Dr. E. White, V, of Smith, Kline and French Laboratories, and Dr. Ned Heindel of Lehigh University for nmr spectra. The author is especially grateful to Dr. Lyle for his consultation and encouragement.

Registry No.—**1a**, 52195-27-4; **1a** hydrochloride, 52195-28-5; **1b** hydrochloride, 52195-29-6; **1c**, 52195-30-9; **1c** hydrochloride, 52195-31-0; **1d** hydrochloride, 52195-32-1; **1e**, 52195-33-2; **1e** hydrochlorides, 52195-34-3; **1f** hydrochloride, 52195-35-4; **1g** hydrochloride, 52195-36-5; **1h**, 52195-37-6; **3**, 34737-89-8; **4a**, 52195-38-7; **4b**, 52195-39-8; **5**, 40240-24-2.

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(7) In addition to the nmr methods summarized in ref 4, an X-ray crystallographic analysis[3] of the slower eluting major isomer obtained from phenyllithium addition to 1,3-dimethyl-4-piperidone (**6**) established the 4-Ph/3-Me stereochemistry as trans. Our stereochemical assignments were then made on the warranted assumption that replacement of the *N*-methyl group by *N*-benzyl does not reverse the preferred pathway of lithium reagent attack. Additionally, these stereochemical assignments and nmr results are in accord with those reported earlier for similar piperidines obtained by catalytic hydrogenation of the parent pyridines.[1]

(8) Free-energy differences between conformers were calculated using a decrease of 0.6–0.8 kcal/mol in the unfavorable axial methyl interaction on replacement of one syn-axial hydrogen by the nitrogen free pair[9] and the best $-\Delta G_X$ values listed by Hirsch.[10]

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(11) As one referee has correctly suggested, there are several hazards in making predictions on conformational equilibria based on additive free energies of substituent groups when two or more are present.[12] In our case, conformational distortions are considered to be negligible.

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Hydration of 3-Methyl-3-buten-2-one (Isopropenyl Methyl Ketone)

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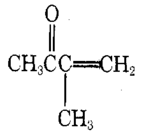
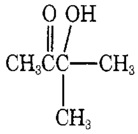
Experience shows that the acid-catalyzed addition of water to a carbon–carbon double bond conjugated with a carbonyl group occurs such that hydrogen appears on the α carbon atom and hydroxyl on the β. Thus methyl vinyl ketone affords 4-hydroxy-2-butanone,[1] and acrylaldehyde and acrylic acid yield respectively 3-hydroxypropionaldehyde and 3-hydroxypropionic acid.[2] This direction of addition can be rationalized in terms of the strong electron-withdrawing influence of the carbonyl group, especially when protonated by the mineral acid catalyst.[2]

It has been reported that 3-methyl-3-buten-2-one (isopropenyl methyl ketone, **1**) behaves abnormally in this reaction, yielding 3-hydroxy-3-methyl-2-butanone (**2**) instead of the anticipated 4-hydroxy-3-methyl-2-butanone (**3**).[3] The formation of this unexpected product has been explained in terms of a possible methyl migration in **1** subsequent to protonation,[3] or of Markovnikov addition of water to the enolic form of **1**.[4]



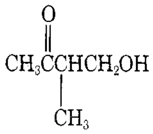
$$CH_3\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{C}{=}CH_2$$

1



$$CH_3\overset{\overset{O}{\|}}{C}\overset{\overset{OH}{/}}{\underset{\underset{CH_3}{|}}{C}}{-}CH_3$$

2



$$CH_3\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{CH}CH_2OH$$

3

Since there appeared to be no compelling reason why **1** should be hydrated in this unusual manner, we have carefully reinvestigated the reaction, and our findings show that in fact the sole product of the addition (aside from polymeric material and unchanged ketone) is the expected 4-hydroxy-3-methyl-2-butanone (**3**). None of the isomeric ketol **2** could be detected.

3-Methyl-3-buten-2-one (**1**) was prepared by reaction between ethyl methyl ketone and formaldehyde,[5] leading to **3**, the ir and nmr spectra of which (see Experimental Section) were in complete agreement with the assigned structure; dehydration of the ketol with anhydrous oxalic acid[6] afforded **1**. The structure **1** was in harmony with its spectral properties, and the melting points of the 2,4-dinitrophenylhydrazones of both ketol and enone were in agreement with values in the literature (see Experimental Section).

