C_5), 131.0 (imidazole CH), 144.1, 155.1, 161.2 (pyrimidone C_2 and C_4 and imidazole C_4), 154.8 (pyrimidone C_6); MS *m/e* (relative intensity) 309 (6), M^+, 177 (90), M – ribose. Anal. Calcd for $C_{12}H_{15}N_5O_5$: C, 46.60; H, 4.89; N, 22.65. Found: C, 46.5; H, 5.0; N, 22.65.

The same product was neatly obtained when compound **1b** was heated to 80 °C in water for 48 h.

Determination of Ionization Constants of Modified Nucleosides. The spectrophotometric method described by Albert and Sergeant[47] was used. Standard 10^{-3} M solutions of nucleosides were made in 10^{-2} M borate, phosphate, or acetate buffers which have very low UV absorption.

Acknowledgment. We are indebted to Drs. J. C. Brochon and F. Merola for the determination of the fluorescence properties of compound **2a**.

(47) Albert, A.; Sergeant, E. P. *The Determination of Ionization Constants*; Chapman and Hall Ltd.: New York, 1971.

Notes

One-Step Preparation of Hydrazinium Nitrates from Tertiary Amines and Azaarenes with $H_2NOSO_3H/Ba(NO_3)_2/BaO$ and Conversion to Energetic Amine–Nitroimides[1]

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Hydrazine derivatives, in which one of the nitrogens is quaternized, have been known since 1876, when Emil Fischer first described the isolation of a water-soluble, crystalline material from a complex mixture of products obtained by the reaction of phenylhydrazine with ethyl bromide (eq 1).[2] Since then analogous compounds were prepared with the exclusion of unwanted side products by treating 1,1-disubstituted hydrazines with alkyl halides (eq 2).[3-5]

$$PhNHNH_2 \xrightarrow{EtBr} PhN^+(Et)_2NH_2\ Br^- + \text{other products} \quad (1)$$

$$R_2NNH_2 \xrightarrow{R'X} R_2N^+(R')NH_2\ X^- \quad (2)$$

Hydrazinium salts have also been obtained by the reactions of pyridine with sulfonyl azides;[6] chloramine with tertiary amines;[7] hydroxylamine-*O*-sulfonic acid with tertiary and aromatic heterocyclic amines;[8] by rearrangement of diazepinones;[9] and by the reaction of hydrazine with pyridinones.[10] More recently Tartakovskii et al. have prepared nitrohydrazine and their imido salts by a desilylative nitration procedure.[11a]

The chemistry of these compounds has not been well-studied, although an excellent review has been published.[11b] Relevant to hydrazinium salts is the formation of highly stable, covalently bonded "ylide" or "betaine" compounds, in which the negative charge is stabilized by both Coulombic attraction and by delocalization into an adjacent electron-withdrawing group, referred to as **amine–imides** (zwitterionic structures A) and are pre-

$$\underset{A}{R_3\overset{+}{N}-\overset{-}{N}-Z} \qquad Z = \text{aryl, acyl, sulfonyl, nitro}$$

pared directly from the corresponding hydrazinium salts. Such compounds derived from azaarenes function as 1,3-dipoles in cycloadditions[12] and, in addition, undergo the types of reactions described for the aliphatic series.[13a]

The amine–nitroimides, where $Z = NO_2$, were introduced as a new class of compounds by Katritzky in 1969[13b] and studied in an impressive body of work.[13a-f] The amine–nitroimides were prepared from hydrazinium nitrates in acetic acid–acetic anhydride–nitric acid, trifluoroacetic acid–trifluoroacetic anhydride, or by treatment with nitronium tetrafluoroborate in acetonitrile.[13c] The hydrazinium nitrates, in turn, were obtained from the halides by metathesis with silver nitrate.[7] In all, a three-step process was required to prepare the nitrates and a fourth step used to obtain the amine–nitroimides.

