cm^{-1}) was linear. The isomer composition of the above mixture was easily determined from this plot.

Treatment of *threo* VIII with 1.5 Equiv of *n*-Butyllithium.—To a magnetically stirred suspension of 4.15 g (0.0172 mole) of *threo* VIII in 50 ml of dry ether was added 16.3 ml (0.027 mole) of 1.6 *M* *n*-butyllithium[15] in hexane and the resulting suspension was heated to reflux. After 30 min, the mixture was inversely neutralized by addition to 3 ml of glacial acetic acid in ether. The mixture was shaken with two 50-ml portions of cold 10% sodium bicarbonate solution. The ether–water-insoluble material was filtered off and dried to give 2.48 g (60%) of a product shown by tlc to be a mixture of diastereomers of VIII. Vpc analysis of the ether layer indicated the presence of 0.005 mole (30%) of benzaldehyde.

Registry No.—VIII (*erythro*), 13144-04-2; VIII (*threo*), 13143-85-6; XII, 13143-86-7; XIII, 13144-05-3; XVa (*erythro*), 13143-87-8; XVa (*threo*), 13143-88-9; XVb (*erythro*), 13143-89-0; XVb (*threo*), 13143-90-3.

Notes

Alkylation of Acetylacetone with Isopropyl Alcohol by Means of Boron Fluoride[1]

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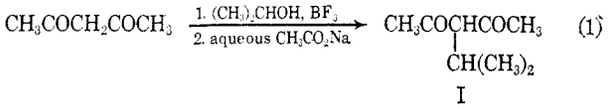
It has previously been shown that ethyl acetoacetate can be alkylated with isopropyl and *t*-butyl alcohols by means of boron fluoride to form the corresponding 3-alkyl derivatives in yields of 65 and 12%, respectively.[2]

It has now been found that acetylacetone can be alkylated similarly with isopropyl alcohol to give 3-isopropylacetylacetone (I) in 58% yield (eq 1). The

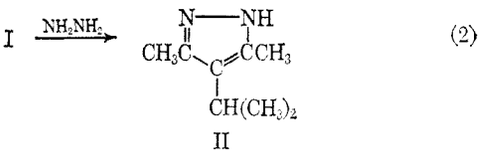


(1)

I

product was identified as I by essential agreement of its boiling point with the reported value, by identity of its vpc retention time with an authentic sample, and by its nmr spectrum. This spectrum exhibited a doublet at 0.90 ppm (assigned to the methyl hydrogens of the isopropyl group), a singlet at 2.14 ppm (assigned to the methyl hydrogens of the acetylacetone moiety), a multiplet centered at 2.41 ppm (assigned to the tertiary hydrogen on the isopropyl group), and a doublet at 3.53 ppm (assigned to the tertiary hydrogen on the acetylacetone moiety). It is not surprising that an enol signal was not observed since the nmr spectrum was determined from 0 to 8.3 ppm. Enol hydrogens resonate from 14 to 15 ppm.[3]

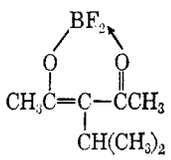
Also, I underwent cleavage with sodium hydroxide to form methyl isobutyl ketone and cyclization with hydrazine to give pyrazole II (eq 2). The nmr spectrum of II showed a doublet at 1.21 ppm (assigned to the methyl groups of the isopropyl moiety), a singlet at 2.20 ppm (assigned to the methyl groups of the pyrazole ring), and a multiplet centered at 2.70 ppm (assigned to the hydrogen of the pyrazole ring, the tertiary hydrogen of the isopropyl moiety, or possibly both).



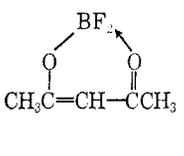
(2)

II

The isopropylation of acetylacetone evidently involved formation of the boron difluoride complex III, from which I was obtained on treatment with hot sodium acetate solution (see eq 1). Thus, III was isolated from the reaction mixture and subsequently converted to I (see Experimental Section). A possible course for the formation of boron difluoride complex III would involve initial conversion of the acetylacetone to its boron difluoride complex IV,[4] which undergoes isopropylation; however, a blank experiment with IV showed that complex III did not arise appreciably in this manner. The mechanism of formation of the boron difluoride complex III is suggested to involve a carbon–carbon condensation between enol-type intermediate VI and the isopropyl carbonium ion, followed by loss, in two steps, of hydrogen fluoride (Scheme I). As indicated in Scheme I, ionizations of boron trifluoride coordination complexes V and VII are analogous. Since the enol-type intermediate VIII loses a fluoride ion to afford difluoride complex III, enol-type intermediate VI might be expected to do likewise to afford the boron difluoride complex of acetylacetone (IV). The latter reaction may have occurred to some extent but, under the conditions employed, VI evidently underwent preferential isopropylation followed by loss of the elements of hydrogen fluoride (see Scheme I). Incidentally, enol-type intermediate VI must lose a



