obtained as a mixture of α and β epimers which upon subsequent chromatography on silica gel provided the pure α derivative and the β epimer containing small amounts of the α product; total yield, 49.4%. α derivative: mp 86 °C; $[a]^{25}_D$ + 108.9° (*c* 1.0, $CHCl_3$); MS (CI), *m/e* (relative intensity) 447 (M + 41) (2), 435 (M + 29) (32), 391 (M – Me) (38), 347 (M – OAc) (1), 317 (M – Me_3Si) (100).

Acknowledgment. We thank the Israel National Council for Research and Development for their generous financial support of this work.

Registry No. **3a** (α-isomer), 92420-79-6; **3b** (β-isomer), 92420-80-9; **3b** (α-isomer), 92420-81-0; **3c** (β-isomer), 3080-47-5; **3d** (β-isomer), 92456-17-2; **3e** (β-isomer), 92420-82-1; **3f** (β-isomer), 92420-83-2; **3f** (α-isomer), 92420-84-3; **3g** (β-isomer), 4630-61-9; **3g** (α-isomer), 37797-57-2; **3h** (β-isomer), 92420-85-4; **3j** (β-isomer), 92420-93-4; **3i** (β-isomer), 92420-86-5; **3k** (β-isomer), 92420-87-6; **3l** (β-isomer), 92420-88-7; **3m** (β-isomer), 75410-50-3; **4a** (β-isomer), 3082-95-9; **5a** (α-isomer), 92420-89-8; **8** (β-isomer), 92420-90-1; **8** (α-isomer), 92420-91-2; Me_3SiOTF, 27607-77-8; Ph_2CHOH, 91-01-0; PhCH(Me)OH, 98-85-1; $PhCH_2OH$, 100-51-6; Br_3CCH_2OH, 75-80-9; Fe_3CCH_2OH, 75-89-8; Me_2CHOH, 67-63-0; PhOH, 108-95-2; MeC_6H_4OH, 106-44-5; MeCH(CN)OH, 78-97-7; $MeCH_2CH(CN)OH$, 4476-02-2; $Me_2CHCH(CN)OH$, 15344-34-0; $Me_2C(CN)OH$, 75-86-5; PhCH(CN)OH, 532-28-5; methyl (*p*-nitrophenyl-2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate, 92420-92-3.

Notes

Chemical Ionization Mass Spectra of α-Hydroxy Carbonyl Derivatives. Formation of Stable Electron-Deficient Carbocations

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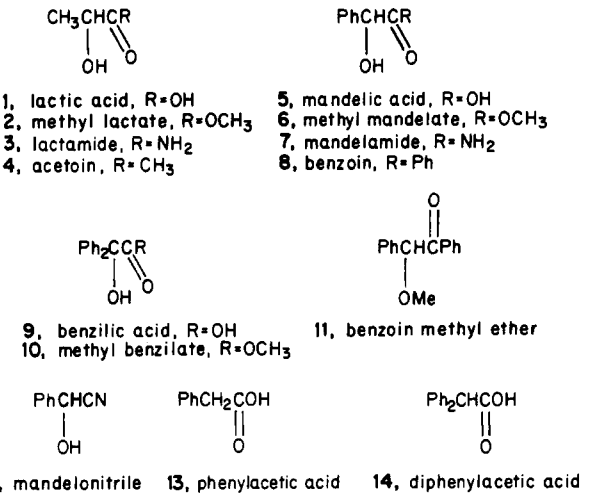
A number of recent studies have demonstrated clearly both the formation and the stability of so-called electron-deficient carbocations, i.e., carbocations substituted with potent electron-withdrawing substituents (groups or atoms).[1-4] Of particular interest to the present work is the surprising ease of generation during solvolysis of carbocations carrying an α-carbonyl moiety from secondary and tertiary benzylic, dialkyl acyclic, and tertiary cycloalkyl substrates.[5] In comparison, considerable structural reorganization occurs during the solvolysis of secondary cycloalkyl systems[6,7] while in the lone case of a secondary acyclic system reported so far solvolysis takes place via a k_Δ process involving methyl migration.[6] Further, with the (*S*-(+)-mesylate of methyl mandelate the observed high rate of racemization compared to solvolysis is compatible with an open-chain cation as against a cyclic oxirane structure which would result in retention of configuration.[5] On the other hand with the mesylate of acetoin (CH_3CH-(OMs)$COCH_3$) very little solvolysis was observed,[8] indicating that the phenyl group plays a stabilizing role in the secondary benzylic series. Several long-lived carbocations belonging to the secondary and tertiary benzylic type $Ar^+C(R)C(O)Ar$ (R = H or Ar) have been observed directly by ^{13}C NMR spectroscopy.[9-11]

