teractions in water have been amply demonstrated in the past for heterodimeric systems of type $Ar_1(CH_2)_nAr_2$, where Ar are nucleic bases and intercalators.[7] The geometry of the stacked complex is favorable for an attack on the C-8 position of guanine by the developing nitrenium ion. The arrangement of the two rings is close to the geometry of the transition state required for the electrophilic attack at C-8 by the nitrenium ion. This hypothetical scheme explains both the efficiency of the attack at the C-8 site of guanine and the dramatic effect of the solvent conditions on the yield.[16]

These observations, based upon our carefully designed molecule, suggest the importance of stacking interactions. In addition, they permit a more general comment on the process of adduct formation between DNA and polycylic aromatic amine metabolites that can intercalate in DNA. Intercalation, closely analogous to our intramolecular complexation, determines the relative position of a DNA base and a carcinogen substance. Our results suggest that in such a situation, following the generation of the reactive species, in our case a nitrenium ion, the site of attack on the base and the efficiency of this process are controlled by the stacking phenomenon. Our model provides evidence for a frequently quoted hypothesis, inadequately substantiated previously because of the complexity of the biological system.

(15) Direct experimental evidence for intramolecular ring–ring stacking in 3 could not be obtained, due to its high reactivity in water ($t_{1/2}$ = 10 min at 25 °C) combined with poor solubility in water (smaller than 10^{-3} at 25 °C). These preclude a ^1H NMR or UV study, as was achieved in other examples.[7]

(16) See, for example: Jiang, X. K.; Hui, Y. Z.; Fei, Z. X. *J. Chem. Soc., Chem. Commun*, 1988, 680–690 and Jiang, X. K. *Acc. Chem. Res.* 1988, *21*, 362–367 for precedents in the literature in applying the concept of making use of hydrophobic forces to increase the yield of intramolecular reactions.

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Concerted Mechanism of the Aminolysis of *O*-Ethyl *S*-(2,4-Dinitrophenyl) Thiocarbonate

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Summary: The linear Brönsted-type plot with slope β = 0.56 found in the aminolysis of *O*-ethyl *S*-(2,4-dinitrophenyl) thiocarbonate indicates a concerted mechanism, which is explained through instability of the putative zwitterionic tetrahedral intermediate, caused by the EtO group. Had the mechanism been stepwise the position of the Brönsted break should have been at pK_a 9.3 (the experimental pK_a range is 6.4–11.5).

The mechanism of the aminolysis of oxyesters[1,2] and carbonates[3] has been extensively studied and the influence of the nucleofuge and nonleaving groups of the substrate on the kinetics has been assessed.[3] Since the mechanism of the aminolysis of thioesters and thiocarbonates has been less studied,[4-6] we now report on the kinetics of the reaction of *O*-ethyl *S*-(2,4-dinitrophenyl) thiocarbonate (DNPTC) with a series of secondary alicyclic amines. The object is to shed more light into the mechanism of the aminolysis of thio compounds and to analyze the influence of the nonleaving group of the substrate on the above mechanism, by comparison with the aminolysis of 2,4-dinitrophenyl thiolacetate (DNPTA).[6] We report in this paper that there is an abrupt change in mechanism from a stepwise, via a tetrahedral intermediate for the thiolacetate aminolysis, to a concerted one for the thiocarbonate reactions. That is, this remarkable change in mechanism occurs when the Me group of DNPTA is replaced by a EtO group.

DNPTC was prepared by a similar method described for analogous thiocarbonates.[7] Previously, 2,4-dinitrophenol was obtained by a modification of a reported procedure.[6,8] The purification of the amines, kinetic measurements and product studies were carried out as described.[6]

In all cases, under amine excess, pseudo-first-order rate coefficients (k_{obsd}) were obtained. The plots k_{obsd} vs free-amine concentration ([N]) at constant pH were linear with the slopes (k_N) independent of pH, except for the reactions with piperazine (PA) at low pH values, where the above slopes were pH dependent. This fact is due to the competing reactions of PA and its conjugate acid (PAH) with DNPTC; in this case the k_N values were determined as previously.[6] The experimental conditions, and k_{obsd} and k_N values are shown in Table I.

