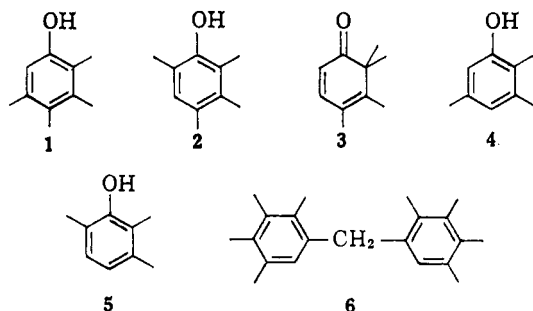


to phenols and quinones in low yield.<sup>4</sup> We reasoned that coordination of a Lewis acid with an organic peracid might facilitate departure of ionic electrophilic hydroxyl from the latter and furnish a potent oxidant under mild conditions.

This communication reports preliminary results on the use of peroxytrifluoroacetic acid with boron fluoride as a source of positive hydroxyl. Mesitylene was converted directly and rapidly to mesitol in 88% yield, with efficient use of the peracid.<sup>5</sup> Similarly, isodurene gave isodurenol in 62% yield (one experiment).

Extension of the reaction to prehnitene gave, in addition to the expected 2,3,4,5-tetramethylphenol (**1**), a number of other products (**2-6**) which reveal the potency of the reactive intermediate formed by this



reagent.<sup>6-9</sup> Attack of  $\text{OH}^+$  at a vacant ring position furnishes **1** (9.0%). Similar attack at C-1, followed by a methyl shift, accounts for **2** (3.6%) and **3** (1.8%).<sup>10</sup> The tarry residue (about 27%), which showed no aromatic protons in the n.m.r. and strong  $\text{C}=\text{O}$  and  $\text{C}=\text{C}$  absorption (bands at 1634, 1661, 1695, 1736 and 1750  $\text{cm}^{-1}$ ), probably contains dimer or polymer from **3** and analogous cyclohexadienones from attack of  $\text{OH}^+$  at C-2.

The remaining products (which account for a major fraction of the prehnitene consumed) either lack (**4** and **5**) or have an extra (**6**) carbon atom. Complete absence of trimethylbenzenes and of isomeric trimethylphenols suggests that **4** and **5** arise from loss of the *para* methyl group of **1** and **2**, respectively, according to the scheme shown (for **1**).<sup>11</sup>

(4) J. D. McClure and P. H. Williams, *J. Org. Chem.*, **27**, 24 (1962). It was, however, effective in the Baeyer-Villiger conversion of ketones to esters.

(5) Although the yield when boron fluoride is omitted is reasonably good,<sup>1</sup> the conversion is very poor.

(6) Identification of the products, which were isolated by a combination of distillation and chromatographic techniques, will be described in a full account. All are previously known except **3**, whose structure is based on a satisfactory analysis of its 2,4-dinitrophenylhydrazones, m.p. 153–156°, and on its spectra. In carbon tetrachloride, **3** had bands at 1663 and 1630  $\text{cm}^{-1}$ , and in ethanol it had  $\lambda_{\text{max}}$  327  $\text{m}\mu$  ( $\log \epsilon$  3.48), which compare favorably with suitable models.<sup>9</sup> Its n.m.r. spectrum in carbon tetrachloride showed singlets at 8.85 and 8.15  $\tau$ , corresponding to six protons each, and doublets at 4.19 and 3.15  $\tau$  ( $J = 19$  c.p.s.) each corresponding to a single proton.

(7) When the reaction was repeated with boron fluoride, but without the peracid, prehnitene was recovered (94%) unchanged. Study of the reverse conditions (peracid but no boron fluoride) will be reported in a full account.

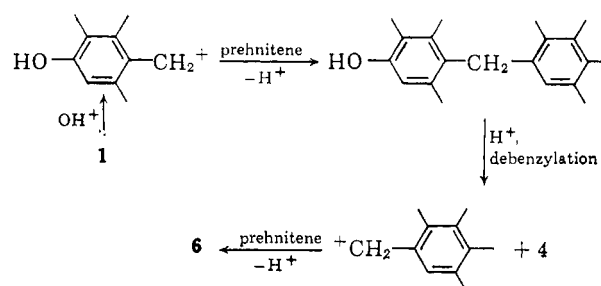
(8) For simplicity, this intermediate will be referred to as  $\text{OH}^+$ .