In continuation of our studies on the preparation of nitro compounds we undertook a study of the highly energetic but stable amine–nitroimides, with the goal to find simplified, less costly route (without silver salts) to starting hydrazinium nitrates. These compounds are subsequently

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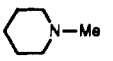
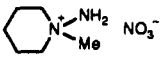
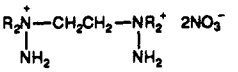
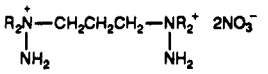
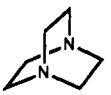
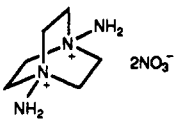
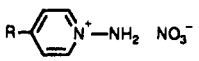
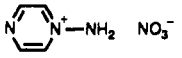
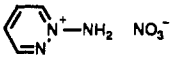
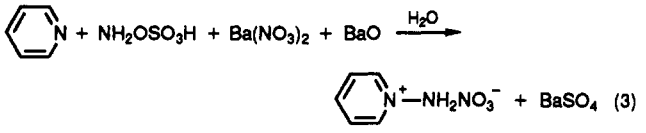
0022-3263/92/1957-1585$03.00/0

Table I. Hydrazinium Nitrates

entry	amine	R	hydrazinium nitrate	yield (%)
1	R_3N	Me	$R_3\overset{+}{N}\text{-}NH_2\ NO_3^-$	85
2		Et		90
3				90
4	$R_2NCH_2CH_2NR_2$	Me		87
5		Et		82
6	$R_2NCH_2CH_2CH_2NR_2$	Me		83
7				63
8		H		96
9		Me_2N		78
10				38
11				34

easily transformed into amine–nitroimides.[13a] Whereas in the past energetic nitramines could be prepared only from primary and secondary amines, nitroimides allow the nitrofunctionalization of tertiary amines, including some bridgehead systems, such as 1,4-diazabicyclo[2.2.2]octane (Dabco). Single-crystal X-ray structures of representative hydrazinium nitrates and amine–nitroimides are also reported, including that of Dabco-1,4-bis(nitroimide), fully substantiating the suggested structures.

Hydrazinium Nitrates. When an aqueous suspension of tertiary or aromatic heterocyclic amine, barium nitrate, and barium oxide or barium hydroxide (mono- or octahydrate) is treated with a freshly prepared solution of hydroxylamine-*O*-sulfonic acid, an exothermic reaction occurs in accordance with eq 3. The precipitate of barium



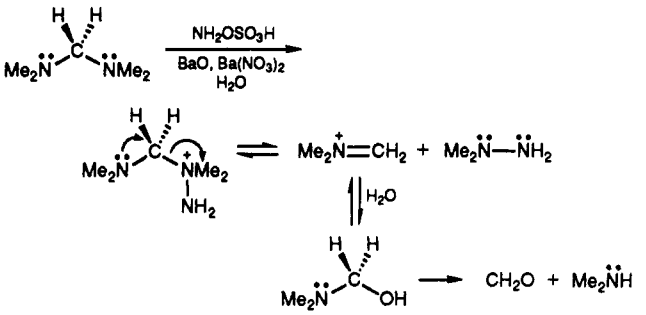
(3)

sulfate is removed by filtration and the water-soluble hydrazinium nitrate easily isolated by evaporation of the filtrate under reduced pressure. Products obtained in this way are sufficiently pure for most purposes, but may be recrystallized from ethanol, ethanol–water, or (less frequently) ethanol–ether, if so desired. Hydrazinium nitrates prepared by this method are listed in Table I.

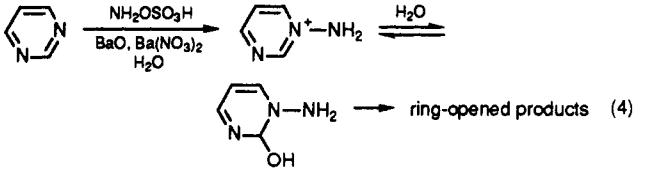
Scope and Limitations. Excellent results were obtained with monoamines in both the aliphatic and aromatic series. Di- and polyamines in either series present limitations. The amino groups in aliphatic compounds must be separated by two or more carbons in order for the reaction to proceed normally. When a carbon atom is geminally substituted by amino groups, the aminal linkage is hydrolyzed under the reaction conditions as exemplified in Scheme I. Thus, in the reactions of *N,N,N′,N′*-tetramethyldiaminomethane, 1,3,5,7-tetraazatricyclo[3.3.1.1^{3,7}]decane (tetraazaadamantane), and 1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}]dodecane (tetraazabishomoadamantane), only hydrolysis products are observed.