Figure 1 shows the linear Brönsted-type plot, statistically corrected,[5,9] obtained for the present reactions (correlation coefficient 0.997). The magnitude of the slope (β = 0.56 ± 0.05) is much smaller than those found for curved Brönsted plots at low pK_a values in the aminolyses of several oxyesters and thioesters and carbonates.[1-3,5,6,10-12] These curved Brönsted plots have been interpreted in terms of a tetrahedral intermediate ($T^{\pm}$) in the reaction path and a change in the rate-determining step. The large Brönsted slope at low pK_a values ($\beta \approx 0.8$–1.0) is indicative of the breakdown of $T^{\pm}$ being the rate-determining step.[2,3,5,6,10-12]

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Table I. Experimental Conditions and k_{obsd} and k_N/q Values for the Reactions of DNPTC with Alicyclic Amines in Aqueous Solution at 25 °C, Ionic Strength 0.2 M (KCl)[a]

amine (pK_a + log p/q)	pH	$10^3[N]_{tot}$,[b] M	10^3k_{obs}, s^{-1}	no. of runs	k_N/q,[c] s^{-1} M^{-1}
piperidine (PI) (11.54)	10.54	0.3–70	2.6–160	7	14
	10.94	0.3–35	6.3–92	7	
	11.24	1.0–25	23–190	6	
piperazine (PA) (9.94)	9.64	0.3–40	0.50–60	7	2.3
	9.94	0.3–27	1.7–61	6	
	10.21	0.3–18	2.0–57	7	
1-(β-hydroxyethyl)piperazine (BHPA) (9.68)	9.08	6.0–130	2.8–59	7	1.4
	9.38	3.0–75	2.2–51	7	
	9.68	2.0–50	1.7–46	7	
morpholine (M) (9.08)	8.48	7.0–250	1.8–73	6	0.84
	8.78	3.0–250	1.3–100	7	
	9.08	10.0–180	5.9–103	6	
1-formylpiperazine (FPA) (8.28)	7.68	9.0–290	0.50–19	7	0.19
	7.98	7.0–400	0.78–37	7	
	8.28	10.0–200	1.4–26	7	
piperazinium ion (PAH)[d] (6.41)	7.20	20–140	0.48–3.4	5	0.020
	7.50	40–120	1.3–4.2	5	
	7.80	80–160	4.0–8.1	5	
	8.10	20–140	1.7–11	6	

[a] Values of pK_a were taken from ref 5. These and the k_N values are statistically corrected.[5,9] [b] Concentration of total amine: [N] + [NH^+]. [c] Values of k_N were obtained as average values of the slopes of plots of k_{obs} vs [N] at constant pH, except in the reactions with PAH (see text). [d] In the presence of 0.01 M phosphate buffer.

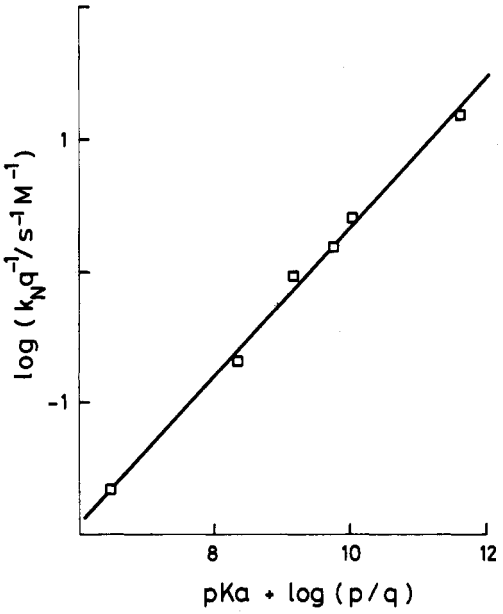

Figure 1. Brönsted-type plot (statistically corrected) found in the reactions of DNPTC with secondary alicyclic amines. The value of the slope is 0.56 ± 0.05.