Chart I



During the course of our investigations of the proton-transfer chemical ionization behavior of the α-hydroxy carbonyl derivatives **1–12**, we have observed results which closely parallel solution phase results. These are reported in the present paper. The predominant ionization reaction under chemical ionization conditions using CH_4 as the reagent gas is protonation of the substrate molecule by the gaseous Brønsted acids CH_5^+ and $C_2H_5^+$.[12] Since the proton affinities of the conjugate bases CH_4 and C_2H_4 are relatively low (130 and 164 kcal mol^{-1}, respectively[12]), the proton-transfer reaction is exothermic and fragmentation of the MH^+ ion formed from the substrate may occur. Normally the fragmentation reactions observed will be those of low critical energy, i.e., those forming stable ionic and neutral products, and the intensity of the fragment ions relative to the MH^+ ion can be taken as a measure of the stability of the product species formed.

The essential features of the CH_4 chemical ionization (CI) mass spectra of the 14 compounds studied (Chart I) are summarized in Table I. Lactic acid and its derivations (**1–4**) show abundant MH^+ ions, indicating the absence of

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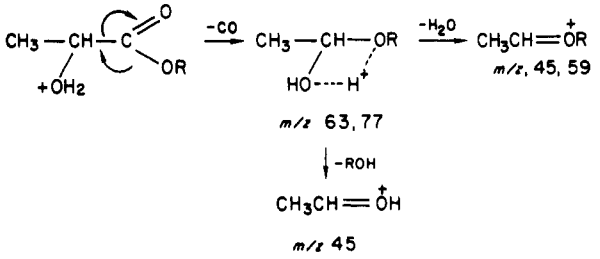
0022-3263/84/1949-4993$01.50/0

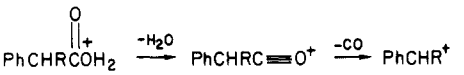
Table I. CH_4 Chemical Ionization Mass Spectra (Intensities as Percent of Base Peak)

	compound	MH^+	$MH^+ - H_2O$	$[MH^+ - H_2O]/MH^+$	other ions, m/z (RA)
1	$CH_3CH(OH)CO_2H$	100	33	0.33	63 (52), 45 (66)
2	$CH_3CH(OH)CO_2CH_3$	75			77 (50), 73 (22), 59 (50), 45 (100)
3	$CH_3CH(OH)CONH_2$	100	6	0.06	73 (5)
4	$CH_3CH(OH)COCH_3$	100	57	0.57	45 (11), 43 (23)
5	PhCH(OH)COOH	<1	100	>100	107 (12)
6	$PhCH(OH)COOCH_3$	<1	100	>100	121 (4), 107 (10)
7	$PhCH(OH)CONH_2$	69	100	1.4	
8	PhCH(OH)COPh	53	100	2.0	167 (18), 105 (5)
9	$Ph_2C(OH)COOH$	<1	100	>100	183 (20), 105 (12)
10	$Ph_2C(OH)COOCH_3$	<1	100	>100	183 (22), 105 (12)
11	PhCH(OMe)COPh	<1			$[MH^+ - MeOH]$ (100), 167 (17), 121 (7), 105 (16)
12	PhCH(OH)CN	<1			$[MH^+ - HCN]$ (100)
13	$PhCH_2COOH$	77	40	0.5	$PhCH_2^+$ (100)
14	$Ph_2CHCOOH$	36	6	0.16	Ph_2CH^+ (100)

Scheme I



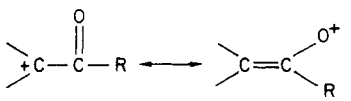
Scheme II



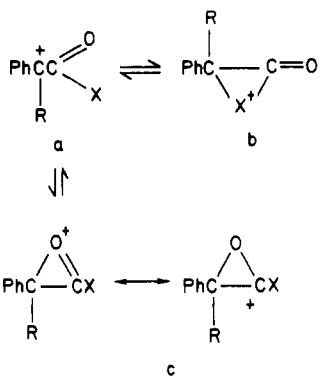
facile fragmentation pathways. The MH^+-H_2O ion signal observed for lactic acid appears to correspond largely to loss of the carboxylic hydroxyl group since H_2O loss from the methyl ester is not observed but rather MH^+-CH_3OH (m/z 73) is observed as a significant fragment ion. In both cases, the acyl ions so formed can fragment further by elimination of CO to give $CH_3CH{=}OH^+$ ion (m/z 45). A unique fragmentation pathway for protonated lactic acid and its methyl ester is the loss of CO from MH^+ to yield, respectively, m/z 63 and 77 (Scheme I). Protonated lactamide and protonated acetoin fragment to a minor extent by elimination of H_2O, and here one must assume that the carbonyl-substituted carbocation is formed, although there is clearly no strong driving force for fragmentation.