III



IV

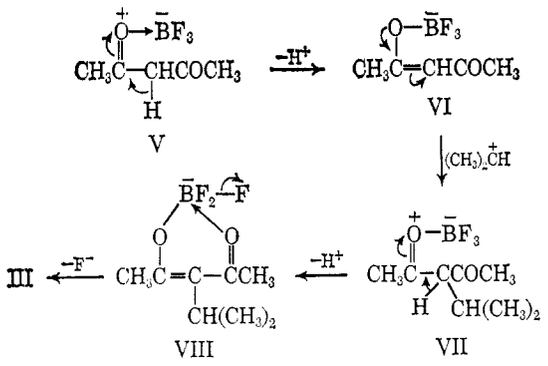
(1) Supported by the National Science Foundation.

(2) J. T. Adams, B. Abramovitch, and C. R. Hauser, *J. Am. Chem. Soc.*, **65**, 552 (1943); J. T. Adams, R. Levine, and C. R. Hauser, *Org. Syn.*, **27**, 35 (1947).

(3) See J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 91.

(4) See G. T. Morgan and R. B. Tunstall, *J. Chem. Soc.*, **125**, 1963 (1924).

SCHEME I



fluoride ion in the presence of acetic anhydride to form difluoride complex IV, since IV was prepared in this manner in connection with the blank experiment mentioned above (see Experimental Section).

The present method of preparation of 3-isopropylacetylacetone (I) is superior to that involving acetylation of methyl isobutyl ketone by boron fluoride (which afforded mixtures)[5] and to the reaction of the sodium salt of acetylacetone with isopropyl iodide at 180° under pressure.[6] Although *t*-butylation of ethyl acetoacetate has been realized in low yield by this boron fluoride method,[2] that of acetylacetone afforded unsatisfactory results. Thus, the *t*-butyl derivative of this β-diketone was apparently obtained in about 15% yield in two experiments, but none was isolated in two other runs. Possibly the loss of fluoride ion from enol-type intermediate VI to form difluoride complex IV competed favorably with the condensation of VI with the *t*-butyl carbonium ion, which might be expected to be less reactive than the isopropyl carbonium ion.

Experimental Section[7]

3-Isopropylacetylacetone (I).—In a 500-ml flask equipped with a thermometer, gas inlet and outlet tubes, a drying tube, and a stirrer were placed 30.0 g (0.50 mole) of acetylacetone and 30.0 g (0.50 mole) of isopropyl alcohol. The flask was kept in an ice–alcohol bath while boron fluoride was passed into the flask. The rate of addition of boron fluoride was so regulated that the temperature of the reaction mixture was generally 0–10° and did not exceed 25°. After the mixture was saturated with boron fluoride, as evidenced by the presence of copious white fumes at the exit tube, the flask was stored overnight in a refrigerator. The resulting mixture was refluxed with 200 ml of 4 *M* sodium acetate solution for 1 hr. After cooling in an ice bath, the organic and aqueous layers were separated. The aqueous layer was extracted three times with ether and the extracts were combined with the organic layer. The ethereal solution was dried over Drierite. After filtering, the solution was condensed on a rotary evaporator. The residue was distilled to give 40.5 g (58%) of 2-isopropylacetylacetone (I), bp 79° (19 mm) [lit.[8] bp 80–84° (20 mm)], n^{29}D 1.4250.

