DL-desmethycotinine and nornicotine.[1] Previous syntheses have been by the condensation of ethyl nicotinate and diethyl succinate[1] in the presence of sodamide[2] or by the condensation of ethyl bromoacetate with ethyl nicotinoyl acetate.[3]

The present method involving the condensation of diethyl sodiomalonate with bromomethyl ketone, reduces the possibility of concurrently formed condensation products to a minimum, and gives a good yield. The intermediate bromomethyl pyridyl ketone should also be a useful intermediate for synthesis of keto alcohols, esters, substituted malonic esters, keto aldehydes, thiazoles, and similar compounds.

EXPERIMENTAL

Bromomethyl pyridyl ketone. A solution of 6 g. of 3-pyridyl methyl ketone in 20 ml. of acetic acid containing 32% hydrobromic acid was cooled and a solution of 16 g. of pyridine hydrobromide perbromide[4] in 200 ml. of glacial acetic acid was added. Warming slightly and shaking intermittently brought about decolorization and the precipitation of the bromoketone hydrobromide.

The contents of the flask were cooled and 400 ml. of ether were added. After standing at 4° overnight, the precipitate was filtered off, washed well with ether, vacuum dried, and placed in an icebox in a closed container. Under these conditions the hydrobromide was stable and was used in the next step without further purification. A small sample was dissolved in hot acetic acid and precipitated with ether several times to procure a pure sample for analysis.

Anal. Calcd. for $C_7H_7NOBr_2$: Br, 56.94. Found: Br, 56.98, 57.00. The yield of crude material was nearly quantitative.

4-(3-Pyridyl)-4-ketobutyric acid. To a solution of 0.2 mole of diethyl sodiomalonate in an excess of malonic ester as a solvent was gradually added 0.1 mole bromomethyl-3-pyridyl ketone, stirring continuously. If, after part of the ketone has been added, the reaction remains sluggish, about 20 ml. of ethanol may be added. Care was taken to prevent a rise in temperature.

After about 12 hr. stirring, while in an ice bath, the temperature was permitted to rise to about 25° and stirring continued for another 12 hr. The salt formed was removed by filtration and the filtrate made acid with hydrochloric acid and refluxed to hydrolyze the ester. After 16 hr. the solution was cooled, extracted with ether once, and evaporated to near dryness in a rotating film evaporator. The solution was brought to a *p*H of 5.7 and allowed to crystallize at 4°. The yield averaged about 60% of crude material based on the bromoketone used.

Anal. Calcd. for $C_9H_9NO_3$: C, 60.33; H, 5.08. Found: C, 60.32, 60.55; H, 5.13, 5.20.

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The Structure of the Trimethylsilyl Derivative of Methyl Cyanoacetate

PETER L. DEBENNEVILLE, MARVIN J. HURWITZ, AND LAWRENCE J. EXNER

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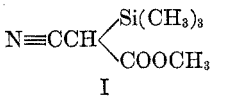
A recent note[1] corrects the structure which two of us had assigned to the trimethylsilyl derivative of ethyl acetoacetate. Since we presented the original paper,[2] we have had occasion ourselves to reexamine by spectral methods one other product which we had disclosed there. We had withheld publication pending a more complete clarification; however, none of us at present is working in this field, and it seems appropriate now to present what data we have.

Our original assignment was based primarily on the reaction of trimethylchlorosilane with methyl cyanoacetate.[3] The reported reactions of alkylating agents with cyanoacetic esters have, as far as we know, been observed to give only C-alkylation,[4] and our assignment of C-silylation to give structure I seemed to be a proper deduction. However, examination of the infrared spectrum of the carefully distilled compound showed strong absorption bands at 1623 cm.$^{-1}$ and at 2222 cm.$^{-1}$ The band at 2222 cm.$^{-1}$ is very likely displaced and strengthened absorption attributable to C≡N in a conjugated position.[5] The band at 1623 cm.$^{-1}$ is attributed to the absorption due to a carbon-carbon double bond in conjugation with the nitrile group. A relatively small absorption at 1761 cm.$^{-1}$, which progressively disappeared in successive fractions, is attributed to methyl cyanoacetate contaminant; otherwise no major carbonyl peak was apparent. Two strong bands at 850 cm.$^{-1}$ and 1250 cm.$^{-1}$ correspond to $Si(CH_3)_3$ absorption. There was no absorption in the reported range for normal Si—O stretching vibrations, but there were strong bands at 965 cm.$^{-1}$ and 1105 cm.$^{-1}$, either of which could be so assigned, in view of the evidently unusual structure.[6] A weak band at 3100 cm.$^{-1}$ is a



I

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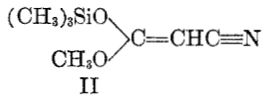
(6) Bellamy (footnote 5, p. 340) suggests 1090–1020 cm.$^{-1}$ for normal Si—O absorption. West (footnote 1) reports "near 1000 cm.$^{-1}$" for Si—O in a more closely related structure.

probable CH stretching vibration arising from the structural unit =CH—.