The hydration of **1** was effected at 100 and at 50°, by simply mixing the ketone and 2 *N* sulfuric acid and heating under reflux at these temperatures. At the higher temperature the major product was polymeric material; volatile material consisted of unchanged ketone and 4-hydroxy-3-methyl-2-butanone (**3**), separable by fractional distillation and identified by their 2,4-dinitrophenylhydrazones and by comparison of their ir and nmr spectra with those of authentic specimens. Glc of the volatile product showed three peaks; two of these had retention times identical with those of authentic samples, and the third small peak was not identified. There was no peak corresponding to 3-hydroxy-3-methyl-2-butanone. At 50° for a longer period a similar result was obtained, except that there was very little polymeric material formed, and most of the ketone was recovered unchanged. Two glc peaks were observed with the volatile product; these corresponded exactly in retention times with unchanged ketone and 4-hydroxy-3-methyl-2-butanone. Neither of the peaks corresponded with 3-hydroxy-3-methyl-2-butanone, which could not be detected in the product.

We conclude that the hydration of isopropenyl methyl ketone occurs in the expected manner, to yield 4-hydroxy-3-methyl-2-butanone (**3**). It would seem almost certain that this was also the product encountered in the original report,[3] since the 2,4-dinitrophenylhydrazone of the product there described had mp 192°, which coincides with that of isopropenyl methyl ketone, and 4-hydroxy-3-methyl-2-butanone is known to yield this derivative under the acid conditions normally used for 2,4-dinitrophenylhydrazone formation.[7] Further, 3-hydroxy-3-methyl-2-butanone (**2**) with 2,4-dinitrophenylhydrazine in alcoholic acid media yields not the simple derivative, but that of the *O*-alkyl ketone $CH_3CO(CH_3)_2OR$.[8] Finally, the *p*-nitrobenzoates of both isomeric alcohols **2** and **3** were prepared. The former had mp 123–123.5°, as opposed to the reported[3] value of 194°, and the latter had mp 54°, in agreement with that reported.[5]

Experimental Section

Gas chromatography was conducted on a Carbowax column at 150°, on an F and M Model 810 apparatus. Nmr measurements were carried out using a Hitachi Perkin-Elmer R-24 Instrument, in deuteriochloroform solution, and using TMS as internal standard. Analyses are by Galbraith Laboratories, Inc., Knoxville, Tenn.

4-Hydroxy-3-methyl-2-butanone (3). This hydroxy ketone was prepared by a modification of Morgan and Holmes' method.[5] Freshly distilled ethyl methyl ketone (500 ml), 40% aqueous formaldehyde (375 ml), and 2 *N* aqueous sodium hydroxide (5 ml) were mixed and stirred at 65°. The temperature rose gradually to 80° and was maintained so, with gentle refluxing, for 2–3 hr. A further quantity (5 ml) of alkali was added and the mixture was stirred at room temperature overnight. Acetic acid (10 ml of 2 *N*) was added, the liquid was distilled until the distillation temperature reached 105°, and the residue was distilled fractionally *in vacuo*. A fraction, bp 86–94° (25–35 mm) (127 g), consisting of 4-hydroxy-3-methyl-2-butanone, was collected. It showed a single peak on glc: ir (film) 3425 (OH) and 1709 cm^{-1} (C=O); nmr δ 1.09 (d, *J* = 7 Hz, 3 H, $CHCH_3$), 2.19 (s, 3 H, $COCH_3$), 2.80 (m, 1 H, CH), 3.34 (s, 1 H, OH), and 3.69 ppm (d, *J* = 7 Hz, 2 H, CH_2OH). The 2,4-dinitrophenylhydrazone, prepared under mild conditions in diglyme,[7] had mp 108–109° (lit.[7] mp 107–109°); under strongly acidic conditions the derivative of isopropenyl methyl ketone was formed[7] (see below). The *p*-nitrobenzoate separated from light petroleum (bp 60–90°) in very pale yellow plates, mp 54° (lit.[5] mp 54°).