Similarly, aromatic heterocyclic di- and triamines, in which nitrogens are separated by a single carbon atom, lead

Scheme I



to unstable acid aminals under the reaction conditions and spontaneously decompose (see eq 4). Reactions with pyrimidine and 1,3,5-triazine give only ring-opened products.



(4)

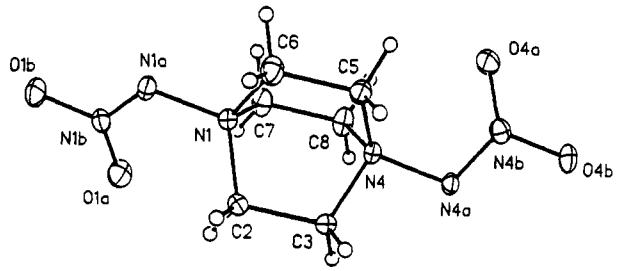
Azaarenes, in which two nitrogens can interact through the π-system, exhibit marked alterations in reactivity patterns. The susceptibility of these compounds to electrophilic attack at nitrogen is directly related to their pK_a values. While formally dibasic, protonation of one nitrogen substantially removes electron density from the other through resonance to the extent that a second protonation does not occur in aqueous media. Consequently, only monoaminated products are obtained for the reactions with 4-(dimethylamino)pyridine, pyrazine, and pyridazine (entries 9–11, Table I). In addition, the weak basicity of pyrazine (pK_a = 0.6) and pyridazine (pK_a = 2.33)[14] severely retards their reactivity and poor yields are obtained even after prolonged reaction times.

Amine–Nitroimides. Katritzky has reported three general methods for the conversion of hydrazinium nitrates

(14) Jacobs, T. L. In *Heterocyclic Compounds*; Elderfield, R. C., Ed.; John Wiley and Sons: New York, 1957; Vol. 6, p 110.

to amine–nitroimides (vide supra). The method of choice must be determined experimentally for each compound. In our laboratory, several hydrazinium nitrates were transformed to amine–nitroimides by treatment with trifluoroacetic anhydride in trifluoroacetic acid according to Katritzky's procedure.[13c] The de facto nitrating agent in this case is presumed to be trifluoroacetyl nitrate,[15] which is formed in situ from the counterion and trifluoroacetic anhydride. This procedure proved to be very effective in two cases and ineffective in five. Thus, *N,N'*-diamino-*N,N,N',N'*-tetramethyl-1,3-propanediylbis(ammonium nitrate) (entry 6, Table I) and *N,N'*-diamino-1,4-diazoniabicyclo[2.2.2]octane (entry 7, Table I) were converted to the corresponding amine–nitroimides B and C in 80% and 85% yields, respectively. Under identical conditions, *N,N'*-diamino-*N,N,N',N'*-tetramethyl-1,2-ethanediylbis(ammonium nitrate) (entry 4, Table I), *N,N'*-diamino-*N,N,N',N'*-tetraethyl-1,2-ethanediylbis(diammonium nitrate) (entry 5, Table I), 1-amino-4-(dimethylamino)pyridinium nitrate (entry 9, Table I), 1-aminopyrazinium nitrate (entry 10, Table I), and 1-aminopyridazimium nitrate (entry 11, Table I) decomposed. These results are in agreement with those observed by Katritzky for similar compounds.[13c]

