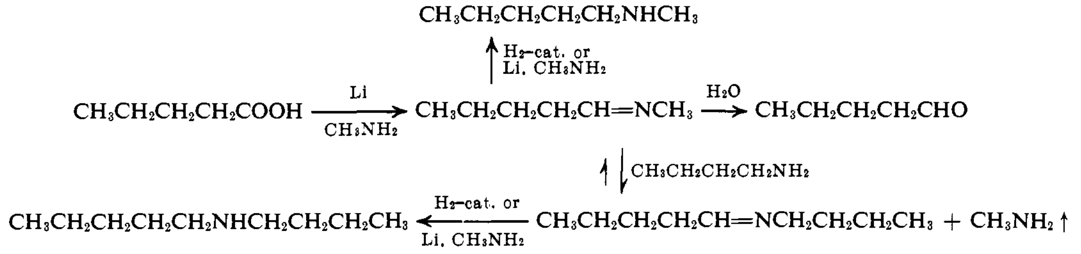
Scheme I



procedure used in the reduction of the acids. One reaction intermediate is thought to be a carbinolamine salt which is converted to the imine during the isolation procedure. The imine which is readily reduced to the corresponding amine cannot be present during the reduction since no amine is isolated. The imine (which can be isolated in good yield) is hydrolyzed to the aldehyde (slowly in neutral aqueous solution, rapidly in acidic aqueous solution), reduced to the corresponding amine (catalytically or with lithium in methylamine), and can undergo any other reaction of an imine. These conversions are illustrated using pentanoic acid as the starting material (Scheme I).

Because Burgstahler, Worden, and Lewis[2] acidified their product mixture, the imine which is rapidly hydrolyzed to the aldehyde was not noted by them. Basic aqueous solutions maintained during our work-up procedure enabled us to isolate the imine.

Saturated acids ranging from five to fourteen carbons (Table I), an unsaturated acid (8-octadecenoic), and a diacid (nonadioic[5]) were reduced with good results (yield ~60%). Use of the lithium–methylamine system converted *N*-(8-octadecenylidene)methylamine to the unsaturated compound, *N*-methyl-8-octadecenylamine, in 64% yield.

Table I. Conversion of Carboxylic Acids to Aldehydes and *N*-Methylamines by Lithium in Methylamine

	Yield, %[a]	
RCOOH	RCHO	RCH_2NHCH_3
$CH_3(CH_2)_3COOH$	66	52
$CH_3(CH_2)_6COOH$	59	
$CH_3(CH_2)_8COOH$	61	68
$CH_3(CH_2)_{10}COOH$	61	51
$CH_3(CH_2)_{12}COOH$	84	51
$(CH_3)_3C(CH_2)_2COOH$	62	

[a] The yields are of distilled product with no more than a 3° boiling range.

Reduction, in addition to that of the carboxyl group, was observed when compounds containing conjugated double bonds (C=CC=C, C=CCOOH, or ArCOOH) or nonconjugated double bonds separated by one methylene group ($C{=}CCH_2C{=}C$ and $C{=}CCH_2COOH$) were subjected to lithium in methylamine.

When benzoic acid reacted with lithium in methylamine, reduction of the benzene ring as well as the carboxyl group occurred. However, addition of ammonium nitrate to the reduction medium resulted in reduction of benzoic acid to benzaldehyde (~25%). This investigation involving the use of additives in the reduction is continuing.

The versatility of the reaction sequence in preparing secondary amines has been demonstrated in this laboratory by the conversion of *N*-pentylidenemethylamine *via* transimination with butylamine[6] (Scheme I). The resulting imine can be reduced either catalytically or with the lithium–methylamine solution.

The reduction of pentanoic acid to pentanal has also been shown to occur by an electrolytic process using platinum electrodes, methylamine, and lithium chloride. Further studies of the electrolytic reduction of carboxylic acids in methylamine are being undertaken.

