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2-Methoxyallyl Bromide. A Superior Acetonyl Alkylating Agent

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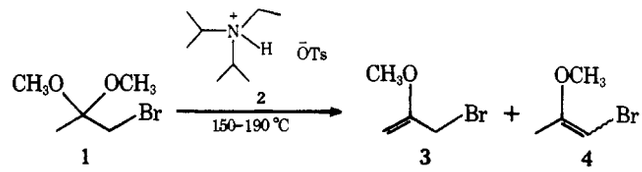
Heating 1-bromo-2,2-dimethoxypropane (1) in the presence of a catalytic amount of diisopropylethylammonium *p*-toluenesulfonate (2) gives 3-bromo-2-methoxy-1-propene (3) in greatly improved yield. Bromide 3 is a good alkylating agent monoalkylating acids, nitriles, esters, ketones, dialkylamides, enamines, and imines in yields of 44–96%. Alkylation of the lithium salt of imines with 3 followed by hydrolysis leads to α-acetonyl ketones which can be cyclized to 3,4-disubstituted cyclopentenones.

In our attempts to extend the Robinson annelation[1] to the formation of cyclopentenones via a three-carbon annelating agent, we desired an effective method of adding an acetonyl side chain to the α carbon of ketones or their equivalents. Several possible reagents for addition of this side chain have been described previously; however, each has problems in its use. The direct alkylation with haloacetones is useful only with the most acidic carbons due to the predominance of side reactions.[2,3] Alkylations with 2,3-dichloro-1-propene have been successful, but difficulties occur in that the vigorous conditions necessary for the unmasking of the vinyl chloride usually lead to the isolation of furans.[4] Lansbury has developed a nongeneral method of electrophilic cyclization to cyclopent*an*ones from these alkylated intermediates, requiring solvolytic conditions.[5] Alkylations with propargyl bromide are troubled by allene formation.[6] Better results have been obtained with the use of the protected 3-bromo-1-trimethylsilyl-1-propyne,[6] but, again, rather stringent conditions are required for conversion of the silylated alkyne to the acetonyl group. The use of methallyl halides as alkylating agents has also been described, but conditions for the subsequent conversion to the acetonyl side chain, ozonolysis or treatment with osmium tetroxide/periodate, are undesirable in many cases.[7] Yoshikoshi and co-workers have recently described the successful addition of an acetonyl side chain synthon to trimethylsilyl enol ethers via a $SnCl_4$-catalyzed Michael addition to 2-nitropropene.[8] Jung has reported the use of 2-trimethylsilyl-3-iodo-1-propene as an acetonyl synthon but unmasking of the ketone requires epoxidation followed by strong acid again limiting the applicability of the reagent.[9] Ketals such as 1-bromo-2,2-dimethoxypropane (1) are, of course, extremely poor alkylating agents.

Results and Discussion

Our solution to the problem of alkylating with a masked acetonyl side chain was found in the use of 2-methoxyallyl bromide (3). The 2-methoxyallyl halides have been synthesized by three groups.[10–12] The alkylation chemistry of 2-methoxyallyl bromide and the analogous 2-tetrahydropyranyloxyallyl bromide have been briefly studied by Bruce and Ban[10] and by Horning et al.[11] We felt that a further investigation of their alkylation chemistry was in order.

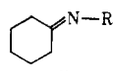
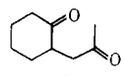
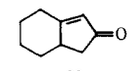
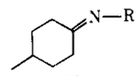
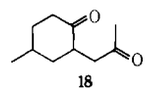
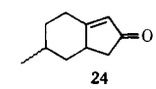
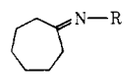
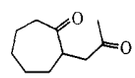
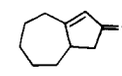
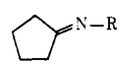
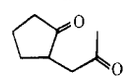
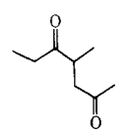
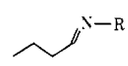
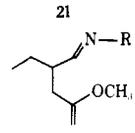
Access to the 2-methoxyallyl halides previously has been obtained by the reaction of *N*-halosuccinimides with 2-methoxypropene, or by the pyrolysis of 1-halo-2,2-dimethoxypropanes.[10,12] The former method resulted in a carbon tetrachloride solution of the 2-methoxyallyl halide contaminated with products resulting from the addition of succinimide to the enol ether double bond. The latter method resulted in only 10–20% conversion to the desired 2-methoxyallyl halide. We have found that pyrolytic cracking of 1-bromo-2,2-dimethoxypropane[12] (1) in the presence of diisopropylethylammonium tosylate (2) leads to a mixture, **5**, of 2-methoxyallyl bromide (3), 1-bromo-2-methoxy-1-propene (4), and starting material 1 (in an average ratio of 65:21:14).[13] Attempts to separate this mixture by distillation, even through spinning band columns, failed due to decomposition, but direct use of the product mixture in alkylation reactions was found to be satisfactory. The cracking is best accomplished by heating the 1-bromo-2,2-dimethoxypropane (1) and 0.016 equiv of the ammonium salt 2 to 150–190 °C while distilling off the methanol formed through a 12-in. fractionating column. After all of the methanol has been removed, quick distillation of the remaining liquid through a short-path distillation apparatus yields the product mixture, crude **3 ≡ 5**. Best results are obtained if the cracking time is kept to less than 90 min, i.e., retaining a small amount of starting material, as 2-methoxyallyl bromide (3) will polymerize slowly under these conditions. The product mixture, which contains less than 1% protic impurities, is stable for long periods of time if stored below 0 °C; samples stored at 25 °C darken after a month or so. Mass recoveries via this method are in the range of 85–90%. This procedure works well on a scale of 30 g but scaling up of the reaction size much beyond this point results in a decrease in the yield, probably due to polymerization of the 2-methoxyallyl bromide. This polymerization results from the increased time necessary for conversion to products if the size of the reaction is increased.



