servations may be rationalized, if we assume reasonably that *cation-anion* bands follow the same pattern and that alkylation of the ammonium ion causes a shift to lower frequencies by increasing the cation mass and radius. We also realize that the effective radii of loosely solvated alkali cations are undoubtedly greater than their Pauling radii.[11]

The fact that Bu_4N^+ salts behave similarly to the alkali ones actually lends further support to the notion that the latter are ionic. For ion pairs there is no strict geometric requirement for binding the cations to particular regions of the anions, as is true in the transition metal chelates. Thus, the Bu_4N^+ cation might be oriented above the plane of a U-shaped β-ketonolate anion, while a smaller alkali cation might be accommodated better in the plane and between the oxygen atoms.

The pattern of methine shifts in Me_2SO is closely parallel (linear correlation coefficients = 0.966 (I), 0.985 (II)) to that of the far-infrared bands in THF, including the position of Bu_4N^+. The trend is reasonable, the greatest downfield shift being produced by Li^+ and the least by Cs^+.

Our conductance data also support the spectral picture of ion pairing and the effects of charge density and delocalization in cation and anion. Finally, our observations are consistent with a variety of other studies on related systems in which the presence of contact ion pairs has been inferred, from ultraviolet spectra,[3] infrared spectra,[12] NMR spectra,[13-15] conductance,[16] and kinetics.[16,17] House[18] and LeNoble[19] have provided extensive reviews of the ambident nucleophilicity of enolate anions. We will present our own observations on this question in subsequent articles.

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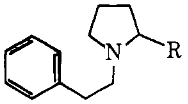
A High Yield Regiospecific Preparation of Iminium Salts

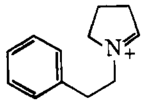
Sir:

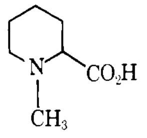
Iminium salts are highly versatile synthetic intermediates[1] since they present an extremely electrophilic carbon for nucleophilic attack. Their use, however, is often rendered unattractive because they are obtained in poor yield or as isomeric mixtures, or both. Currently, the most popular modes of preparing these salts involve (a) oxidation of a tertiary amine,[2] (b) condensation of a carbonyl component and a secondary amine,[3] and (c) addition to amides.[4] There are a number of specialized and limited methods[5] as well. These procedures sometimes produce adequate yields of iminium salts, but frequently suffer seriously from a lack of regiospecificity. We not report the development of a high yield, single-step, regiospecific method for preparing iminium salts from α-tertiary amino acids.

Our method is based on the frequently reported observation that acid chlorides of α-tertiary amino acids are unstable. These observations were first rationalized by Maksimov[6] who reported that activated acyl derivatives of α-tertiary amino acids were thermally decarbonylated, yielding in part a secondary amine and an aldehyde after decomposition with water. This instability, a drawback in utilization of the acyl derivatives, could become a virtue for the preparation of specific iminium salts if a convenient, high yielding procedure could be developed. Such a procedure is now at hand.

The iminium salts are obtained by briefly (3–5 min) heating the α-tertiary amino acids in phosphorus oxychloride. At this point, starting acid has been completely consumed, and a single product has been formed as demonstrated by thin layer chromatography. This organic product is iminium salt as shown in the infrared where the only absorption is between ~1670 and 1700 cm^{-1} and is due to the iminium ion. As an example, N-β-phenylethylproline hydrochloride (**1**, mp 186–189 °C)[7] was decarbonylated in this manner and, after adding the reaction mixture to water, the N-β-phenylethyl-Δ^1-pyrrolinium ion (**2**)


1, R = COOH
3, R = H


2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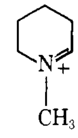
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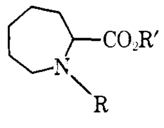
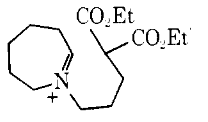
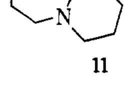
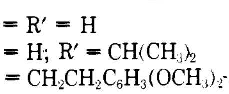
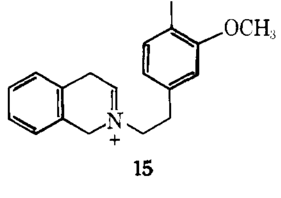
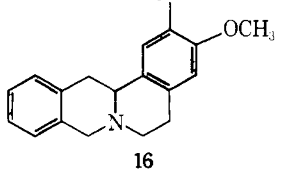

6, R = R′ = H
7, R = H; R′ = Bn
8, R = $(CH_2)_3CH(CO_2Et)_2$; R′ = Bn
9, R = $(CH_2)_3CH(CO_2Et)_2$; R′ = H


10


11


12, R = R′ = H
13, R = H; R′ = $CH(CH_3)_2$
14, R = $CH_2CH_2C_6H_3(OCH_3)_2$-3,4


15


16

was precipitated as the crystalline perchlorate (mp 116–117 °C; IR 1680 cm^{-1}) in 93% yield. Alternatively, the reaction mixture could be treated with hydrogen after the addition of 10% Pd-on-carbon to produce *N*-β-phenylethylpyrrolidine (bp 131 °C (21 mm); lit.[8] bp 139° (21 mm)) in 91% yield. Similarly, *N*-methylpipecolic acid (**4**)[9] was converted to *N*-methyl-Δ^1-tetrahydropyridinium (**5**) perchlorate (mp 85–86 °C; IR 1700 cm^{-1}) or tetraphenylborate (mp 184 °C), both in 94% yield.