Single-Crystal X-ray Diffraction Analysis. In order to supplement the synthetic work and IR and NMR spectroscopic studies, three representative hydrazinium nitrates (table entries 4, 5, and 7) and one bis(amine–nitroimide) C were analyzed by single-crystal X-ray diffraction. The structures were solved and refined with the aid of the SHELXTL system of programs.[16] The structural details of the three hydrazinium nitrates (Table I, entries 4, 5, and 7) are given in the supplementary material. The compound of interest 1,4-bis(nitroimino)-1,4-diazabicyclo[2.2.2]octane, C (Dabco-1,4-bis(nitroimide)), had the following crystal data: $C_6H_{12}N_6O_4$, FW = 232.2, orthorhombic space group $Pb2_1a$, a = 7.334 (1) Å, b = 11.236 (2) Å, c = 11.625 (1) Å, V = 958.0 (3) Å^3, Z = 4, ρ_{calc} = 1.610 mg mm^{-3}, λ(Cu Kα) = 1.541 84 Å, μ = 1.12 mm^{-1}, $F(000)$ = 488, T = 295 K. A clear colorless 0.05 × 0.15 × 0.20 mm crystal, in the shape of a flat plate, was used for data collection. Lattice parameters were determined from 25 centered reflections within $60.2 \le 2\theta \le 83.1°$. The data collection range of hkl was: $0 \le h \le 8$, $0 \le k \le 12$, $-12 \le l \le 13$, with $[(\sin\theta/\lambda)]_{max}$ = 0.580. Three standards, monitored every 97 reflections, exhibited random variations with deviations up to ±3.5% during the data collection. A set of 3044 reflections was collected in the $\theta/2\theta$ scan mode, with scan width $[2\theta(K_{\alpha 1}) - 0.5]$ to $[2\theta(K_{\alpha 1}) + 0.5]°$ and a constant ω scan rate (a function of count rate) of 14.65 deg/min. There were 847 unique reflections, and 746 were observed with $F_o > 3\sigma(F_o)$. The full-matrix least-squares refinement varied 144 parameters: atom coordinates and anisotropic thermal parameters for all non-H atoms and H atoms included using riding model [coordinate shifts of C applied to attached H atoms, C–H distance set to 0.96 Å, H angles idealized, U_{iso}(H) set to $1.1U_{eq}$(C) or, if methyl, $1.2U_{eq}$(C)]. Final residuals were R = 0.052 and R_w = 0.054 with final difference Fourier excursions of 0.23 and −0.27 e Å^{-3}.



C

The details of the bond distances and angles are included in the supplementary material. The N_1–N_{1a} and N_4–N_{4a} bond lengths are 1.473 (6) and 1.476 (8) Å, respectively, indicating almost equidistance. The corresponding distance in the reported pyridinium *N*-nitroimide[13e] is much shorter (1.423 Å). This indicates that in the Dabco case the N–N bond is weaker. Such a conclusion is also supported by the shortness of N_{1a}–N_{1b} and N_{4a}–N_{4b} bonds (1.320 (7) and 1.309 (7) Å, respectively). In the pyridinium case the corresponding bond is longer (1.336 Å). These crystal structure data seem to indicate that the Dabco-1,4-bis(nitroimide) should be less stable than the pyridine analogue. None the less this 1,4-bis(nitroimide) is a rather remarkable, stable but highly energetic[17] double-bridgehead nitrohydrazine derivative.

Experimental Section

^{13}C and ^{1}H NMR data were obtained at 50 and 200 MHz, respectively. All chemicals were purchased from commercial sources, and used without further purification. *Caution: All nitro compounds as well as nitrates should be considered potential hazards and extreme care must be exercised in working with them.* While no problems were encountered during our studies, laboratory explosions of related compounds have been reported.[13d] The known compounds, entries 1, 2, 3, 4, 7, and 8 and C gave satisfactory data as reported in the literature.[7,13a,e]

