The enthalpy of transfer of the reactants from dioxane to CH_2Cl_2, $\delta\Delta H_{soln}$ (reactants) = $\Delta H^r{}_{soln}$ (CH_2Cl_2) − $\Delta H^r{}_{soln}$ (dioxane), is 1.2 kcal/mol. The heat of solution of N in dioxane is unknown. If it is assumed to be equal to the value in CH_2Cl_2, the small difference between our value and that of Rogers and Quan reduces to 0.3 kcal/mol, which is well within experimental error. Even if one assumes a value as large as 1 kcal/mol for the enthalpy of transfer of the product from dioxane to CH_2Cl_2, one would still find that our results are in good agreement with the values determined by standard solution calorimetry.[7]

In conclusion, we wish to emphasize that the flow calorimetric method employed is fast, convenient, and requires small amounts of sample. It is potentially applicable to measurement of enthalpies of a wide variety of fast organic reactions in solution.

Experimental Section

Materials. Maleic anhydride (Eastman Organic Chemicals) was recrystallized from $CHCl_3$, sublimed under vacuum, and stored in a desiccator until use. Dioxane was purified by refluxing over sodium followed by distillation (onto molecular sieves) immediately before use. CPD was obtained by cracking *endo*-dicyclopentadiene which had been purified by the method of Harkness, *et al.*[10]

Calorimetry. The flow calorimeter (a modified Beckman Model 190 microcalorimeter) has been described in detail elsewhere.[3,11] Calibration was accomplished by measuring the enthalpy of reaction of 1.000 × 10^{-3} *N* HCl and 2.000 × 10^{-3} *N* NaOH, employing the values given by Grenthe, *et al.*,[12] for the enthalpy of formation of water.

The temperature of the calorimeter was regulated to within ±0.005° at both temperatures at which the reaction was investigated. The output of the thermopile during the steady-state period was integrated using a ball and disk integrator. The integration precision is estimated to be better than ±1%.

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Registry No. CPD, 542-92-7; MA, 108-31-6.

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(6) A reviewer has questioned whether the product is 100% endo adduct. Although we did not determine this, the paper by Rogers and Quan[1] states that "Wilder and Gratz fractionally crystallized a kinetically determined reaction mixture and found 1.4% exo." The citation to the above experiment is erroneous, neither has this work been done by P. Wilder, Jr. (private communication). We have been unable to find the source of the report; however, even if it is substantiated, the enthalpy difference between N and X is expected to be quite small, so that the effect on our measured enthalpy is negligible.

(7) Using their data Rogers and Quan calculated a value for $\Delta H_r(g)$, and suggested an empirical equation for estimation of the heat of any DA reaction

$$\Delta H_r{}^d(g) - \Delta H_r{}^e(g) = \Delta H_H{}^d - \Delta H_H{}^e \qquad (1)$$

where $\Delta H_r{}^d(g)$ is the heat of addition of any diene to dienophile (d), $\Delta H_r{}^e(g)$ is the enthalpy of addition to ethylene, and $\Delta H_H{}^d$ and $\Delta H_H{}^e$ are the heats of hydrogenation of the dienophile and ethylene. Applying this equation to the reaction of CPD + MA they calculated a value for $\Delta H_r(g)$ which was 2.6 kcal/mol less exothermic than the experimental value. It should be noted that the value of $\Delta H_r{}^e(g)$ is derived from the heat of formation of norbornene. The value used by Rogers and Quan of 20.6 kcal/mol has been updated by the work of Hall, *et al.*,[8] who find $\Delta H^\circ{}_f$ (norbornene) = 15.1 kcal/mol. The calculated value according to eq 1 should therefore be higher than the experimental value by 2.9 kcal/mol. In addition, their conclusion that the strain energy of N contains only a small contribution from the succinic anhydride moiety (1.1 kcal/mol) now seems to be incorrect, in view of the new value for strain energy (SE) of norbornene (17.6 kcal/mol), and a revised value (4.5 kcal) for the strain contribution of a succinic anhydride moiety recently published by Eigenmann, Golden, and Benson.[9] Using the revised group additivity parameters for enthalpies of formation of oxygen-containing compounds,[9] we calculate $\Delta H_f(g)$ (N) = −111.8 kcal/mol. Comparing this value with the experimental value of −89.8 kcal/mol, the strain energy in N is 22 kcal/mol. [Note: SE (norbornene) + SE (succinic anhydride) = 22.1 kcal/mol].