1 3 4

Several tertiary alkylammonium salts were investigated for use as cracking catalysts, including the *p*-toluenesulfonate salts of dicyclohexylethylamine, diisopropylethylamine, benzyldiisopropylamine, tributylamine, and quinaldine.[12] Other acidic catalysts included H_2SO_4, *p*-toluenesulfonic acid,

Table I. Imine Alkylations

Starting material (R = C_6H_{11})	Product	Yield, %	Cyclopentenone	% yield from alkn product
 11	 17	84	 23	68
 12	 18	81	 24	70
 13	 19	75	 25	74
 14	 20	43	*a*	
 15	 21	65		
 16	 22	76 *b*		

a Cyclization resulted in a mixture of several products. *b* Hydrolysis in oxalic acid resulted in the formation of tars.

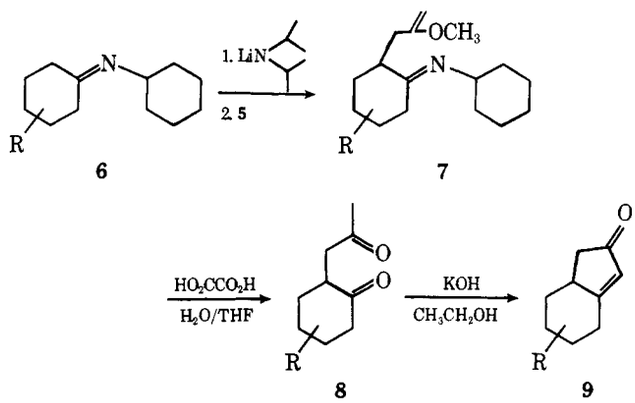
KSO_4H, and Rexyn 101. Of all these tested, diisopropylethylammonium *p*-toluenesulfonate (**2**) was found to be vastly superior. Use of the other salts listed above as catalysts resulted in less favorable ratios of 2-methoxyallyl bromide to 1-bromo-2-methoxypropene and/or a lower total conversion of the starting ketal **1** to product.

A similar but alternate method of cracking bromo ketal **1** was also investigated. A cracking column was prepared from about 12 in. of 15-mm glass tubing. This column was packed with 3-mm glass beads coated with the cracking catalyst desired. The column was heated to 260 °C with a flow of argon through it, and the bromo ketal **1** was dropwise added to the top of the column. The effluent gases were collected in a trap cooled to −78 °C. Subsequent distillation of the mixture, first to remove the methanol and then to purify the product, resulted in a product of the same average composition as that obtained previously. However, mass recoveries were in the 40–50% range and the catalyst decomposed on the column beads after two or three runs, rendering the method less practical than the simple cracking.

We also investigated the preparation of 2-methoxyallyl chloride[12] and iodide[12] via the same procedure used to prepare the bromide. Attempted cracking of 1-chloro-2,2-dimethoxypropane[12] resulted in a very low conversion to products, while the attempted cracking of 1-iodo-2,2-dimethoxypropane[12] resulted in explosive decomposition. Preparation of 2-methoxyallyl iodide (**10**) by reaction of 2-methoxyallyl bromide (**3**) with sodium iodide in methyl formate resulted in a solution of 2-methoxyallyl iodide (**10**) that, when concentrated in vacuo at 25 °C, underwent a vigorous exothermic decomposition liberating iodine. Subsequently, 2-methoxyallyl iodide (**10**) was prepared in situ from bromide **3** by addition of 1 equiv of a solution of anhydrous lithium iodide in THF. For direct preparation, therefore, the bromide **3** is the preferred reagent.