In another experiment on the same scale, the reaction mixture was stored overnight in a refrigerator and then suction filtered (without treating it with sodium acetate). The solid residue was washed with water, dried in a desiccator over Drierite, and finally recrystallized from chloroform–hexane to give 40 g (42%) of the boron difluoride complex III. The nmr spectrum of complex III showed a doublet at 1.25 ppm (assigned to the methyl groups of the isopropyl moiety), a singlet at 2.38 ppm (assigned to the methyl groups on the acetylacetone moiety), and a multiplet centered at 2.92 ppm (assigned to the tertiary hydrogen of the isopropyl group). The integrated peak areas agreed with the theoretical values. **Decomposition** of complex III by means of hot aqueous sodium acetate gave 3-isopropylacetylacetone (I) in 79% yield, bp 81° (20 mm). **Cleavage** of a 7.1-g (0.05 mole) sample of the free β-diketone I with 2.2 g (0.055 mole) of sodium hydroxide in 40 ml of water (refluxed 1.5 hr) afforded 2.7 g (54%) of methyl isobutyl ketone, bp 115–118° (lit.[9] bp 119°). The vpc retention time of the methyl isobutyl ketone was identical with that of an authentic sample.

Blank Experiment with Boron Difluoride Complex IV.—This complex was prepared by saturating a solution of 20 g (0.20 mole) of acetylacetone in 61.2 g (0.6 mole) of acetic anhydride with boron fluoride at 0–10° and refluxing the reaction mixture on the steam bath for 3 hr. After the mixture was stored overnight in a refrigerator, the precipitate was collected on a funnel and recrystallized from aqueous methanol to give 6 g (20%) of complex IV, mp 43–44° (lit.[4] mp 43°). A suspension of 7.1 g (0.048 mole) of complex IV in 50 ml of isopropyl alcohol was saturated with boron fluoride and the reaction mixture refluxed with aqueous sodium acetate essentially as described above for the preparation of isopropylacetylacetone (I). Vpc analysis of the crude product showed that it consisted largely of recovered acetylacetone and only a trace of the isopropyl derivative I.

3,5-Dimethyl-4-isopropylpyrazole (II).—Into a flask equipped with a dropping funnel and condenser was placed 14.2 g (0.1 mole) of 3-isopropylacetylacetone (I) in 40 ml of absolute ethanol. The flask was cooled in an ice bath while 5.5 g of 64% hydrazine (0.11 mole) in 10 ml of ethanol was added; the solution was stirred with a magnetic stirring bar during the addition. The ice bath was removed and the solution was refluxed for 18 hr. Solvent was then removed on a rotary evaporator and the resulting oil was distilled *in vacuo* to give 7.8 g (57%) of 3,5-dimethyl-4-isopropylpyrazole (II), bp, 142–143° (15 mm).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.50; H, 10.23; N, 20.27. Found: C, 69.11; H, 10.14; N, 20.39.

Registry No.—I, 1540-38-1; II, 13084-76-9; acetylacetone, 123-54-6; isopropyl alcohol, 67-63-0; boron fluoride, 7637-07-2.

(5) C. R. Hauser and J. T. Adams, *J. Am. Chem. Soc.*, **66**, 345 (1944).

(6) G. T. Morgan and R. W. Thomason, *J. Chem. Soc.*, **125**, 754 (1924).

(7) Gas chromatograms were obtained on F & M Model 500 and 700 gas chromatographs equipped with 6 ft × 1/8 in. Se-30 columns. The nmr spectra were obtained on a Varian A-60 high-resolution spectrometer. Microanalyses were performed by Jansses Pharmaceutica, Beerse, Belgium. Reagents were obtained from commercial sources and used without purification. Boron fluoride was passed through concentrated sulfuric acid before use.

(8) C. R. Hauser, F. C. Frostick, and E. H. Man, *J. Am. Chem. Soc.*, **74**, 3231 (1952).

(9) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., p 316.

Naphthyridine Chemistry. VII. Syntheses and Spectral Data on Some Benzo[*f*][1,7]naphthyridines

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Several publications[1-4] describe the cyclization of 3-aminoquinoline under the conditions of the Skraup, Conrad–Limpach, and ethoxymethylenemalonic ester (EMME) condensations. These reactions could potentially afford derivatives of either the linear benzo-1,5-naphthyridines (pyrido[3,2-*b*]quinolines) **1** or the angular benzo-1,7-naphthyridines (pyrido[2,3-*c*]quino-

(1) M. Shimizu, *J. Pharm. Soc.* (Japan), **64**, 489 (1944).

(2) C. Hauser and G. Reynolds, *J. Org. Chem.*, **15**, 1224 (1950).

(3) N. Buu-Hoi, R. Royer, and M. Hubert-Hubart, *J. Chem. Soc.*, 2048 (1956).

(4) C. F. H. Allen, "The Chemistry of Heterocyclic Compounds," Vol. 12, Interscience Publishers, Inc., New York, N. Y., 1958, pp 98–100.