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Reaction of *N*-Iodosuccinimide with Secondary Alcohols

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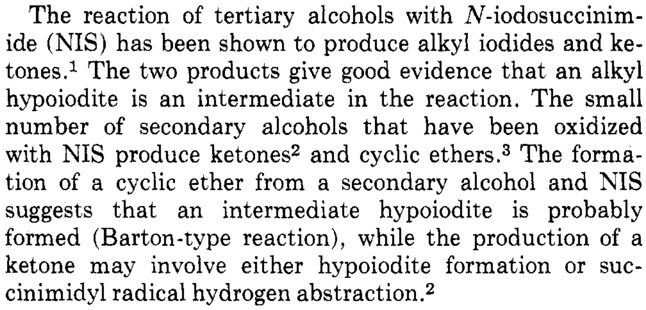
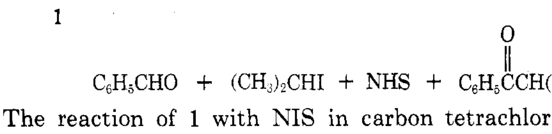
The reaction of tertiary alcohols with *N*-iodosuccinimide (NIS) has been shown to produce alkyl iodides and ketones.[1] The two products give good evidence that an alkyl hypoiodite is an intermediate in the reaction. The small number of secondary alcohols that have been oxidized with NIS produce ketones[2] and cyclic ethers.[3] The formation of a cyclic ether from a secondary alcohol and NIS suggests that an intermediate hypoiodite is probably formed (Barton-type reaction), while the production of a ketone may involve either hypoiodite formation or succinimidyl radical hydrogen abstraction.[2]

To gain more evidence for the general mechanistic pathway involved in the oxidation of secondary alcohols with NIS, NIS was allowed to react with three secondary alcohols, 2-methyl-1-phenyl-1-propanol (**1**, Table I), cyclopentanol (**2**), and 2,6-dimethyl-4-heptanol (**3**), that we believed would not form ketones if an intermediate hypoiodite was involved in the oxidation. Two of the secondary alcohols had previously been oxidized with reagents that are thought to produce hypohalite intermediates, and ketones were not the major product. Cyclopentanol gives 5-iodopentanal when treated with iodine and mercuric oxide in carbon tetrachloride[4] and 2,6-dimethyl-4-heptanol gives a furan when treated with bromine and silver acetate.[5]



$$\underset{\mathbf{1}}{C_6H_5\overset{\overset{OH}{|}}{C}HCH(CH_3)_2} + NIS \longrightarrow C_6H_5CHO + (CH_3)_2CHI + NHS + C_6H_5\overset{\overset{O}{\|}}{C}CH(CH_3)_2$$

The reaction of **1** with NIS in carbon tetrachloride at reflux in the presence of visible light[6] produced 78–87% benzaldehyde and 4–12% isobutyrophenone.[7] The 2-iodopropane product was found to be produced in 83% yield when no solvent was present. Succinimide was produced in 75–80% yield.