***N,N'*-Diamino-1,4-diazoniabicyclo[2.2.2]octane Dinitrate**[13c] **(7).** 1,4-Diazabicyclo[2.2.2]octane (5.61 g, 50.0 mmol), $Ba(NO_3)_2$ (13.07 g, 50.0 mmol), and BaO[18] were combined in 100 mL of distilled H_2O and heated with vigorous stirring until a homogeneous suspension resulted. While still hot, the suspension was added in ~2-mL portions to a freshly prepared solution of hydroxylamine-*O*-sulfonic acid (14.14 g, 125.0 mmol) in 50 mL of distilled H_2O. The precipitation of $BaSO_4$ occurred immediately. After allowing 2 h of stirring at rt, $BaSO_4$ was removed by suction filtration and water removed from the filtrate by evaporative distillation (rotavap) at water-aspirator pressure. The residue was recrystallized from EtOH/H_2O, and the crystals were collected on a Büchner funnel, washed with ether, and air-dried: yield 8.50 g, 63%; ^{13}C NMR (DMSO-d_6) δ 56.8; ^{1}H NMR (DMSO-d_6) δ 6.62 (s, 4 H), 4.09 (s, 12 H); IR (KBr) 1383 cm^{-1}.

1,1,1-Trimethylhydrazinium nitrate[13b,c] **(1):** ^{13}C NMR (DMSO-d_6) δ 57.3; ^{1}H NMR (DMSO-d_6) δ 5.85 (s, 2 H), 3.25 (s, 9 H); IR (KBr) 3445, 1634, 1484, 1385, 945, 826 cm^{-1}.

1,1,1-Triethylhydrazinium nitrate[7] **(2):** ^{13}C NMR (DMSO-d_6) δ 57.4, 7.4; ^{1}H NMR (DMSO-d_6) δ 5.70 (s, 2 H), 3.34 (q, 6 H), 1.20 (t, 9 H); IR (film) 3268, 3159, 1342, 1106, 927, 814 cm^{-1}.

1-Amino-1-methylpiperidinium nitrate[13b,c] **(3):** ^{13}C NMR (CD_3OD) δ 66.2, 57.0, 21.7, 21.5; IR (film) 3249, 3128, 3005, 1384, 847, 507 cm^{-1}.

***N,N'*-Diamino-*N,N,N',N'*-tetramethyl-1,2-ethanediylbis(ammonium nitrate)**[13c] **(4):** ^{13}C NMR (DMSO-d_6) δ 59.5, 56.2; ^{1}H NMR (DMSO-d_6) δ 6.01 (s, 4 H), 3.87 (s, 4 H), 3.19 (s, 12 H); IR (KBr) 3427, 3235, 3119, 2986, 1384, 826 cm^{-1}.

(15) For a discussion of trifluoroacetyl nitrate, see: Olah, G. A.; Malhotra, R.; Narang, S. C. *Nitration Methods and Mechanisms*; VCH Publishers, Inc.: New York, 1989; pp 44–5.

(16) Sheldrick, G. M. *Solving, Refining, and Displaying Crystal Structures from Diffraction Data*; University of Göttingen: Federal Republic of Germany, 1980.

(17) Preliminary tests at China Lake Naval Weapons Center on this compound has shown its highly energetic nature.

(18) Barium oxide is extremely hygroscopic and precautions must be taken to ensure accurate weight determination. A freshly opened bottle provides sufficient accuracy without additional predrying. Hydrates of barium hydroxide may be substituted for barium oxide with equally good results.

N,N'-Diamino-N,N,N',N'-tetraethyl-1,2-ethanediylbis(ammonium nitrate) (5): ^{13}C NMR (DMSO-d_6) δ 59.0, 54.4, 7.7; ^{1}H NMR (DMSO-d_6) δ 5.95 (s, 4 H), 3.84 (s, 4 H), 3.46 (q, 8 H, J = 6.6 Hz), 1.26 (t, 12 H, J = 6.6 Hz); IR (KBr) 3462, 3444, 3134, 1384 cm^{-1}.