Having acquired an easy access to 2-methoxyallyl bromide, uncontaminated by protic impurities, its alkylation chemistry was investigated. Alkylation of metalloenamines, derived from imines and lithium diisopropylamide,[14] resulted in excellent yields (85–98%) of the monomethoxyallylated imines **7**, which could be hydrolyzed in good to excellent yields to 2-acetonyl ketones[15] **8**. The 2-acetonyl ketones **8** could then easily be cyclized to the corresponding cyclopentenones **9** with potassium hydroxide in refluxing ethanol;[16] of course, the resulting 1,4-diketones can be made to undergo any of their other characteristic reactions. Scheme I represents the reactions studied.

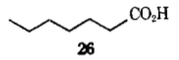
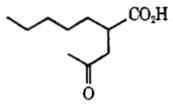
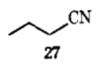
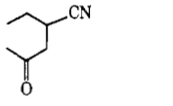
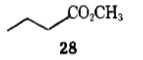
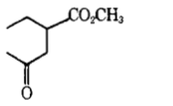
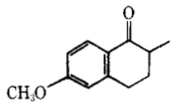
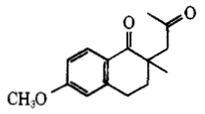
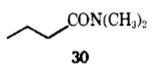
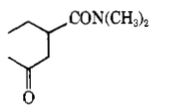
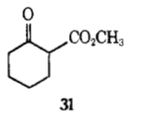
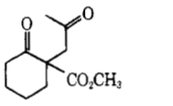
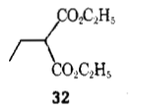
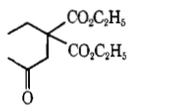
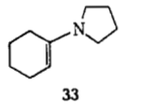
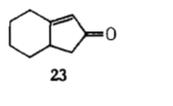
Scheme I



The procedure represents a general and convenient access to substituted cyclopentenones in about 60% overall yield from readily available starting materials. Alkylation of other activated methylene compounds with 2-methoxyallyl bromide (**3**) also proved successful. Acids, esters, amides, nitriles, and β-keto esters will readily monoalkylate with this reagent at −78 °C giving good to excellent yields of methoxyallylated product. Hydrolysis of the enol ether obtained was easily accomplished in dilute aqueous acid.

All alkylated compounds had satisfactory spectral data and were determined to be greater than 95% pure on the basis of

Table II. Other Alkylations

Starting material	Product	Yield, %
 26	 34	85
 27	 35	96
 28	 36	74
 29	 37	81
 30	 38	44
 31	 39	80
 32	 40	94
 33	 23	45

GC analysis. Alkylation results are summarized in Tables I and II.

The mildness of the conditions required to unmask the acetonyl group, water at pH 3 if desired, compared to the severe conditions required for previously available acetonyl synthons, and the effectiveness of the monoalkylation of a variety of functional groups should prove 2-methoxyallyl bromide (3) to be the reagent of choice for adding an acetonyl group to an active methylene compound. Thus, a highly efficient method for introducing the acetonyl side chain, useful for ultimate transformation to substituted cyclopentenones where applicable, has been realized via the use of 2-methoxyallyl bromide.

Experimental Section

All boiling points given are uncorrected. ^{1}H NMR spectra were obtained on a Varian EM-360 (60 MHz) spectrometer using tetramethylsilane as an internal standard. Infrared spectra were obtained from a Perkin-Elmer 467 grating infrared spectrometer. Mass spectra were obtained from a Varian-MAT CH-7 mass spectrometer. All starting materials were distilled before use. Tetrahydrofuran was dried over potassium benzophenone dianion and was freshly distilled under argon prior to use.

Diisopropylethylammonium *p*-Toluenesulfonate (2). To 3.80 g (20 mmol) of *p*-toluenesulfonic acid monohydrate in 10 mL of anhydrous methanol was added 2.80 g (22 mmol) of diisopropylethylamine. The resulting solution was concentrated in vacuo, yielding an oil which on standing crystallized. The solid was crushed and the last traces of solvent were removed by drying at 0.05 Torr: yield 6.00 g (100%); mp 87–88.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.37 (m, 15 H), 2.35 (s, 3 H), 2.8–3.3 (m, 2 H), 3.3–3.9 (m, 2 H), 7.17 (d, 2 H), 7.82 (d, 2 H), 9.18 (br s, 1 H).