Reaction of pentanoic acid (25.2 g; 0.250 mol), methylamine (500 ml), and lithium wire (1.77 g; 0.255 g-atom) for 10–20 min resulted in a blue solution. If gelling occurred this could be eliminated by addition of more methylamine. An additional 3.43 g of lithium (0.495 g-atom) was then added. After 4.5 hr the reaction mixture was decomposed (250 ml of saturated aqueous NH_4Cl) and extracted with ether (best for aldehyde conversion) or pentane (best for amine conversion). A 66% yield of distilled pentanal was obtained by washing the ether extract consecutively with 10% hydrochloric acid (until the washings remained acidic), aqueous sodium bicarbonate solution, and water, and finally drying (Na_2SO_4). Alternately a 52% yield (see Table I) of distilled *N*-methylpentylamine was obtained after the pentane extracts were dried (Na_2SO_4), the solution concentrated (to 300 ml), and the imine reduced in a low-pressure Parr hydrogenation apparatus with 3.0 g of 10% Pd–C catalyst.

The imines obtained from this reduction contained considerably less condensation products than those prepared by Tiollais' method of combining aldehydes with methylamine (R. Tiollais, *Bull. Soc. Chim. Fr.*, 708 (1947); R. Tiollais and H. Guillerm, *C. R. Acad. Sci.*, **236**, 1798 (1953)).

(5) Both carboxyl groups of the diacid were reduced because the lithium:acid ratio was 6:1 as compared with 3:1 used in monocarboxylic acids. Attempts to isolate aldehydo acids from the reduction mixture are currently in progress.

(6) The low boiling point of methylamine is one reason why it is preferable to ethylamine as the reaction medium.

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Negative-Ion Mass Spectrometry of Polynitroaromatics

Sir:

Numerous correlations have been established between positive ions found in the gas phase in the mass spectrometer and carbonium-ion intermediates in solution. By comparison, few correlations yet exist between carbanion or anion-radical solution chemistry and the gas-phase behavior of negative ions.

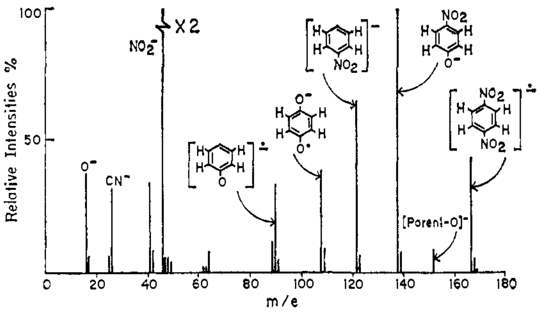

Figure 1. Negative-ion mass spectrum of *p*-dinitrobenzene at 10 eV.

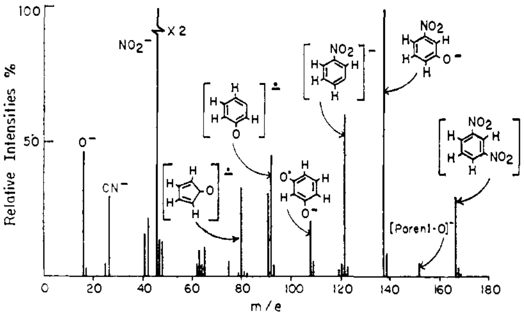

Figure 2. Negative-ion mass spectrum of *m*-dinitrobenzene at 10 eV.

This deficiency exists because negative-ion mass spectrometry is a virtually unexplored field. This may be attributed to certain technical problems associated with negative-ion mass spectrometry. First, in negative-ion mass spectrometry most workers report a 1000-fold decrease in sensitivity due to inefficiency of electron-capture processes for most organic molecules.[1,2] Second, the spectra observed are frequently found to be highly dependent on the energy of the electron beam. This is partially caused by the variety of electron-capture processes which are involved in the formation of negative ions.