However, in contrast to these systems mandelic (**5**) and benzilic (**9**) acids and their methyl esters (**6**, **10**) show very low intensity MH^+ ion signals, the base peak in the spectra in all cases corresponding to MH^+-H_2O. For both mandelamide (**7**) and benzoin (**8**), the MH^+ ion signal is appreciable but MH^+-H_2O is the base peak, while for benzoin methyl ester MH^+-CH_3OH constitutes the base peak. Clearly in all these phenyl-substituted systems facile elimination of H_2O (or for the methyl ether CH_3OH) from the protonated molecule is occurring. The loss of H_2O from protonated mandelic and benzilic acids appears to involve primarily the α-hydroxy group and not the carboxylic hydroxyl group. The corresponding methyl esters show essentially no elimination of CH_3OH from MH^+. In addition, the spectra of phenylacetic and diphenylacetic acids (**13**, **14**) show only low intensity signals corresponding to MH^+-H_2O, the base peak in each spectrum corresponding to MH^+-H_2O-CO) indicating facile loss of CO from the MH^+-H_2O fragment (Scheme II). The loss of CO from the acyl ions formed by elimination of the carboxylic hydroxyl from mandelic and benzilic acids should be equally facile, yet the corresponding fragment ions (m/z 107 from **5** and m/z 183 from **9**) are of low intensity.

Scheme III



Scheme IV



The facile loss of the α-hydroxyl or α-methoxyl group from the protonated α-hydroxy or α-methoxy carbonyl compounds compared to the much less facile loss of H_2O from the protonated aliphatic α-hydroxy carbonyl compounds closely parallels the behavior of these compounds in solution-phase acid-catalyzed hydrolysis. The high MH^+-H_2O/MH^+ ratio for the aromatic series points to a low critical energy for fragmentation of MH^+ and thus to a stable carbocation despite α-substitution by the electron-withdrawing carbonyl group. Although such α-keto carbocations undoubtedly are stabilized by carbonyl conjugation as indicated in Scheme III, it is clear from the comparison of the aliphatic and aromatic compounds that the adjacent phenyl group plays a larger role in stabilizing the electron-deficient α-keto carbocations.

The structures of the MH^+-H_2O ions from the aromatic series may be represented by the open-chain cations a or the oxiranyl cations b or c derived by participations of the σ-heteroatom (X = O in **5**, **6**, **9**, and **10** and N in **7**) or the carbonyl oxygen, respectively (Scheme IV). It is not possible to define clearly the structure of the stable gas-phase ion; however, in view of the strong stabilizing effect of the phenyl group a significant participation of a appears to be indicated (note that in both b and c the charge site is at a distance from the phenyl group). There is very little information available concerning the relative stabilities of these ions. For the simplest system $C_2H_3O^+$ Radom et al.[13] have calculated that the formyl methyl cation ($^+CH_2CHO$) is 86 kJ/mol^{-1} less stable than the oxiranyl cation

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($\overline{OCH_2CH^+}$) and 330 kJ mol^{-1} less stable than the acetyl cation ($CH_3C{\equiv}O^+$) to which it collapses without an energy barrier. However, by charge reversal of the enolates of acetaldehyde and acetone Lehman et al.[14] have produced the formyl methyl and acetyl methyl carbocations and have shown that they give distinctive fragment ion spectra although this requires only a very short lifetime of the carbocations. Further experiments are in progress in an attempt to characterize the gaseous ion structures more completely.

Finally, the behavior of mandelonitrile in the gas phase is at variance with its solution behavior. In the gas phase protonated mandelonitrile fragments, entirely by elimination of HCN, to give the stable hydroxybenzyl (or hydroxytropylium) carbocation, while in solution mandelonitrile[15] or its mesylate[16] when treated with strong acids form the electron-deficient carbocation Ph^+CHCN. The reasons for this difference are not clear.

Experimental Section

The chemical ionization mass spectra were obtained on a DuPont 21-490 mass spectrometer equipped with a high-pressure source using methane as reagent gas at ~0.3-torr pressure. Source temperatures of 50–100 °C were employed and samples were introduced through a heated inlet system (100–110 °C) for liquids or by direct insertion probe for solids. The spectra reported are the averages of at least three runs on each sample.