1-Bromo-2,2-dimethoxypropane(1).[12] To 42 mL ($\leq$0.50 mol) of bromoacetone prepared according to the method of Levene[17] and containing 5–15% 1,1-dibromoacetone were added 60 mL (0.55 mol) of trimethyl orthoformate, 25 mL of CH_3OH, and 10 drops of H_2SO_4. After stirring for 2 h, all the bromoacetone had been converted to the ketal. The mixture was basified with 2 mL of triethylamine and concentrated in vacuo to remove most of the methyl formate. The resulting reaction mixture was added to an ice-cold solution of 20 g of sodium hydroxide in 200 mL of methanol, destroying the unketalized 1,1-dibromoacetone.

The resulting reaction mixture was partitioned between 300 mL of pentane and 200 mL of H_2O. The aqueous layer was extracted with 100 mL of pentane and the combined pentane layers were washed with 50 mL of water and dried over potassium carbonate. Concentration in vacuo and distillation gave 73 g (0.40 mol, $\geq$80%) of 1-bromo-2,2-dimethoxypropane (1): bp (80 Torr) 83–87 °C, (760 Torr) 156 °C; ^{1}H NMR (CCl_4) δ 1.36 (s, 3 H), 3.16 (s, 6 H), 3.26 (s, 2 H); IR (neat) 1219 (CH_2Br), 1110, 1077, 1049 cm^{-1} (C—O); mass spectrum (70 eV) 182 (M^+) (absent), 153 (43), 151 (44), 89 (100), 57 (69), 43 (83), 29 (34).

Cracking of Bromo Ketal 1. Preparation of 3-Bromo-2-methoxypropene (2-Methoxyallyl Bromide) (3 and 5). A mixture of 25 g of 1-bromo-2,2-dimethoxypropane (1) and 0.4 g of diisopropylethylammonium *p*-toluenesulfonate (2) was heated at 150–190 °C (bath temperature) while distilling off the methanol through a 12-in. Vigreaux fractionating column about 15 mm in diameter. The temperature of the heating bath was never allowed to exceed 200 °C, and the rate of methanol distillation was kept at a moderate rate (~1 drop/s) so as to be complete in less than 1.5 h. After removal of the methanol was complete, as shown by a rise of the head temperature to >130 °C, the distilling column was removed and the product mixture was rapidly distilled through a short-path distillation head, resulting in collection of 17.9 g (87% mass recovery) of the product mixture, **5**, i.e., crude **3**: bp (760 Torr) 134–137 °C, *d* 1.16; ^{1}H NMR 3-bromo-2-methoxy-1-propene (**3**) (CCl_4) δ 3.55 (s, 3 H), 3.79 (s, 2 H), 4.03 (d, 1 H, J = 2.6 Hz), 4.23 (d, 1 H, J = 2.6 Hz); 1-bromo-2-methoxy-1-propene (**4**) (CCl_4) δ 1.92 (br s, 3 H), 3.51 (s, 3 H), 5.11 (br s, 1 H). The mixture was found to contain ~65% 2-methoxyallyl bromide (**3**), ~21% 1-bromo-2-methoxypropene (**4**), and ~14% of the starting bromoketal (**1**) by gas chromatography at 150 °C on a 2 m × 6 mm ID column containing 15% OV17 on Chromosorb W AWDMCS: retention time 3.1 min, **4**; 3.6 min, **3**; 5.5 min, **1**. This mixture, **5**, was used as such in subsequent alkylations, and was stored at −20 °C when not in use.

Preparation of Imines. The procedure of Stork and Benaim was used to prepare the starting imines.[14] The following imines were prepared.

***N*-Cyclohexylidenecyclohexylamine[18] (11):** 95%; bp (10 Torr) 121–123.4 °C; ^{1}H NMR (CCl_4) δ 0.95–1.90 (m, 16 H), 19.5–2.40 (m, 4 H), 3.0–3.4 (m, 1 H); IR (neat) 1658 cm^{-1} (C=N); mass spectrum (70 eV) 179 (M^+) (31), 136 (49), 98 (100), 56 (37), 55 (85), 41 (50).

***N*-(4-Methylcyclohexylidene)cyclohexylamine[19] (12):** 83%; bp (7 Torr) 119–121 °C; ^{1}H NMR (CCl_4) δ 0.97 (d, 3 H), 1.2–3.0 (m, 19 H), 3.0–3.4 (m, 1 H); IR (neat) 1652 cm^{-1} (C=N); mass spectrum (70 eV) 193 (M^+) (20), 136 (43), 112 (48), 83 (38), 56 (67), 55 (78), 54 (35), 43 (100), 41 (50).