N,N'-Diamino-N,N,N',N'-tetramethyl-1,3-propanediylbis(ammonium nitrate) (6): ^{13}C NMR (DMSO-d_6) δ 64.6, 55.5, 17.3; ^{1}H NMR (DMSO-d_6) δ 6.11 (s, 4 H), 3.53 (t, 4 H, J = 7.8 Hz), 3.29 (s, 12 H), 2.34 (quint, 2 H, J = 7.8 Hz); IR (KBr) 3437, 3226, 3101, 1629, 1385, 1013 cm^{-1}.

1-Aminopyridinium nitrate[13a,b,e] **(8):** ^{13}C NMR (DMSO-d_6) δ 139.8, 138.4, 128.2; ^{1}H NMR (DMSO-d_6) δ 8.83 (d, 2 H), 8.60 (s, 2 H), 8.31 (t, 1 H), 8.06 (pseudo t, 2 H); IR (KBr) 3180, 3109, 3055, 1515, 1482, 1385 cm^{-1}.

1-Amino-4-(dimethylamino)pyridinium nitrate (9): ^{13}C NMR (DMSO-d_6) δ 156.8, 154.7, 142.2, 139.0, 107.1, 106.8, 39.6, 39.5; ^{1}H NMR (DMSO-d_6) δ 8.23–8.18 (d, 2 H), 7.15 (br s, 1 H), 7.01–6.88 (d, 2 H), 3.19–3.17 (s, 6 H); IR (KBr) 3440, 1646, 1569, 1385, 1211, 826 cm^{-1}.

1-Aminopyrazinium nitrate (10): ^{13}C NMR (DMSO-d_6) δ 150.1, 128.0; ^{1}H NMR (DMSO-d_6) δ 9.63 (br s, 2 H), 9.16 (m, 2 H), 8.76 (m, 2 H); IR (KBr) 3459, 3206, 3043, 1385, 916, 831 cm^{-1}.

1-Aminopyridazinium nitrate (11): ^{13}C NMR (DMSO-d_6) δ 154.2, 136.5, 134.5, 128.5; ^{1}H NMR (DMSO-d_6) δ 9.90 (s, 2 H), 9.28 (ddd, 6 H, J^1 = 5.3 Hz, J^2 = 2.0 Hz, J^3 = 1.0 Hz), 9.15 (ddd, 3 H, J^1 = 6.2 Hz, J^2 = 1.0 Hz, J^3 = 1.0 Hz), 8.51 (ddd, 4 H, J^1 = 8.1 Hz, J^2 = 6.2 Hz, J^3 = 2.0 Hz), 8.14 (ddd, 5 H, J^1 = 8.1 Hz, J^2 = 5.3 Hz, J^3 = 1.0 Hz); IR (KBr) 3447, 1435, 1385, 786 cm^{-1}.

N,N,N',N'-Tetramethyl-1,3-propanediamine 1,3-bis(nitroimide), B: ^{13}C NMR (DMSO-d_6) δ 63.5, 53.3, 18.9; ^{1}H NMR (DMSO-d_6) δ 3.65 (t, 4 H, J = 7.8 Hz), 3.24 (s, 12 H), 1.92 (quint, 2 H, J = 7.8 Hz); IR (KBr) 3052, 1364, 1305, 873, 775 cm^{-1}.

1,4-Diazabicyclo[2.2.2]octane 1,4-bis(nitroimide), C:[13c] ^{13}C NMR (solid) δ 52.0.

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Registry No. 1, 51470-59-8; 2, 1185-49-5; 3, 25230-43-7; 4, 51518-00-4; 5, 138385-72-5; 6, 138385-73-6; 7, 51470-64-5; 8, 28460-22-2; 9, 138407-38-2; 10, 138385-74-7; 11, 138385-75-8; B, 138385-76-9; C, 51470-74-7; NMe_3, 75-50-3; NEt_3, 121-44-8; *N*-methylpiperidine, 626-67-5; *N,N,N',N'*-tetramethylethylenediamine, 110-18-9; *N,N,N',N'*-tetraethylethylenediamine, 150-77-6; *N,N,N',N'*-tetramethyl-1,3-propanediamine, 110-95-2; 1,4-diazobicyclo[2.2.2]octane, 280-57-9; pyridine, 110-86-1; 4-(dimethylamino)pyridine, 1122-58-3; Pyrazine, 290-37-9; Pyridazine, 289-80-5; bis(dimethylamino)methane, 51-80-9; tetraazaadamantane, 100-97-0; tetraazabishomoadamantane, 51-46-7; pyrimidine, 289-95-2; 1,3,5-triazine, 290-87-9; hydroxylamine-*O*-sulfonic acid, 2950-43-8; barium nitrate, 10022-31-8; barium oxide, 1304-28-5.