Unlike positive-ion mass spectrometry, the question of sensitivity in the production of negative ions is highly related to the type of molecules being examined. This is true because while all organic molecules have electrons which can be removed by ionization to produce a positive ion, not all molecules have a high affinity for adding an electron. Clearly, organic molecules with a high electron affinity will tend to capture an electron more efficiently. With this thought in mind, we have examined the negative-ion mass spectra of polynitroaromatics, molecules which are well known to form anion radicals in solution.[3,4] We find that such molecules easily form negative ions in the mass spectrometer. For this reason we have had no problem with sensitivity using a normal Hitachi RMU-6E instrument at sample pressures of 1–2 × 10^{-6} mm and ionizing voltages of 2–20 eV. Furthermore, polynitroaromatics are molecules whose positive-ion mass spectral behavior has been extensively studied, providing an excellent opportunity for comparison.[5,6] We find that the negative-ion mass spectra of polynitroaromatics are very rich in structural information. In many cases, owing to the appearance of "flat-top" metastable ions,[7–11] we have been able to determine the amount of excess kinetic energy released in decomposition of these particular ions in the gas phase.

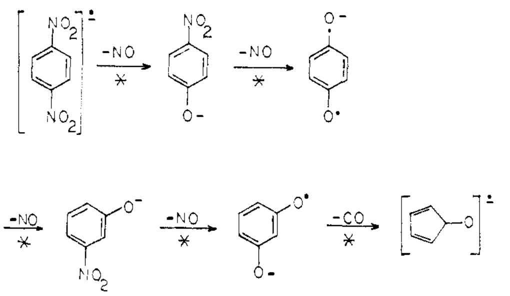

Figure 3. Fragmentation patterns of *p*- and *m*-dinitrobenzenes. An asterisk denotes observation of a metastable peak.

The ion at highest mass in the spectra of both *m*- and *p*-dinitrobenzene is the parent ion (M) at *m/e* 168. The next peak is the M − O ion at *m/e* 152. In both compounds this ion is relatively small. The major peak at *m/e* 138 is due to loss of NO from the parent ion to yield the corresponding nitro-substituted phenolate anion. In both the *m*- and *p*-dinitrobenzenes we observe a "flat-top" metastable peak at *m/e* 113 (calcd *m/e* 113.4) due to this process. The width of these flat-top metastable peaks combined with our knowledge of the accelerating voltage (1.8 kV) permit determination of the kinetic energy released in the formation of these daughter ions.[9,10] McLafferty has shown that the product-ion stability quantitatively governs the kinetic energy released in their formation.[7] The energy change for the *p*-dinitrobenzene (0.89 ± 0.09 eV) is greater than for the *m*-dinitrobenzene (0.36 ± 0.04 eV). This is expected since a *m*-nitro group can stabilize a phenolate anion only by inductive electron withdrawal, whereas a *p*-nitro group can also stabilize a negative charge by direct resonance interaction. A similar process involving loss of NO has been observed in the positive-ion mass spectra of aromatic nitro compounds in general,[5] and flat-top metastable ions have been observed in those cases where there is a strong electron-donating substituent capable of stabilizing the positive charge. Our observation is particularly noteworthy in that Beynon has only observed[5] flat-top metastable transitions for the loss of NO from the parent ion in the positive-ion mass spectra of *o*- and *p*-nitroanilines but not in the case of the meta compound. This has been explained in terms of a need for direct resonance interaction of a donor group to stabilize the positive charge.[7]

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Both the *p*- and *m*-nitro-substituted phenolate anions at m/e 138 decompose further by loss of NO to form ions at m/e 108. This decomposition is substantiated in both compounds by the observation of a flat-top metastable ion at m/e 85 (calcd m/e 84.6). Our calculations of the kinetic energy released in these processes indicate that these daughter ions at m/e 108 are structurally different. The energy change in formation of the *p*-semiquinone anion radical is greater (0.3 ± 0.03 eV) than for the meta radical anion (0.13 ± 0.01 eV). Independent evidence for the stability of the *p*-semiquinone anion radical in the gas phase was found in our observation that in the negative-ion mass spectrum of benzoquinone the only ion formed is at m/e 108.[12,13] On the other hand, the proposed *m*-semiquinone anion radical decomposes further by loss of CO to go to an ion m/e 80. The observation that no peak at m/e 80 is found in the case of the para compound supports the view that the *p*-semiquinone anion radical is particularly stable. In fact, this is perhaps the most obvious difference between the two spectra. A proposed structure for this ion at m/e 80 is a cyclopentadienone ketyl. This process is substantiated by the observation of a flat-top metastable ion at m/e 59 (calcd m/e 59.2). The excess kinetic energy released in this process was found to be 0.15 ± 0.02 eV.