***N*-Cycloheptylidenecyclohexylamine[20] (13):** 70%; bp (0.05 Torr) 102–105 °C; ^{1}H NMR (CCl_4) δ 1.0–2.0 (m, 18 H), 2.1–2.8 (m, 4 H), 3.0–3.4 (m, 1 H); IR (neat) 1640 cm^{-1} (C=N); mass spectrum (70 eV) 193 (M^+) (19), 112 (65), 83 (50), 68 (35), 56 (54), 55 (100), 41 (71).

***N*-Cyclopentylidenecyclohexylamine[21] (14):** 83%; bp (0.05 Torr) 64–67 °C; ^{1}H NMR (CCl_4) δ 1.0–1.9 (m, 14 H), 1.95–2.4 (m, 4 H), 2.8–3.3 (m, 1 H); IR (neat) 1680 cm^{-1} (C=N); mass spectrum (70 eV) 165 (M^+) (28), 136 (45), 84 (100), 83 (34), 55 (66), 54 (41), 41 (41).

***N*-(3-Pentylidene)cyclohexylamine[20] (15):** 81%; bp (0.02 Torr) 60–63 °C; ^{1}H NMR (CCl_4) δ 1.0 (t, 6 H), 1.2–1.9 (m, 10 H), 2.2 (q, 4 H), 3.0–3.5 (m, 1 H); IR (neat) 1660 cm^{-1} (C=N); mass spectrum (70 eV) 167 (M^+) (24), 138 (42), 86 (35), 83 (85), 56 (100), 55 (63), 41 (35).

***N*-Butylidenecyclohexylamine[22] (16):** 78%; bp (80 Torr) 118–119 °C; ^{1}H NMR (CCl_4) = 0.8–1.1 (m, 3 H), 1.2–2.3 (m, 14 H), 2.7–3.2 (m, 1 H), 7.69 (d, 1 H); IR (neat) 1666 cm^{-1} (C=N); mass spectrum (70 eV) 153 (M^+) (2), 125 (70), 110 (100), 83 (30), 82 (34), 55 (69), 44 (64), 43 (33), 41 (48).

General Procedure for Alkylation of Imines. Alkylations were run using a variation of the procedure of Stork and Benaim.[14] To a solution of 1.3 mmol of lithium diisopropylamide (generated in situ from diisopropylamine and butyllithium) in 5 mL of anhydrous THF

at 0 °C containing two crystals of 1,10-phenanthroline as an indicator was added 1 mmol of the imine. The rust-colored solution was stirred at 0 °C for 0.5 h and then 0.3 mL (1.5 mmol) of **5** was added, followed by stirring an additional 15 min at 0 °C. The solution was slowly warmed to room temperature and stirred for 4–6 h. The solvent was removed in vacuo, and the residue was dissolved in 9 mL of THF. To this solution was added 1.5 mL of 1 M aqueous oxalic acid, and the solution was stirred at room temperature for 2 h. The solvent was again removed in vacuo and the residue was dissolved in ether and washed twice with water. The ether layer was separated, dried over $MgSO_4$, and filtered. The ether was removed in vacuo, leaving the crude alkylated product which was purified by bulb to bulb distillation. The following compounds were prepared from their respective imines via the above procedure.

2-Acetonylcyclohexanone[16] (17): 84%; bp (0.02 Torr) 105–107 °C; ^1H NMR (CCl_4) δ 2.1 (s, 3 H), 1.0–3.2 (m, 11 H); IR (neat) 1710 cm^{-1} (C=O); mass spectrum (70 eV) 154 (M^+) (21), 97 (38), 55 (40), 43 (100), 18 (35).

2-Acetonyl-4-methylcyclohexanone (18): 81%; bp (0.02 Torr) 109–111 °C; ^1H NMR (CCl_4) δ 1.0 (d, 3 H, trans), 1.31 (d, 3 H, cis), 2.09 (s, 3 H), 1.5–3.5 (m, 10 H); IR (neat) 1710 cm^{-1} (C=O); mass spectrum (70 eV) 168 (M^+) (12), 111 (36), 55 (41), 43 (100), 41 (28), 18 (57). Ratio c/t = 3/1.

2-Acetonylcycloheptanone[23] (19): 75%; bp (0.02 Torr) 116–119 °C; ^1H NMR (CCl_4) δ 0.8–3.3 (m, 13 H), 2.07 (s, 3H); IR (neat) 1710 cm^{-1} (C=O); mass spectrum (70 eV) 168 (M^+) (7), 111 (25), 98 (25), 55 (48), 43 (100).