Isopropenyl Methyl Ketone (3-Methyl-3-buten-2-one[6] 1). The foregoing keto alcohol (107 g, 1.05 mol), anhydrous oxalic acid (2.0 g), and a few crystals of hydroquinone were placed in a distillation flask and distilled slowly until the vapor temperature reached 115°. The heterogeneous distillate was separated, and the upper layer was dried with anhydrous potassium carbonate. The liquid was filtered and distilled, bp 42–45° (85–90 mm), to yield isopropenyl methyl ketone (42 g, 41%): ir (film) 1678 (C=O), 1629 (C=C), and 935 cm^{-1} (=CH_2); nmr δ 1.83 (s, 3 H, =CCH_3), 2.28 (s, 3 H, $COCH_3$), and 5.79 ppm (d, *J* = 10 Hz, 2 H, =CH_2); uv λ_{max} (EtOH) 220 nm (ε 9175). The product showed a single peak on glc. The 2,4-dinitrophenylhydrazone separated from 95% ethanol as red needles, mp 192–193° (lit. mp 190,[9] 192.7–193.7° [7]), uv λ_{max} (EtOH) 372 nm (ε 21,800).

Hydration of Isopropenyl Methyl Ketone. A. At 100°. Isopropenyl methyl ketone (12.0 g) and 2 *N* sulfuric acid (240 ml) were heated under reflux at 100° (steam bath) for 3 hr. After being cooled the solution was saturated with anhydrous potassium carbonate and subjected to continuous ether extraction overnight. The extract was dried ($MgSO_4$) and concentrated by flask evaporation. The residue distilled at 92–95° (24 mm) (1.0 g), leaving a large residue of polymeric material. The ir and nmr spectra of the volatile product were identical with those of authentic 4-hydroxy-3-methyl-2-butanone (*vide supra*). Glc of the product showed one major peak (73%) corresponding in retention time with that of 4-hydroxy-3-methyl-2-butanone. A minor peak corresponded to unchanged isopropenyl methyl ketone (16%); a third peak (11%) was unidentified. None of the peaks corresponded in retention time with authentic 3-hydroxy-3-methyl-2-butanone. The 2,4-dinitrophenylhydrazone of the major product, prepared in diglyme under mild conditions,[7] had mp 108–109°, alone or mixed with an authentic sample (*vide supra*).

B. At 50°. Isopropenyl methyl ketone (7.5 g) and 2 *N* sulfuric acid (135 ml) were heated under reflux at 50° (internal temperature) for 7 hr. No polymeric material seemed to be formed. The mixture was cooled, saturated with potassium carbonate, and subjected to continuous ether extraction for 22 hr. The extract was dried (K_2CO_3), concentrated, and distilled, bp 90–95° (24 mm) (2.5 g), ir (film) 3425 (OH) and 1709 cm^{-1} (C=O). Glc of the product showed a major peak (73%) corresponding in retention time to authentic 4-hydroxy-3-methyl-2-butanone, and a minor peak (27%) corresponding to unchanged isopropenyl methyl ketone. Both retention times were quite different from that of authentic 3-hydroxy-3-methyl-2-butanone.

3-Hydroxy-3-methyl-2-butanone (2). The commercial product (Aldrich Chemical Co.) was purified by distillation, bp 140°, nmr δ 1.40 [s, 6 H, $C(CH_3)_2$], 2.25 (s, 3 H, $COCH_3$), and 3.95 ppm (s, 1 H, OH); it showed a single peak on glc. The 2,4-dinitrophenylhydrazone, prepared in dilute hydrochloric acid, separated from ethyl acetate as orange prisms, mp 144–145° (lit.[8] mp 138–139°), λ_{max} (EtOH) 359 nm (ε 23,300).

Anal. Calcd for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.85. Found: C, 46.81; H, 5.00; N, 19.85.

The *p*-nitrobenzoate was prepared by heating the alcohol and *p*-nitrobenzoyl chloride (1.05 mol) in pyridine on the steam bath for 2 hr, and then cooling and adding ether and a slight excess of dilute HCl. The ether layer was separated, washed with water and sodium bicarbonate, dried, and evaporated. The residual crystalline ester separated from light petroleum (bp 60–90°) in very pale yellow plates, mp 123–123.5°.

Anal. Calcd for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.57. Found: C, 57.33; H, 5.23; N, 5.54.

Registry No.—1, 814-78-8; **1** 2,4-DNP, 5077-59-8; **2,** 115-22-0; **2** 2,4-DNP, 52123-60-1; **2** *p*-nitrobenzoate, 52123-61-2; **3,** 3393-64-4; formaldehyde, 50-00-0; ethyl methyl ketone, 78-93-3; *p*-nitrobenzoyl chloride, 122-04-3.

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