Finally, in both compounds ions are observed at m/e 122 due to loss of NO_2 from the parent ion. The ion at m/e 92 may be formed by the loss of NO from the m/e 122 ion. However, no metastable peak was observed for this process. The ion of greatest abundance in all the nitroaromatic compounds investigated is at m/e 46 due to the NO_2^- anion. This ion was extremely useful in calibration of our modified mass marker.[14]

Aplin, *et al.*, have concluded for a wide range of organic compounds including nitrobenzene that negative-ion mass spectrometry is "of limited value" for the determination of structure and molecular weight.[2] Our experience with nitroaromatics at least indicates that negative ion mass spectroscopy can provide complementary structural information to that obtained in positive ion mass spectrometry.

Acknowledgments. We wish to acknowledge a National Science Foundation grant for purchase of the mass spectrometer. C. L. B. wishes to thank the California State College at Los Angeles Foundation for partial support and W. P. W. thanks the Research Corporation. Both C. L. B. and W. P. W. wish to thank the Caltech President's Fund and NASA Contract No. NAS 7-100 for support.

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[14] We thank Mr. H. Ouchi of the Hitachi Perkin-Elmer Co. for help in modifying our instrument.

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Nucleic Acid Analogs. The Interaction of Poly-9-vinyladenine with Polyuridylic Acid

Sir:

The formation of complementary base-paired complexes between both ribo- and deoxypolynucleotides is a well-known phenomena.[1,2]

We now wish to report that base-paired complex formation can also occur between poly-9-vinyladenine[3] (PVAd) and polyuridylic acid (Poly U) even though the backbones of these polymers are considerably different. Continuous variation[4a-c] mixing experiments (Figure 1) at neutral pH in both 0.01 *M* Na$^+$ and 0.1 *M* Na$^+$ have shown that PVAd[4d] (M_n, 106,000) and Poly U[4e] (S_{20}, 6.06) form a stable complex with 1:1 stoichiometry in bases.

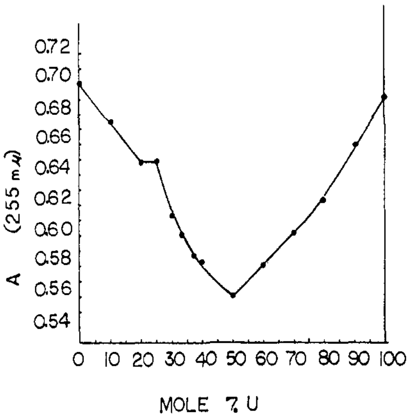

Figure 1. Continuous variation mixing curve for PVAd and Poly U in 0.01 *M* Tris buffer, pH 7.4, 0.01 *M* NaCl after 3 days at 25°.

The absorbance–temperature profile (Figure 2) indicated some cooperative character to the transition but it was not reversible. In the range of 0.005 *M* Na$^+$–0.1 *M* Na$^+$ the thermal transition curves remained monophasic and the dissociation temperature (T_m) varied linearly with the logarithm of the salt concentration. The slope of this plot (Figure 3) was 0.32 that of the double-stranded Poly U–Poly A[2] complex suggestive of a lower charge density[5,6] for the hybrid complex.

The intrinsic viscosities of the complex at neutral pH were 2.86 dl/g (0.1 *M* NaCl) and 4.35 dl/g (0.01 *M* NaCl). These values, because of their magnitude and low sensitivity to the change in salt concentration,[7] are consistent with a semirigid rod in analogy to DNA.

The circular dichroism[8] curve for this complex (λ_{max} 259 mμ, $R = +31.1 \times 10^{-40}$; λ_{min} 244 mμ, $R =$

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