2-Acetonylcyclopentanone[24] (20): 43%; bp (0.02 Torr) 108–111 °C; ^1H NMR (CCl_4) δ 2.07 (s, 3 H), 0.8–3.1 (m, 9 H); IR (neat) 1738 (C=O); 1719 cm^{-1} (C=O); mass spectrum (70 eV) 140 (M^+) (14), 97 (38), 83 (40), 43 (100).

4-Methyl-2,5-heptanedione (21): 65%; bp (0.02 Torr) 92–95 °C; ^1H NMR (CCl_4) δ 0.85–1.35 (m, 6 H), 2.06 (s, 3 H), 1.8–3.2 (M, 5 H); IR (neat) 1712 cm^{-1} (C=O); mass spectrum (70 eV) 142 (M^+) (2), 113 (42), 57 (78), 43 (100), 29 (38).

2-(2-Methoxy-2-propenyl)butylidenecyclohexylamine (22): 76%; bp (0.02 Torr) 116–119 °C; ^1H NMR (CCl_4) δ 0.89 (t, 3 H), 0.95–2.0 (m, 14 H), 2.0–2.6 (m, 2 H), 3.47 (s, 3 H), 3.78 (s, 2 H), 7.46 (d, 1 H); IR (neat) 1660 (C=N), 1625 cm^{-1} (C=C); mass spectrum (70 eV) 223 (M^+) (2), 208 (83), 192 (34), 126 (35), 110 (49), 83 (66), 55 (100), 43 (30), 41 (91), 29 (33).

Preparation of Cyclopentenones from 2-Acetonyl Ketones. The 2-acetonyl ketones were cyclized with KOH in refluxing ethanol by the procedure of Islam and Raphael.[16] The following compounds were obtained in this manner.

Bicyclo[4.3.0]non-6-en-8-one[16] (23): 68%; bp (0.05 Torr) 59–62 °C; ^1H NMR (CCl_4) δ 0.8–3.1 (m, 11 H), 5.73 (s, 1 H); IR (neat) 1705 (C–O), 1620 cm^{-1} (C=C); mass spectrum (70 eV) 136 (M^+) (100), 121 (31), 108 (58), 107 (39), 95 (48), 94 (25), 93 (35), 80 (27), 79 (64), 77 (28), 39 (42).

3-Methylbicyclo[4.3.0]non-6-en-8-one[25] (24): 70%; bp (0.025 Torr) 109–111 °C; ^1H NMR (CCl_4) δ 0.99 (m, 3 H), 0.8–3.0 (m, 10 H), 5.74 (s, 1 H); IR (neat) 1708 (C=O), 1623 cm^{-1} (C=C); mass spectrum (70 eV), 150 (M^+) (100), 135 (32), 122 (41), 108 (52), 107 (67), 95 (65), 94 (36), 93 (66), 91 (31), 82 (35), 80 (41), 79 (76), 77 (38), 55 (31), 41 (39), 39 (56).

Bicyclo[5.3.0]dec-7-en-9-one[23] (25): 75%; bp (0.025 Torr) 117–119 °C; ^1H NMR (CCl_4) δ 1.0–2.0 (m, 10 H), 2.3–3.0 (m, 3 H), 5.75 (s, 1 H); IR (neat) 1700 (C=O), 1608 cm^{-1} (C=C); mass spectrum (70 eV) 150 (M^+) (100), 122 (31), 108 (38), 107 (84), 95 (72), 94 (46), 93 (46), 82 (41), 79 (75), 77 (37), 41 (31), 38 (38).

Alkylation of Other Activated Methylene Compounds with 2-Methoxyallyl Bromide (3). The following compounds were alkylated via the published procedure: *n*-heptanoic acid[26] (**26**), methyl butyrate[27] (**28**), and *N,N*-dimethylbutyramide[28] (**30**). Other compounds were alkylated via the following general procedure.

To a solution of 1.3 mmol of lithium diisopropylamide (generated in situ from diisopropylamine and butyllithium) in 5 mL of anhydrous THF at −78 °C containing two crystals of 1,10-phenanthroline as an indicator was added 1 mmol of the active methylene compound. The rust-colored solution was stirred for about 45 min at −78 °C and then 0.3 mL (1.5 mmol) of **5** was added, followed by stirring for 30 min at −78 °C. The solution was slowly warmed to room temperature and stirred for 4–6 h. The reaction was then quenched with about 3 mL of water. The solvent was removed in vacuo and the residue was taken up in 15 mL of ether. This ether solution was washed twice with 0.1 N HCl and once with water. The ether layer was separated and dried over $MgSO_4$. Removal of the ether in vacuo left the crude 2-acetonyl compound which was purified by bulb-to-bulb distillation. The following compounds were obtained.