Linear Brönsted plots with slope β = 0.8–1.0 have been obtained in the aminolyses of less reactive esters and carbonates.[1,2,13] These reactions have also been shown to proceed through $T^{\pm}$, with rapid preequilibrium formation and slow rate-determining decomposition of $T^{\pm}$.[2,13]

The value of the Brönsted slope found in the present reactions (Figure 1) is consistent with a concerted process where the structure of the transition state remains constant with the variation of the nucleophile basicity. Linear Brönsted plots with similar slope values have been obtained in the methoxycarbonyl group transfer from *N*-(methoxycarbonyl)isoquinolinium ion to substituted pyridines (β = 0.58) for nucleophiles of pK_a comprising that of isoquinoline,[14] in the acetyl group transfer between 4-chloro-2-nitrophenolate anion and substituted phenolate anions (β = 0.64),[15] in the phosphoryl group transfer between 4-nitrophenolate anion and substituted phenolate anions (β = 0.46),[16] and in the reactions of oxyanions with 4-nitrophenyl 4-nitrobenzenesulfonate (β = 0.5).[17] All these reactions have been shown to follow a concerted mechanism.[14-17]

Not all concerted reactions have values of the Brönsted slopes (β) in the range 0.4–0.7. Some β values smaller than 0.4 for concerted processes have been reported in phosphoryl group transfer reactions.[18,19] Also β values larger than 0.7 have been found in other concerted reactions.[15]

A value of the Brönsted slope in the region 0.4–0.7 alone does not prove that the reaction is concerted. One must be sure that the hypothetical break of the Brönsted plot, due to change in the rate-limiting step associated with a putative intermediate, is located at a pK_a value within the pK_a range used in the plot.[20] For the present reactions the predicted pK_a value at the break of the Brönsted plot ($pK_a°$) is 9.3 (see below), which is within the pK_a range of the nucleophiles employed (Figure 1); therefore, we believe that the reactions under scrutiny are concerted.

The reactions of alicyclic amines with 2,4-dinitrophenyl acetate (DNPA) and DNPTA show nonlinear Brönsted relationships with $pK_a°$ = 9.1[21] and 8.9,[6] respectively; namely, there is pK_a lowering of 0.2 unit in the position of the center of the Brönsted curvature when replacing the O phenolic atom of DNPA by a S atom. A nonlinear Brönsted plot was also found in the reactions of alicyclic amines with 2,4-dinitrophenyl methyl carbonate (DNPMC), with $pK_a°$ = 9.5.[11] Assuming the same $pK_a°$ lowering as that exhibited by the acetate series, a $pK_a°$ value of 9.3 can be predicted for the present reactions.[22] On the other hand, a $pK_a°$ increase of 0.4 unit is noted when going from the aminolysis (alicyclic amines) of DNPA[21] to that of DNPMC.[11] A similar $pK_a°$ increase is

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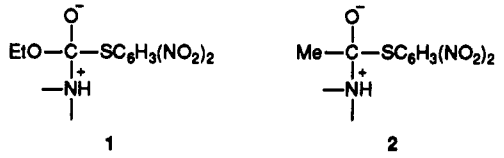
(22) Assuming that EtO and MeO are similar.

found in the pyridinolysis of DNPMC ($pK_a° = 7.8$)[12] compared to that of DNPA ($pK_a° = 7.3$).[13b] Assuming the same $pK_a°$ increase in going from the aminolysis of DNPTA to that of DNPTC,[22] we can predict a $pK_a° = 9.3 \pm 0.1$ for the reactions under study, which satisfactorily agrees with the previous prediction.