This evidence allows a probable assignment of the structure II to the compound. None of these



II

data corresponds to the original structural assignment. We therefore wish to withdraw the assignments that we had previously made.[2,3]

EXPERIMENTAL

Reaction of trimethylchlorosilane with methyl cyanoacetate. To a solution of methyl cyanoacetate (49.5 g., 0.5 mole) and triethylamine (202 g., 2.0 moles) in benzene (264 g.) at −5° was added dropwise a solution of trimethylchlorosilane (54.5 g., 0.5 mole) in benzene (264 g.) over a period of 1.5 hr. During the addition, the temperature was held at 5° with an ice bath. The reaction mixture was filtered, and the filtrate was stripped and carefully distilled through a well dried 6-inch Vigreux column. After removal of unreacted cyanoacetic ester, the product (42.5 g., 50%) distilled as a colorless liquid, very sensitive to moisture, at 75–76°/0.65 mm., n_D^{25} 1.4465.

Anal. Calcd. for $C_7H_{13}O_2NSi$: C, 49.1; H, 7.6; N, 8.2. Found: C, 49.1; H, 7.6; N, 8.2.

Infrared spectra were carried out on films, using a Perkin-Elmer Model 21 spectrophotometer.

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Cleavage of Tetrahydrofuran by Triphenylmethylmagnesium Bromide

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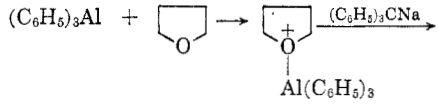
Most ethers, except strained cyclic ethers and allyl ethers, are not cleaved by Grignard reagents at temperatures below 175°.[1] For example, ethylene oxide reacts with Grignard reagents at room temperature,[2] trimethylene oxide is cleaved by Grignard reagents in refluxing benzene,[3] but anisole is cleaved by Grignard reagents at 200°. Cleavage of tetrahydrofuran, which is not highly strained, has not been generally found to occur, and tetrahydrofuran has been widely used as a solvent for the preparation and reaction of Grignard reagents.

In an attempt to prepare *t*-butylmagnesium bromide in tetrahydrofuran, Assarson[4] obtained a white precipitate which he assumed to be a product of the cleavage of tetrahydrofuran by the Grignard reagent, and was unable to find any gas evolved upon hydrolysis of the reaction mixture. However, in a reinvestigation of this reaction, Normant[5] was able to prepare *t*-butylmagnesium bromide in normal fashion in tetrahydrofuran, and obtained the normal addition product from further reaction with acetaldehyde. He proposed that the white precipitate was analogous to the precipitates obtained with dioxane.

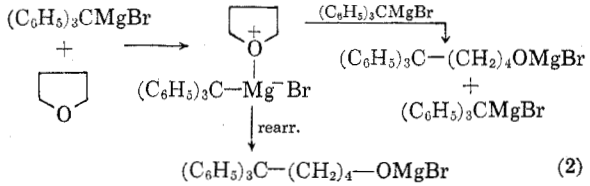
In a study of organometallic complexes, Wittig and co-workers[6] found that in the presence of triphenylaluminum and triphenylboron, triphenylmethylsodium reacts with tetrahydrofuran at room temperature to produce 5,5,5-triphenylpentanol-1 in good yield. Triphenylmethylsodium alone, however, was ineffective as a cleaving agent. These workers also found that 9-fluorenyllithium and 9-phenyl-9-fluorenyllithium also cleave tetrahydrofuran in good yield in the presence of triphenylaluminum.

It seems reasonable that triphenylaluminum forms an etherate complex with tetrahydrofuran, and the complex then undergoes attack by triphenylmethylsodium to lead eventually to the product obtained. The decreased complexing ability of sodium accounts for the fact that no cleavage was observed in the absence of triphenylaluminum.



$$(C_6H_5)_3C-(CH_2)_4-ONa + (C_6H_5)_3Al \quad (1)$$

We have found that triphenylmethylmagnesium bromide also cleaves tetrahydrofuran to produce 5,5,5-triphenylpentanol-1 in excellent yield. In this case, the Grignard reagent complexes strongly with the ether, and the complex can then undergo either further attack by another molecule of Grignard reagent, or intramolecular rearrangement to form the product:



$$(C_6H_5)_3C-(CH_2)_4-OMgBr \quad (2)$$

Triphenylmethylmagnesium bromide is ionized in solution to a sufficient extent to impart the dark red color of the triphenylmethylcarbanion[6] to the solution. Since most Grignard reagents are not highly ionized in solution and do not cleave tetrahydrofuran, it is not unlikely that the cleavage occurs by way of the carbanion.

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(2) For example, see R. C. Huston and A. H. Agett, *J. Org. Chem.*, **6**, 123 (1941).

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