2-Acetonylheptanoic acid[29] (34): 85%; bp (0.02 Torr) 150–153 °C; ^1H NMR (CCl_4) δ 0.91 (m, 3 H), 1.0–1.8 (m, 8 H), 2.09 (s, 3 H), 2.35–2.95 (m, 3 H), 11.0 (s, 1 H); IR (neat) 1765 (C=O) 1710 (C=O), 2500–3600 cm^{-1} (COOH); mass spectrum (70 eV) 173 (M^+) (1), 129 (34), 111 (26), 73 (25), 55 (29), 43 (100).

2-Ethyl-4-oxopentanenitrile (35): 96%; bp (0.05 Torr) 85–87 °C; ^1H NMR (CCl_4) δ 1.08 (t, 3 H), 1.3–1.9 (m, 2 H), 2.13 (s, 3 H), 2.4–3.2 (m, 3 H); IR (neat) 2240 (C≡N), 1719 cm^{-1} (C=O); mass spectrum (70 eV) 125 (M^+) (1), 58 (30), 43 (100).

Methyl 2-ethyl-4-oxopentanoate (36): 74%; bp (0.1 Torr) 82–85 °C; ^1H NMR (CCl_4) δ 0.9 (t, 3 H), 1.2–1.8 (m, 2 H), 2.07 (s, 3 H), 2.0–2.8 (m, 3 H), 3.63 (s, 3 H); IR (neat) 1735 (C=O), 1720 cm^{-1} (C=O); mass spectrum (70 eV) 158 (M^+) (1), 101 (53), 87 (24), 55 (21), 43 (100).

2-Methyl-2-acetonyl-6-methoxy-1-tetralone (37): 81%; bp (0.05 Torr) 150 °C; ^1H NMR (CCl_4) δ 1.13 (s, 3 H), 2.05 (s, 3 H), 1.7–2.6 (m, 4 H), 2.7–3.1 (m, 2 H), 3.73 (s, 3 H), 6.4–6.9 (m, 2 H), 7.85 (d, 2 H); IR (neat) 1712 (C=O), 1669 (C=O), 1598 (C=C), 1253 cm^{-1} (OCH_3); mass spectrum (70 eV) 246 (M^+) (13), 188 (100), 148 (96), 120 (26).

***N,N*-Dimethyl-2-ethyl-4-oxopentanamide (38):** 44%; product decomposed upon attempted distillation; ^1H NMR (CCl_4) δ 0.87 (t, 3 H), 1.2–1.7 (m, 2 H), 2.07 (s, 3 H), 2.0–3.1 (m, 3 H), 2.87 (s, 3 H), 3.10 (s, 3 H); IR (neat) 1715 (C=O), 1640 cm^{-1} (C=O); mass spectrum (70 eV) 171 (M^+) (12), 128 (40), 127 (55), 119 (39), 117 (40), 114 (61), 100 (35), 99 (42), 72 (84), 58 (100), 43 (41).

Methyl 1-Acetonyl-2-oxocyclohexanecarboxylate (39): 80%; bp (0.05 Torr) 123–125 °C; ^1H NMR (CCl_4) δ 1.25–3.0 (m, 8 H), 2.10 (s, 3 H), 2.73 (s, 2 H), 3.71 (s, 3 H); IR (neat) 1735 (C=O), 1714 cm^{-1} (C=O); mass spectrum (70 eV) 212 (M^+) (1), 180 (45), 137 (47) 127 (37), 109 (43), 81 (69), 67 (33), 55 (40), 43 (100), 41 (44).

Alkylation of *N*-(1-Cyclohexenyl)pyrrolidine (33). To a solution of 2.00 g (13 mmol) of *N*-(1-cyclohexenyl)pyrrolidine[30] in 20 mL of dioxane was added 3 mL (15 mmol) of **5**. The red solution was stirred at reflux for 2 h. Hydrolysis and ring closure were accomplished by adding 5 mL of water, 2 g of acetic acid, and 1 g of sodium acetate. This was stirred at reflux overnight and then diluted with pentane. This pentane solution was washed with both dilute aqueous HCl and dilute aqueous NaOH, dried over $MgSO_4$, and filtered. The pentane and dioxane were removed and the product was purified by bulb-to-bulb distillation. The yield of bicyclo[4.3.0]non-6-en-8-one (**23**) was 0.80 g (45%) for this procedure.