All the compounds investigated, except the methyl esters **2**, **6**, and **10**, were commercial samples, the purities of which were checked by gas chromatography. The methyl esters were prepared by esterifying the corresponding acid with methanol using standard procedures and were purified by distillation.

Acknowledgment. We are indebted to the Natural Science and Engineering Research Council of Canada for financial support.

Registry No. 1, 50-21-5; 2, 547-64-8; 3, 2043-43-8; 4, 513-86-0; 5, 90-64-2; 6, 771-90-4; 7, 4410-31-5; 8, 119-53-9; 9, 76-93-7; 10, 76-89-1; 11, 3524-62-7; 12, 532-28-5; 13, 103-82-2; 14, 117-34-0.

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Chloromethylation of 1-Bromo-2-methoxynaphthalene. A Revised Structure for the Product

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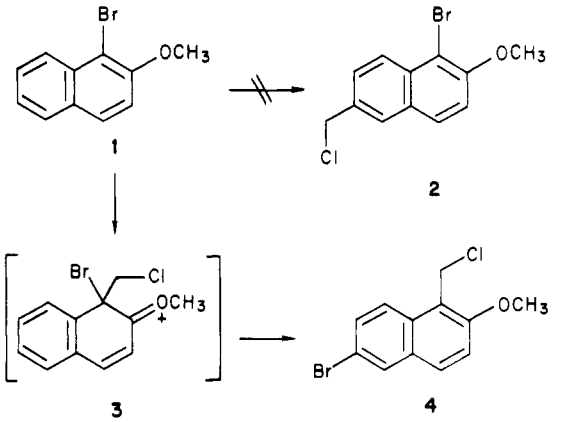
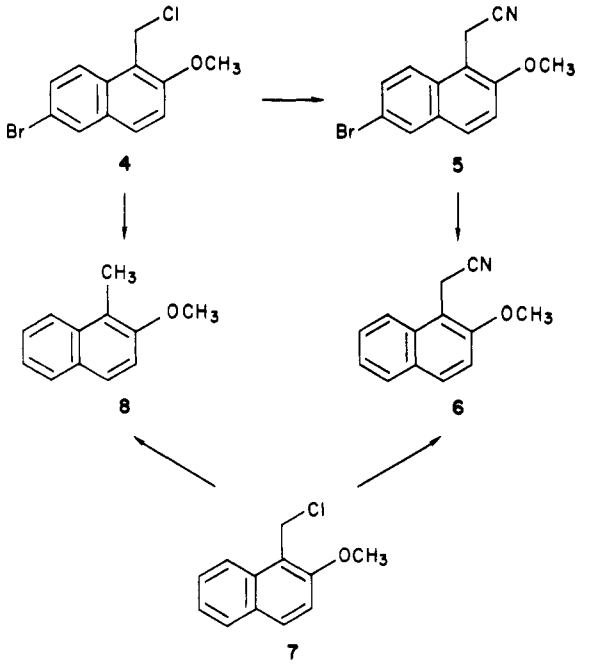
During the course of synthesizing metabolites of napactidine (DL-588) (**12a**),[1] a potential antidepressant agent, a sample of 6-methoxy-2-naphthaleneacetonitrile (**11a**) was required for subsequent demethylation[2] and conversion to the 6-hydroxy metabolite **12b**.[1b] The route initially chosen to prepare **11** utilized 1-bromo-6-(chloromethyl)-2-methoxynaphthalene (**2**)[3] as an intermeidate. On repetition of the procedure of Sy and Oiry[3] for the preparation of **2**, (see Scheme I) a compound was isolated in the same yield, with the same melting point and IR spectrum as those reported. The chloromethylation product (shown to be **4**; vide infra) (see below) was treated with sodium cyanide under

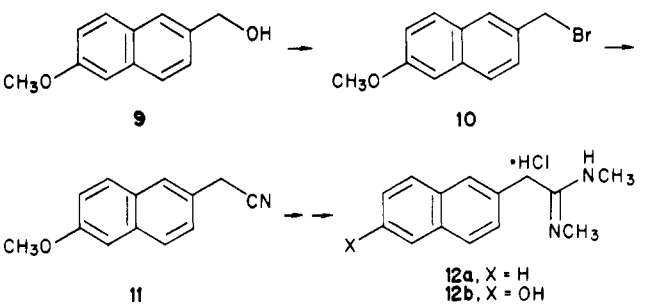
Scheme I



Scheme II



Scheme III



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