); uv max (C_2H_5OH) 209 nm (ϵ 22,200), 277 (22,400), 515 (1040); nmr ($CDCl_3$) δ 6.86 (s, 2), 6.43 (q, 1, J = 1.5 Hz), 4.74 (s, 2), 3.44 (s, 3), 2.32 (s, 3), 2.20 (s, 3), 1.92 ppm (s, 9). Mass spectral data indicated a parent peak at 341.[6] Anil **4** was hydrolyzed with 3 N H_2SO_4 with concurrent steam distillation. Sublimation of the ether-soluble distillate gave the quinone **5**: mp 33°; ir (KBr) 1667, 1117, 1087 cm^{-1}; nmr (CCl_4) δ 6.65 (q, 1, J = 1.5 Hz), 4.36 (s, 2), 340 (s, 3), 2.17 (s, 3), 2.08 ppm (d, 3. J = 1.5 Hz). The acid-soluble portion of the hydrolysate was converted to a benzamide, mp 204°, undepressed on admixture with authentic mesidine benzamide.[7]



The quinone **5** was synthesized *via* a sequence that started with 2,6-dimethylnitrobenzene. The latter compound was alkylated with chloromethyl ether and aluminum chloride to give 2,6-dimethyl-3-chloromethylnitrobenzene, mp 61–62°. Sodium methoxide treatment converted this material to 2,6-dimethyl-3-methoxymethylnitrobenzene, mp 46–47°, which was reduced to the corresponding aniline, mp 62–63°, by means of zinc and sodium hydroxide. This aniline was oxidized with Fremy salt to the quinone **5**. This synthesis lends chemical proof for the structural assignment of anil **4**.

A reaction path for the oxidation of mesidine is shown in Scheme I and is consistent with the dependence of products on the acidity. Cation radicals are assumed to be formed initially and converted to neutral radicals with increasing basicity of the medium. In strongly acidic media their ability to couple is

SCHEME I



---

[5] B. Loew and M. M. Goodman, *Chem. Ind.* (*London*), 2026 (1967).

[6] All new compounds were analyzed to give acceptable values.

[7] H. Huebner and E. von Schack, *Chem. Ber.*, **10**, 1711 (1877).

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.

---

[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).

DEPARTMENT OF CHEMISTRY,
NEW YORK UNIVERSITY
NEW YORK, NEW YORK 10003

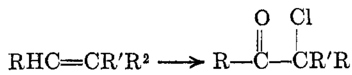
STEPHEN L. GOLDSTEIN
EDWARD MCNELIS*

RECEIVED OCTOBER 3, 1972

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,

---

[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).