2

Scheme I

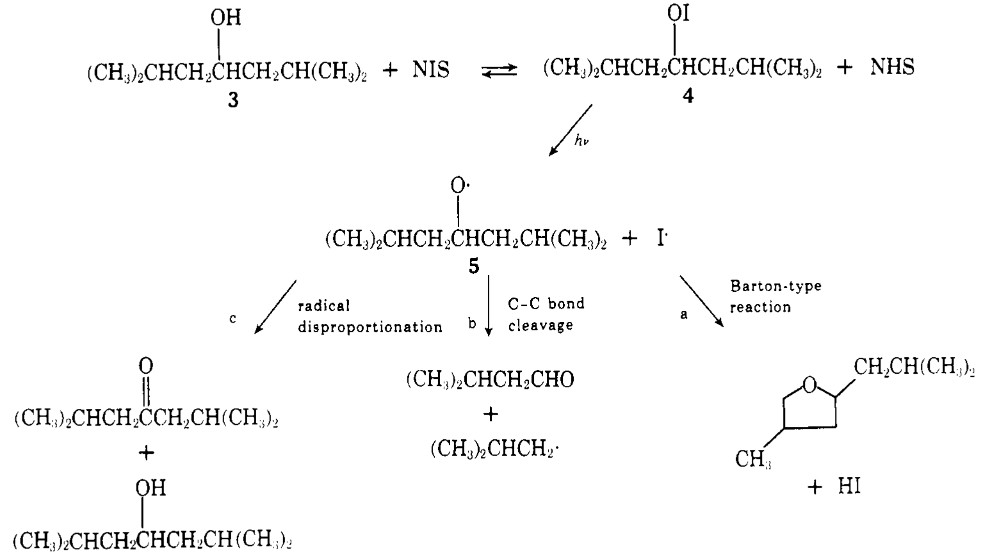
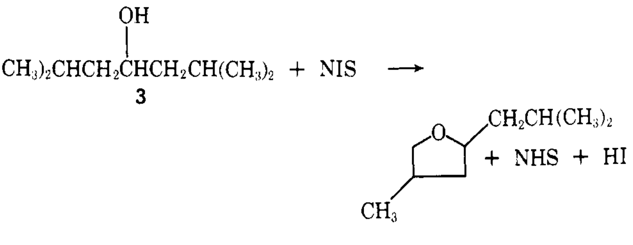


Table I
Oxidation of 2-Methyl-1-phenyl-1-propanol with NIS

Conditions (solvent, irradiation, time)	Yield of products, %: Benzaldehyde	Yield of products, %: Isobutyrophenone
CCl_4, $h\nu$, 2 hr	84	4
CCl_4, dark, 4 hr	87	5
CCl_4, $h\nu$, 3 hr	78	7
CCl_4, $h\nu$, 3 hr	80	12
No solvent, $h\nu$, 2 hr[a]	88	7

[a] The 2-iodopropane peak was not separated on the vpc from the carbon tetrachloride solvent peak. When 2-methyl-1-phenyl-1-propanol was oxidized with NIS with no solvent present 2-iodopropane was found in a yield of 83%.

Irradiation of 2 with NIS in carbon tetrachloride at reflux produced 5-iodopentanal. The 5-indopentanal was isolated as a 2,4-dinitrophenylhydrazone derivative in 15–25% yields. An nmr spectrum ($CDCl_3$) of the crude aldehyde produced triplets at δ 9.61 (CHO) and 3.27 (ICH_2) and a complex multiplet at δ 1.6–2.0 (CH_2). An ir spectrum gave characteristic[8] aldehyde C–H stretching vibrations at 2747 and 2890 cm^{-1} and a carbonyl band at 1754 cm^{-1}. Analyses of the crude aldehyde by vpc showed only trace amounts of cyclopentanone.



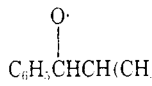
When 3 was treated at reflux with NIS in carbon tetrachloride, 35–40% of the cyclic ether (3-methyl-1-isobutyltetrahydrofuran) was produced with only 3–5% formation of the corresponding ketone. Small amounts (2–3%) of the C–C cleavage products, 2-methyl-1-iodopropane and 3-methylbutanal, were also found.

An nmr analysis of the ether, isolated from the vpc, produced overlapping doublets (δ 0.85, 0.96, 1.09, 9 H, 3 CH_3) and complex multiplets (δ 3.1–4.2, 3 H, 1 CH_2O and 1 CHO and δ 1.2–2.4, 6 H, 2 CH_2 and 2 CH). The mass spectrum of the ether included peaks with *m/e* 142 (M^+) and 85. Infrared analysis of the ether showed an absence of both carbonyl and hydroxyl peaks.

The products formed from the reaction of the above three alcohols with NIS suggest that a hypoiodite intermediate is formed, possibly in an equilibrium step. (Barton and his coworkers[9] have prepared *N*-iodoamides with *tert*-butyl hypoiodite.) An example of the proposed reaction pathway is given in Scheme I using 3 as the alcohol oxidized with NIS.