Supplementary Material Available: Details of the X-ray structure determinations, including atomic coordinates, bond lengths and angles, as well as anisotropic thermal parameters and ^{1}H NMR spectra of 5, 6, 9, 10, and 11 (29 pages). Ordering information is given on any current masthead page.

Synthesis of (+)-(*E*)-(2*S*,5*R*)-5-Acetoxy-3-hexen-2-ol via Enantioselective Enzymatic Hydrolysis. An Enantiodivergent Palladium-Catalyzed Route to (+)- and (−)-*cis*-2-Methyl-5-hexanolide

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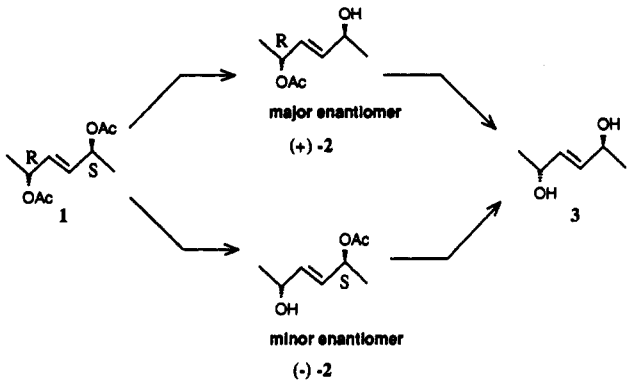
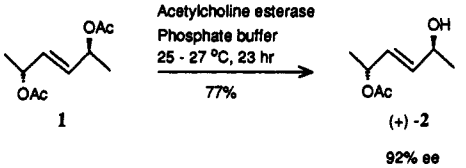
The use of enzymes as a tool in asymmetric organic synthesis has increased dramatically during the last decade.[1] A particularly attractive approach is the use of enzymes for enantioselective transformations (eg. hydrolysis[1b,d,2] reduction,[3] and oxidation[4]) of meso compounds and other compounds having enantiotopic groups. The advantage of employing such substrates in enantioselective reactions is that, theoretically, 100% of the starting material can be transformed into an enantiomerically pure product.

Scheme I



Enantioselective hydrolysis of meso diesters and diacylated meso diols is an extensively used enzyme mediated reaction. The most successfully used enzyme for this purpose is probably pig-liver esterase,[1b,d,2a] but other enzymes, such as lipases[2f] and acetylcholine esterase[2b-e] (ACE), have also proved useful. The enzyme ACE attracted our interest since it has been applied successfully to the asymmetric hydrolysis of cyclic *meso*-1,4-diacetoxy-2-cycloalkenes,[2b,d-e] a type of alkene readily available by the palladium-catalyzed diacetoxylation of 1,3-cycloalkadienes.[5] However, acyclic meso diacetates, such as *meso*-(*E*)-2,5-diacetoxy-3-hexene (1) also available via the diacetoxylation procedure,[5] have not been studied in enzymatic reactions.

In this paper we report a successful enantioselective enzymatic hydrolysis of 1 and the application of the product to the syntheses of both enantiomers of the Carpenter bee pheromone.



(1)

Results and Discussion

Enzymatic Hydrolysis of *meso*-(*E*)-2,5-diacetoxy-3-hexene (1). Performing the hydrolysis of 1, using the conditions described by Johnson,[2c] resulted in a very slow

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