As examples of the synthetic convenience and utility of this method, we have applied it to the synthesis of a 1-azabicyclo[5.4.0]undecane and a tetrahydroberberine. The 1-azabicyclo compound was prepared starting with hexahydroazepine-2-carboxylic acid (**6**)[10] which as the benzyl ester **7** was alkylated with diethyl 3-bromopropylmalonate[11] in benzene/DMF in the presence of K_2CO_3 to the α-tertiary amino ester **8** (bp 205–210 °C (0.1 mm), bulb to bulb). Hydrogenolysis gave acid **9** which was heated at 100 °C in $POCL_3$ for 3 min to form iminium salt **10** (IR 1690 cm^{-1}). Diluting with water, adjusting the pH to 6.5, and standing over night gave diethyl 1-azabicyclo[5.4.0]undecane-8,8-dicarboxylate (**11**, bp 100–105 °C (0.1 mm)) in 77% overall yield.

The tetrahydroberberine example was synthesized from 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid hydrochloride (**12**),[12] which as the isopropyl ester **13** (bp 125 °C (0.1 mm)) was alkylated with β-(3,4-dimethoxyphenyl)ethyl bromide[13] to the α-tertiary amino ester **14** ($R' = CH(CH_3)_2$, bp 180 °C (0.6 mm). Hydrolysis to acid **14** ($R' = H$, mp 157 °C) and heating at 100 °C for 2.5 min in $POCl_3$ gave iminium salt **15** which was warmed in hydrochloric acid to give 2,3-dimethoxy-5,8,13,13a-tetrahydro-6*H*-dibenzo[*a*,*g*]quinolizine hydrochloride (**16**, mp 238–241 °C; lit.[14] mp 236–238 °C) in 79% overall yield from acid **14.**

A significant feature of this scheme for preparing iminium salts is the wide availability of α-amino acids. This broad scope in starting materials provides a potent handle for directing the stereochemical course of a synthesis, including the cyclization step. Further details of these syntheses and that of other 1-azabicyclanes and berberines, as well as applications to other systems and for the preparation of enamines, will be forthcoming.

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Octamethyl-1,4-cyclohexanedione. Chair Conformation in the Crystal State

Sir:

The parent 1,4-cyclohexanedione has been studied by a wide variety of physical and theoretical techniques and, as a consequence, has become the example par excellence of a six-membered ring which adopts a twist-boat conformation in the solid,[1a–c] in solution,[1d–f] and possibly in the gas phase.[1g,h] Similarly, at least four derivatives of 1,4-cyclohexanedione, namely the *cis*- and *trans*-2,5-dimethyl compounds,[2a] as well as *cis*- and *trans*-2,5-di-*tert*-butylcyclohexanedione[2b] have been considered to prefer boat conformations in solution. We have now determined the x-ray crystal structure of octamethyl-1,4-cyclohexanedione[3] (**1**) and report that the molecule exists as a centrosymmetric chair in the solid.[4]

Crystals of **1** were obtained as very thin plates by slow sublimation in a long vertical tube at atmospheric pressure. A fragment of approximate dimensions 0.01 × 0.2 × 0.2 mm was used for x-ray study. Preliminary photography indicated the orthorhombic system with space group *Cmca* or *C2ca*, the former being confirmed during structure analysis. Cell dimensions were determined by least-squares refinement of setting angles for 15 reflections with $30 < \theta < 40°$, centered automatically on a Nonius CAD4 diffractometer, as $a = 15.441$ (5), $b = 10.832$ (4), $c = 7.525$ (2) Å. Using Cu Kα radiation, four octants ($\pm h$, $\pm k$, $+l$) of intensity data (1809 reflections) were recorded, yielding 392 independent, observed ($I > 3\sigma(I)$) reflections after merging ($R = 0.018$).

The structure was solved using the automatic centrosymmetric direct methods routine in the SHELX program[5] and refined by full-matrix least squares (C, O anisotropic, H isotropic, 64 parameters) to a final R_w of 0.037 (unweighted $R = 0.048$) in space group *Cmca*. The alternative space group *C2ca*, which would require the molecule to have only C_2 symmetry, was investigated, but because of correlation effects, no acceptable refinement could be obtained. We decided against any artificial damped refinement since the low R value, the reasonable anisotropic thermal parameters, and the accurate definition of hydrogen atoms ($U_{iso} = 0.047 - 0.073$ (8)) for the space group *Cmca* seemed to us to confirm adequately the centrosymmetric model. The molecule occupies a position of symmetry $2/m$ in the unit cell. Figure 1 shows the atomic numbering used and some of the more important bond lengths and angles; Figure 2 is a Newman projection of the molecule.

It is instructive to compare the molecular geometries of octamethyl-1,4-cyclohexanedione (**1**) and 1,4-cyclohexanedione (**2**).[1a,b] The C1–C2 bond in **1** (1.532 Å) is longer than the corresponding bond in **2** (1.511 Å) and the crowded diquaternary C2–C3 bond in **1** (1.571 Å) is also longer than the C2–C3 bond in **2** (1.545 Å), which in turn is longer than a cyclohexane C–C bond (1.520 Å from electron diffraction[6]).

The internal carbonyl angle C2–C1–C6 in **1** is 4° larger than