(9) See L. Mandell, D. Caine and G. E. Kilpatrick, *J. Am. Chem. Soc.*, **83**, 4457 (1961), and leading earlier references therein.

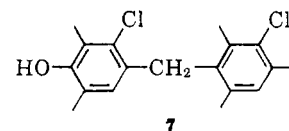
(10) The formation of a cyclohexadienone from 2,6-dimethylphenol and peroxytrifluoroacetic acid<sup>3</sup> is not strictly analogous to the present reaction, since the potential ketonic oxygen was already present in the aromatic substrate. The hydrogen bonding invoked to rationalize the product in ref. 3 is not possible here.

(11) This mechanism requires that the sum of moles of **4** and **5** equal the yield of **6**. In fact, from 0.0332 mole of prehnitene consumed, there was obtained 0.0048 mole of **4**, 0.0017 mole of **5** and 0.0039 mole of **6**. The sum of **4** and **5** is too large, but the yield of these products was determined from v.p.c. curves, whereas that of **6** is of isolated, purified crystalline product and is probably low.

The material balance accounted for 85% of the prehnitene consumed; it is unlikely that any significant products with low molecular weights (under 200) were missed.



Consistent with this scheme is the isolation of **7** as the major product from the reaction of our reagent with



chloromesitylene.<sup>12</sup> The chlorine apparently does not prevent the hydride abstraction, but does inhibit the debenzylation. Nitromesitylene gave a product similar to **7**.

Typical of the experimental procedure is the following preparation of mesitol. To a solution of 56.1 g. (0.468 mole) of mesitylene<sup>13</sup> in 100 ml. of methylene chloride was added peroxytrifluoroacetic acid prepared from 35 g. (0.167 mole) of trifluoroacetic anhydride, 50 ml. of methylene chloride and 4 ml. (0.148 mole) of 90% hydrogen peroxide.<sup>14</sup> Boron fluoride was bubbled through the reaction mixture during the addition, which required 2.5 hr. The reaction was strongly exothermic, and the temperature was kept below 7° by external cooling.<sup>15</sup> After addition was complete, water was added and the organic layer was washed with bisulfite and bicarbonate, dried and distilled. There was obtained 32.0 g. of unchanged mesitylene and 17.7 g. (88%) of mesitol, m.p. 69–70°.

**Acknowledgment.**—We are grateful to the Petroleum Research Fund of the American Chemical Society for financial support (G-488C).

(12) The structure of **7**, m.p. 142.5–143.5°, is based on a satisfactory analysis, hydroxyl at 3535  $\text{cm}^{-1}$ , n.m.r. and mass spectra consistent with the structure, and reduction to products with one or both chlorines removed. We are indebted to Mr. S. Meyerson, American Oil Company, Whiting, Indiana, for mass spectral data and interpretation for **6** and **7**.

(13) Excess hydrocarbon reduces further oxidation of the primary product.

(14) The peracid was prepared by mixing the reagents at 0°, then allowing them to warm to room temperature.

(15) If boron fluoride was omitted, the reaction was much less exothermic and gave mesitol in 47% yield based on peracid; this is, nevertheless, an appreciable improvement over the earlier<sup>1</sup> procedure.

(16) National Science Foundation Cooperative Fellow, 1962–1963.

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RECEIVED MAY 16, 1963

## A New Method for the Alkylation of Ketones and Aldehydes: the C-Alkylation of the Magnesium Salts of N-Substituted Imines

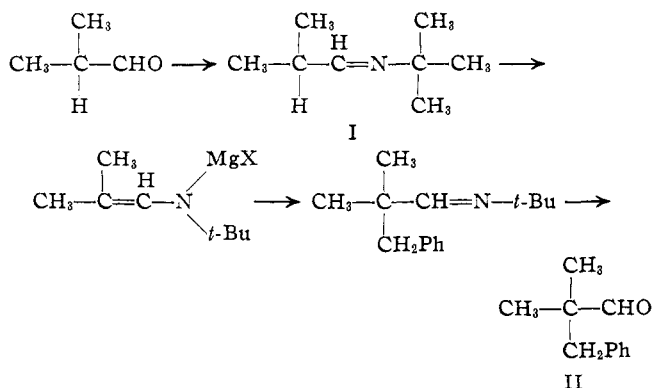
Sir:

The difficulties involved in monoalkylating ketones and aldehydes are well known. As we have pointed out in a previous communication,<sup>1</sup> the enamine alkylation procedure which was devised to circumvent some of these difficulties is general only with electrophilic olefins (conjugated ketones, esters, nitriles, etc.). With alkyl halides, however, it has turned out that although

(1) G. Stork, A. Brizzolarra, H. Laudesman, J. Szmuszkowicz and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

the method is very useful with particularly reactive halides (allyl, benzyl, propargyl halides;  $\alpha$ -halo ethers, esters, nitriles and ketones) it is not very serviceable for ordinary primary and secondary alkyl halides. This is especially true of the reaction with aldehydes, whose enamines give mostly N-alkylation.

We have now found that a wide variety of imines derived from aliphatic primary amines and enolizable aldehydes or ketones<sup>2</sup> can be made to undergo essentially complete enolization with very little, if any, addition<sup>3</sup> by refluxing with one equivalent of ethyl magnesium bromide in tetrahydrofuran. *These readily prepared magnesium salts react with primary and secondary alkyl halides to give, after aqueous acid hydrolysis, high yields of monoalkylated carbonyl compounds.* The process may be illustrated as shown below in the case of the *t*-butylimine (I) from isobutyraldehyde. Formation of the magnesium complex by reaction with ethyl magnesium bromide, followed by alkylation with benzyl chloride and aqueous acid hydrolysis,<sup>4,5</sup> gave 2,2-dimethyl-3-phenylpropanal (II) which vapor phase



chromatography showed to be pure (2,4-dinitrophenylhydrazone, m.p. 150–152°; reported<sup>6</sup> m.p. 154–155°). The yield of distilled product<sup>7</sup> based on the imine used was 80%. In similar fashion, the cyclohexylimine from cyclohexanone gave with butyl iodide 78% of 2-butylcyclohexanone; with butyl toluene sulfonate, 80% of 2-butylcyclohexanone; with allyl bromide,

(2) The imines were prepared, whenever feasible, by condensation of the appropriate amine and ketone or aldehyde using azeotropic distillation with benzene to remove the water. Imines from low boiling ketones or amines were prepared by the procedure of C. W. Smith, D. G. Norton and S. A. Ballard, *J. Am. Chem. Soc.*, **75**, 3316 (1953); those from low boiling aldehydes were made by the method of M. R. Tiollais, *Bull. soc. chim. France*, **14**, 708 (1947).

(3) To the extent that they have been studied, these imines have previously been claimed to undergo addition to the carbon-nitrogen double bond: cf. P. M. Maginnity and R. J. Gair, *J. Am. Chem. Soc.*, **74**, 4958 (1952); V. Evdokimoff, *Gazz. chim. ital.*, **77**, 318 (1947); M. R. Tiollais, *Bull. soc. chim. France*, 959 (1947); cf. U. S. Patents 2,700,681 and 2,700,682 to R. N. Blomberg and W. F. Bruce, *Chem. Abstr.*, **49**, 7589 (1955); P. M. Maginnity and J. B. Cloke, *J. Am. Chem. Soc.*, **73**, 49 (1951); cf. E. F. Godefroi and L. H. Simanyi, *J. Org. Chem.*, **27**, 3882 (1962).

(4) Efforts to use bases such as sodium hydride with imines derived from aliphatic amines have not been very successful. The more acidic Schiff bases from aniline can be enolized with sodium hydride, as well as with Grignard reagents. For instance, the anil of cyclohexanone gave off an equivalent of gas on heating 8 hr. with 10% excess of sodium hydride in toluene. Addition of butyl iodide, refluxing overnight, hydrolysis and work-up as usual gave 62% of distilled 2-butylcyclohexanone.

(5) All these alkylations were carried out by adding the imine to a solution of one equivalent of ethylmagnesium bromide in dry tetrahydrofuran and refluxing under nitrogen until one equivalent of gas had been formed. The alkylating agent then was added with stirring, after cooling to room temperature, and the solution was refluxed until the pH was lowered to 9–10. This usually required 15–20 hr., but there is evidence that the reaction is essentially complete in a much shorter time. Hydrolysis was effected by refluxing for 1–3 hr. with a 2–3-fold excess of 10% hydrochloric acid and the carbonyl compound was extracted and distilled.