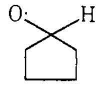
Once the hypoiodite is formed, visible light homolytically cleaves the O–I bond to produce the *sec*-alkoxy radical 5, which has several decomposition pathways available to it. The Barton-type reaction (route a) is the preferred decomposition route for this *sec*-alkoxy radical, while a small percentage of the radicals undergo C–C bond cleavage (route b). The small percentage of ketone occurs (route c) presumably by radical disproportionation[10] rather than by loss of a hydrogen atom or iodine atom hydrogen abstraction.

However, the *sec*-alkoxy radicals 6 and 7 do not have the Barton reaction available to them and their decompositions follow a route similar to pathway b, C–C bond cleavage.



$C_6H_5CH(O\cdot)CH(CH_3)_2$

6



7

The products formed from the reaction of NIS with the three secondary alcohols studied indicate that an alkyl hypoiodite is probably formed as an intermediate. The alkyl hypoiodite then decomposes to produce ethers, aldehydes, and alkyl iodides as major products. However, ketones are produced in small amounts. The mechanistic pathway for the formation of the ketones may involve the alkyl hypoiodite or it may involve hydrogen abstraction by the succinimidyl radical.

Experimental Section

Analyses were carried out using a Perkin-Elmer 810 vpc and a Varian Aerograph Model 700 vpc. Infrared analyses were done using a Perkin-Elmer 337 grating infrared spectrophotometer. Nuclear magnetic resonance spectra were determined using a Varian T-60. Irradiation of the reaction mixtures was effected with a G.E. Projector Spot 150-W, 130-V tungsten lamp. The NIS was purchased from K & K Laboratories and was not recrystallized. The alcohols, ketones, benzaldehyde, isopropyl iodide, and internal standards were purchased from Matheson Scientific and were fractionally distilled. Vpc analyses of the 1-phenyl-1-propanol and 2,6-dimethyl-4-heptanol reactions were performed using a

7% SE-30 and 1.5% Carbowax 20M 6-ft column. All reactions were run at reflux and were irradiated. The reactions were continued until the reaction mixture gave a negative test with starch–potassium iodide paper. A description of the oxidation of 2,6-dimethyl-4-heptanol with NIS is given in detail. The other two reactions were performed in a similar manner.

Reaction of 2,6-Dimethyl-4-heptanol with NIS. Four milliliters of a CCl$_4$ solution containing 2,6-dimethyl-4-heptanol (1.57 mmol) and bromobenzene (0.93 mmol) was added to a 10-ml pear-shaped flask. To this solution was added 0.182 g (0.809 mmol) of NIS. The mixture was irradiated, heated at reflux, and stirred for 6 hr. Vpc analyses indicated a 39% yield of 3-methyl-1-isobutyltetrahydrofuran, a 3% yield of 2,6-dimethyl-4-heptanone, and 2% yields of 2-methyl-1-iodopropane and 3-methylbutanal.

Two reactions (with silver acetate added to reduce the decomposition of NIS by HI) produced 42 and 45% yields of the tetrahydrofuran product with the other products found in the 2–4% range. [The addition of silver acetate generally gave a small (5–7%) increase in the yield of tetrahydrofuran with no change in the percentage of the other products.]

Oxidation of Cyclopentanol with NIS. Five oxidations of cyclopentanol with NIS were performed. Vpc analyses of the reaction mixtures, after 3 hr, showed only trace amounts of cyclopentanone. The ω-iodopentanal was not found on the vpc. Evaporation of the CCl$_4$ solvent, after filtration of the reaction mixture, produced an oil. An nmr analysis of the oil showed a triplet at δ 9.61 (CHO) and 3.27 (ICH$_2$) and a complex multiplet at δ 1.6–2.0 (CH$_2$CH$_2$CH$_2$). A 2,4-dinitrophenylhydrazone derivative of the ω-iodoaldehyde gave a solid melting at 126–128°. (The 2,4-dinitrophenylhydrazone derivative[4] of the product obtained from the oxidation of cyclopentanol with HgO and I$_2$ melted at 127–128°.)

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Registry No. 1, 611-69-8; **2,** 96-41-3; **3,** 108-82-7; NIS, 516-12-1.