The fact that a concerted pathway occurs in the present reactions means that the putative intermediate 1 is too unstable to exist. This is in contrast to the relative stability of intermediate 2 found in the reactions of DNPTA with secondary alicyclic amines, where the mechanism is stepwise.[6,23] The higher instability of 1 relative to 2 could be



1 2

due to the additional push exerted by EtO in 1 to expel either the amine or the thiolate anion. On the other hand, it is known that in the aminolysis of *O*-aryl acetates and carbonates substitution of MeO for Me on a tetrahedral carbon enhances the push provided by the aryloxy group attached to that carbon atom due to an inductive electron-withdrawing effect of the MeO group in $T^{\pm}$.[12,13,25] Therefore, it is possible that EtO in 1 also increases the push provided by the thio group in 1 to expel the amine compared with the same push from 2.[26] Either argument could explain why 1 is much more unstable than 2. The expulsion of the amine from 1 should be as fast as a C-N bond vibration; therefore, 1 would not have a significant lifetime and the concerted pathway is enforced.[27]

Electron donation from the acyl group that destabilizes a zwitterionic tetrahedral intermediate and enforces a concerted mechanism has also been found in methoxycarbonyl group transfer from isoquinoline to pyridines.[14] (The acetyl transfer between pyridines is stepwise.[28]) Another example: In the aminolysis of benzoyl fluoride a concerted process was observed,[27] whereas a stepwise mechanism was found in the aminolysis of acetyl chloride.[29] The higher instability of the putative intermediate formed in the former reactions was attributed to electron donation from the benzene ring.[27]

It is known that aryl methyl carbonates are less reactive than aryl acetates toward amine nucleophiles.[12,13,25,30] Likewise, the aminolyses of methyl chlorocarbonate[30] and DNPTC (this work) are slower than the corresponding reactions of acetyl chloride[29] and DNPTA,[6] respectively. This must be due to the electron-releasing effect of the MeO or EtO group in the substrate, which results in resonance delocalization and, therefore, in stabilization of the carbonate relative to the acetate. This renders the CO carbon of the former substrate less positively charged and therefore less susceptible to amine attack. The $T^{\pm}$ formed in the carbonate reactions would be less stable in view of the great loss of resonance stabilization in going from reactants to $T^{\pm}$ (this resonance is very much inhibited in $T^{\pm}$).

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Supplementary Material Available: Experimental details of the kinetic measurements and product studies and ^1H NMR and IR data for DNPTC (2 pages). Ordering information is given on any current masthead page.

(23) The fact that a curved Brönsted-type plot was found in the aminolysis of DNPTA[6] does not prove per se that the reaction is stepwise. We have shown that the mechanism is stepwise in this and other reactions by fitting a semiempirical equation based on the existence of $T^{\pm}$ to the experimental points.[5,6,10-13,21] In similar reactions, an equation based on an extension of the Hammond postulate, which predicts a curved Brönsted plot for a concerted process, does not account satisfactorily for the experimental points.[24]

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Preparation of *C*-Aryl Glucals via the Palladium-Catalyzed Coupling of Metalated Aromatics with 1-Iodo-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal

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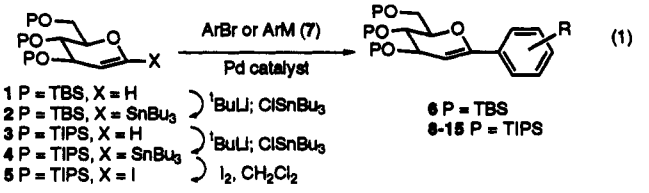
Summary: The preparation of the novel iodo glucal 5 from 3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (4), via a two-step procedure involving C1 stannylation and subsequent tin-iodine exchange, is described. The palladium-catalyzed coupling of 5 with a variety of metalated aromatics provides a facile and high yielding entry into *C*-aryl glucals, compounds that have been demonstrated to be useful precursors for the synthesis of *C*-aryl glycosides.

There is currently a great deal of interest in the synthesis of *C*-glycosides. We have previously reported that the palladium-catalyzed cross-coupling reaction of an aryl bromide and the C1-stannylated glucal 2 is a useful and simple method for the preparation of *C*-aryl glucals 6 (eq 1).[1] The glucal products of these reactions can be effi-



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