(6) G. Opitz, H. Heilmann, H. Mildenerger and H. Suhr, *Ann.*, **649**, 36 (1961).

(7) All yields quoted refer to *distilled* material. The yield by v.p.c. appeared to be appreciably higher.

73% of 2-allylcyclohexanone; and with benzyl chloride, 60% of 2-benzylcyclohexanone.

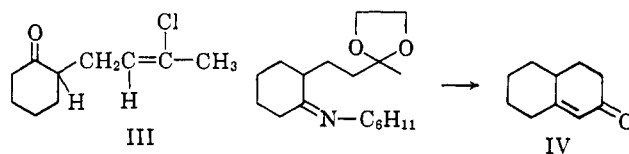
Cyclopentanone *via* its cyclohexylimine gave 72% of 2-butylcyclopentanone. Cycloheptanone similarly gave 2-butylcycloheptanone in 75% yield, and 2-methylcycloheptanone in 70% yield.

Isobutyraldehyde as its cyclohexylimine gave with butyl iodide 70% of 2,2-dimethylhexanal, also obtained in 65% yield from the *t*-butylimine. Heptaldehyde produced (butyl iodide) 50% of 2-butylheptanal from its *t*-butylimine.

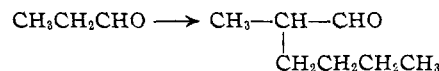
Some special features of the new reaction are worthy of comment.

(1) Some halides which are easily dehydrohalogenated by strong oxygen bases are not dehydrohalogenated by the magnesium salts of imines. For instance, isopropyl iodide gave 61% of 2-isopropylcyclohexanone from the cyclohexylimine of cyclohexanone, and similarly 2-( $\beta$ -phenethyl)-cyclohexanone was obtained in 65% yield with  $\beta$ -phenethyl bromide.

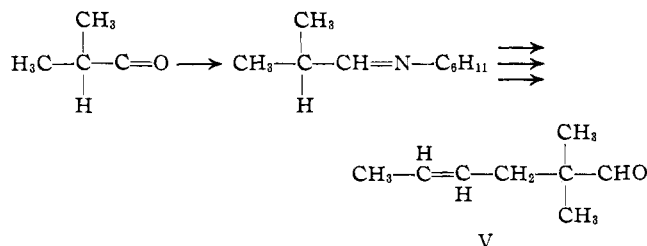
(2) Certain functional groups may be present in the alkylating agent. Alkylation *via* the magnesium complex of the cyclohexylimine from cyclohexanone with 2,4-dichloro-2-butene gave 77% of 2-(3-chloro-2-butenyl)-cyclohexanone (III). Similarly, alkylation with 2-(2-bromoethyl)-2-methyldioxolane gave 66% of  $\Delta^{1,9}$ -2-octalone (IV) the product of hydrolysis and cyclization of the intermediate alkylation product.



(3) The formation of the magnesium complexes of N-alkylimines may be carried out in the presence of alkyl bromides since the latter react only slowly with Grignard reagents. This is helpful with imines which condense easily with their Grignard salts, such as the imines of low molecular weight aldehydes. For instance, addition of the *t*-butylimine of propionaldehyde to a tetrahydrofuran solution of ethyl magnesium bromide containing one equivalent of butyl bromide gave, after acid hydrolysis and distillation, 60% of 2-methylhexanal (semicarbazone m.p. 90–91°; reported<sup>8</sup> m.p. 92–93°).



(4) Allylic halides give alkylation *without rearrangement*. For instance, the cyclohexylimine of isobutyraldehyde gave, on alkylation of its magnesium salt with crotyl bromide, a 71% yield of 2,2-dimethyl-4-hexenal (V). This contrasts with the alkylation of the enamine



of isobutyraldehyde with the same reagent which gives the isomeric product VI resulting from N-alkylation, followed by Claisen rearrangement<sup>9</sup>

(8) M. B. Green and W. J. Hickinbottom, *J. Chem. Soc.*, 3262 (1957).

(9) K. C. Brannock and R. D. Burpitt, *J. Org. Chem.*, **26**, 3576 (1961).

(5) Passage of a pure 1-olefin over the best catalysts under dehydration conditions resulted in 1-2% isomerization to the 2-isomer.