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Intramolecular C-2 → C-1 Hydrogen Transfer Reactions during the Conversion of Aldoses to 2-Furaldehydes[1,2a]

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Sugar 1,2-enediols have been suggested as intermediates in acid-catalyzed dehydration reactions and alkaline degradation reactions, as well as in the interconversion of aldoses and related 2-ketoses[3,4] (the Lobry de Bruyn-Alberda van Eckenstein transformation). In previous experiments designed to test the importance of 1,2-enediols and related enolic structures as intermediates in dehydration reactions, sugars were converted to 2-furaldehydes in acidified deuterium oxide or in tritiated water.[5] The finding that D-xylose is converted in acidified, tritiated water to 2-furaldehyde which is devoid of carbon-bound isotope[5] suggests that 1,2-enediols, if formed, further react immediately. Otherwise significant isotope incorporation would have been detected at the aldehyde carbon atom of 2-furaldehyde as a result of aldose–ketose interconversion. It has recently been found, however, that D-glucose is converted to D-fructose in acidic solution *via* a reaction involving an intramolecular transfer of hydrogen from C-2 of D-glucose to C-1 of D-fructose.[6,7] In strong acid (2 *N* sulfuric acid), the transfer appears to be complete and involves an isotope effect (K_h/K_t) of 4.3. Thus, in this case, the data are more consistent with a reaction mechanism involving an intramolecular C-2 → C-1 hydride transfer rather than the more generally accepted one involving a 1,2-enediol intermediate. These data suggest that aldose–ketose interconversion could easily have occurred, as a result of hydride transfer reactions, during dehydration reactions and remained undetected during isotope acquisition experiments.

The purpose of the present work was to evaluate the importance of C-2 → C-1 hydride transfers during some typical dehydration reactions. This was studied by preparing D-xylose and D-glucose specifically tritiated on C-2 and converting them to respectively 2-furaldehyde (I) and 5-(hydroxymethyl)-2-furaldehyde (II) in acidified water. A determination of the amount of carbon-bound tritium on the aldehyde carbon (which corresponds to C-1 of the original aldose) of I and II would provide information on the extent of C-2 → C-1 transfer occurring during the dehydration reactions and, in addition, provide qualitative information on the extent of aldose–ketose interconversion occurring during the dehydration reactions.

D-Glucose-2-^{3}H was prepared by converting D-fructose 6-phosphate to D-glucose 6-phosphate in tritiated water using phosphoglucose isomerase, followed by treating the resulting crystalline D-glucose 6-phosphate with alkaline phosphatase. This procedure was essentially the same as was used to prepare D-glucose-2-^{2}H.[8,9] That the D-glucose was tritiated only at C-2 is evident from the known[10,11] specificity of the enzyme, which produces, at equilibrium in tritiated water, only D-glucose-2-^{3}H 6-phosphate and D-fructose-*1*-^{3}H 6-phosphate, with no isotope being present at C-1 of the aldose. Further proof of this labeling specificty also observed in the past when the same procedure was used to prepare D-glucose-2-^{2}H,[8] which, from its nmr spectrum, was observed to be deuterated only at C-2. D-Xylose-2-^{3}H was prepared from D-glucose-2-^{3}H by converting the latter to 1,2-*O*-isopropylidene-D-glucofuranose followed by periodate oxidation to give 1,2-*O*-isopropylidene-D-xylo-1,5-dialdose-2-^{3}H. Reduction of the latter derivative with sodium borohydride gave 1,2-*O*-isopropylidene-D-xylofuranose-2-^{3}H, which was hydrolyzed to give chromatographically pure D-xylose-2-^{3}H.

D-Glucose-2-^{3}H was converted to II and a portion isolated as the crystalline bisether[12] oxybis(5-methylene-2-furaldehyde). The specific activity of the compound was 14% that of the starting sugar, indicating that each furan residue retained 7% of the radiochemical activity of the original D-glucose-2-^{3}H. A further portion of II was oxidized to 2-furoic acid which contained negligible activity indicating that all of the carbon-bound tritium was located on the aldehyde carbon of II. Considering the isotope effect involved for the conversion of D-glucose-2-^{3}H to D-fructose-*1*-^{3}H, approximately 30% of the dehydration reaction would involve hydride transfer if the reactant were protiated rather than tritiated.