Preparation of Diethyl (Acetonylethyl)malonate (40). This compound was prepared similarly to the procedure of Muchowski and co-workers.[11] A suspension of 11 mmol of sodium hydride in 20 mL of THF was heated to reflux and 1.87 mL (10 mmol) of diethyl ethylmalonate was added dropwise. After hydrogen evolution was complete, 12 mmol of **5** was added. After stirring for 3 h at reflux, the reaction mixture was poured into dilute HCl and extracted with ether. The ether layer was dried with $MgSO_4$ and filtered. All low-boiling material was removed in vacuo, leaving 2.99 g of crude product. Bulb-to-bulb distillation afforded 2.39 (94% yield) of pure diethyl (acetonylethyl)malonate (**40**): bp (11 Torr) 150 °C; ^1H NMR (CCl_4) δ 0.83 (t, 3 H), 1.26 (t, 6 H), 2.03 (q, 2 H), 2.13 (s, 3 H), 3.00 (s, 2 H), 4.16 (q, 4 H); IR (CCl_4) 1725 cm^{-1} (C=O); mass spectrum (70 eV) 254 (M^+) (absent), 187 (57), 141 (67), 127 (26), 125 (65), 101 (29), 55 (32), 43 (100), 29 (44).

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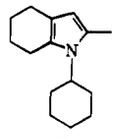

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Carbon-13 and Low-Temperature Proton Nuclear Magnetic Resonance Study of the Interaction of Acetylacetone with Diethylamine and Triethylamine[1a]

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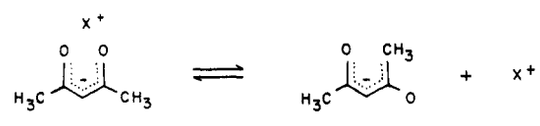
The ^1H NMR spectra of mixtures of acetylacetone with diethylamine and triethylamine have been examined at low temperature under conditions such that torsion about the partial double bonds in the acetylacetonate moiety is slow on the NMR time scale. Configurational assignments and distributions and NMR chemical shifts are used to define the nature of the interaction between the amine and acetylacetonate molecules in methanol and chloroform as solvents. The data suggest that, in methanol, mixtures of chelated ion pairs and solvent separated ions are found for both amines. Proton and carbon spectra indicate that in chloroform diethylamine gives rise to a chelated ion pair, while the diketone–triethylamine complex is best described as one in which the chelated enol form of acetylacetone is hydrogen bonded to triethylamine.

Reeves and Schneider have used proton nuclear magnetic resonance spectroscopy to study the interactions between acetylacetone (Hacac) with diethylamine and triethylamine.[2] Their study of spectra above room temperature was used to provide information about the rates of keto–enol tautomerism and proton exchange. We have shown that low-temperature ^1H NMR spectra of acetylacetonates[3-5] can be used to determine the configuration of the acetylacetonate moiety and draw conclusions about the degree and kind of association of the acac anion with alkali metal cations. For this reason, it seemed likely that examination of the low-temperature spectra of mixtures of Hacac and amines might provide further information about these interactions and could complement and extend the findings of Reeves and Schneider.

Results

The ^1H NMR spectrum of an equimolar mixture of acetylacetone (Hacac) and diethylamine in methanol-d_4 at −57 °C exhibits three singlets deriving from the acetyl methyl groups of the acac moiety. Two of these singlets at δ 1.89 and 2.27 are of equal intensity and must arise from species with the *E,Z* configuration, which have diastereotopic methyl groups. The signal at δ 1.85 arises from species with the *Z,Z* configuration in which the methyl groups are homotopic. Integration of the acetylmethyl signals indicated that the *Z,Z* configuration was present to the extent of 47% under these conditions. The use of triethylamine as base instead of diethylamine changed the situation only slightly. The proportion of acetylacetonate in the *Z,Z* form increased to ca. 60%.



When the solvent was changed to deuteriochloroform, both mixtures exhibited only single resonances for the acetyl methyl peaks at δ 1.92 at −57 °C. Unless the coalescence point for topomerization has been drastically lowered in this solvent, the observation of only a single resonance can be taken to mean that only the *Z,Z* form is present. The chemical shifts observed for the resonances both in the amine and acac moieties can provide further information about the states of association of these ammonium acetylacetonates. These data are given in Tables I and II. The ^{13}C NMR spectra of both mixtures in chloroform were also measured. The ^{13}C chemical shifts of the ethyl carbon atoms provide complementary information about protonation at nitrogen and are given together with the shifts in free amines and their benzoates in Table III.

Discussion

Reeves and Schneider concluded from their study that the keto–enol equilibrium of acetylacetone was markedly shifted