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A C-13 STUDY OF THE REACTION OF 2,4,6-TRIARYLPYRYLIUM CATIONS WITH AMINES[1]

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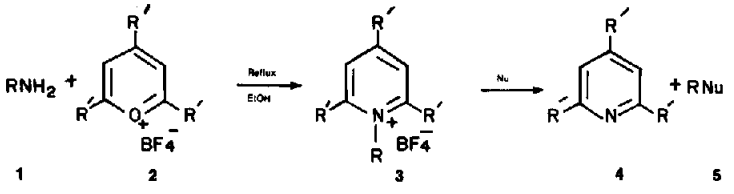
Abstract—The reaction of primary and secondary amines with 2,4,6-triarylpyryliums is shown by C-13 NMR to proceed by fast ring opening to a vinylogous amide; in the case of primary amines this closes slowly to a pyridinium salt. The reaction in DMSO gives the pyridinium salt quantitatively when 2 moles of amines are used, with less amine significant quantities of a diketone intermediate are produced which results in slower conversion.

Considerable work from this laboratory[3] has shown that primary amines (**1**) may be converted in good yields to other functional groups *via* pyridinium salts obtained by reaction with pyrylium cations. The first stage of the sequence is often accomplished synthetically by refluxing the amine **1** in ethanol with the pyrylium salt **2a**. The pyridinium salt **3a** thus produced may be converted into the desired product **5** by nucleophilic attack. The driving force of this reaction is the good leaving group ability, and the high stability of 2,4,6-triphenylpyridine **4a**.

All the compounds in the reaction sequence of Scheme II should have characteristic C-13 spectra. In particular, the chemical shifts of the five pyrylium ring carbons, and the corresponding carbon shifts in the products derived during the reaction are readily identified. Full assignments for these compounds are made (Table 1) and are discussed later in the paper; however, the reaction sequence is initially discussed in terms of these five easily identified ring-carbon signals (first five lines of Table 1): obviously the pyrylium salt **2a**[5] and the pyridinium salt **3a** possess planes of symmetry which simplify their C-13 spectra. The vinylogous amide **8a** has a carbonyl chemical shift at 186.8 ppm, and the diketone two such shifts at 190.1 and 195.9 ppm. We have not observed any signals attributable to 2-amino-2H-pyrans **7** but expect that ring carbon shifts for **7** should be similar to those of 2-methoxy-2H-pyran[5] (**10**) which are also given in Table 1.

[a: R′ = Ph; b: R′ = *p*-FC₆H₄]

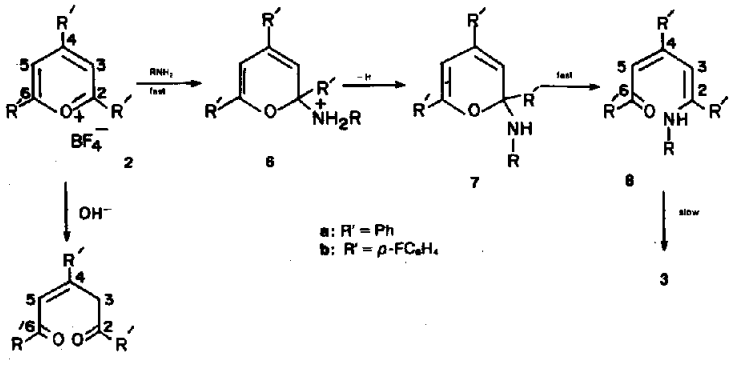


Scheme I.

As part of a wider study on the application of this synthetic method we are investigating the mechanisms of both steps of the sequence.[4] Here we report on the reactions of amines with pyrylium salts to produce pyridinium salts. Such reactions are expected to follow the sequence illustrated in Scheme II: the pyrylium salt **2** and the amine **1** initially yield the 2-amino-2H-pyran **7** which ring opens to give the divinylogous amide **8** which can then ring close to the desired pyridinium salt **3**. Reaction of the pyrylium salt with water competes to give the diketone byproduct **9**.

Reaction of the pyrylium salt with secondary amines

Our initial experiments were conducted with secondary amines as in these cases the final ring-closure of

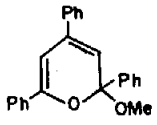


Scheme II.

Table 1. C-13 NMR assignments[a] of compounds derived from 2,4,6-triarylpyrylium salts **2a** and **2b** in DMSO

Comp. C	Pyrylium salt[b] 2a	Pyridinium salt R = n-Bu 3a[c]	p-Fluorophenyl pyridinium salt R = n-Bu 3b[d,e]	Divinylogous amide R = n-Bu 8a[f]	p-Fluorophenyl divinylogous amide R = n-Bu 8b[e,g]	Diketone 9a	2-Methoxy-2H-pyran[b] 10[h]
2	170.0	156.0	155.1	159.2[i]	158.6[i]	195.9	102.2
3	115.1	126.1	126.4	97.5	97.5	42.3	114.6
4	165.1	154.2	153.0	159.9[i]	159.0[i]	152.4	135.7
5	115.1	126.1	126.4	111.9	111.5	122.7	98.9
6	170.0	156.0	155.1	186.8	185.6	190.1	151.7
2-i	129.0	133.1	129.4	141.5[j]	137.9[j]	136.7[j]	133.8[j]
2-o	128.8	129.1[k]	132.0	127.4[l]	130.0[l]	128.3[l]	125.1[l]
2-m	129.9	129.2[k]	116.2	127.2[m]	114.1[m]	128.7[m]	128.7[m]
2-p	135.1	130.9	163.4	128.6[n]	161.5[n]	133.2[n]	128.4[n]
4-i	132.4	133.2	129.7	137.8[j]	134.0[j]	141.1[j]	137.5[j]
4-o	130.0	128.7	131.5	128.8[l]	131.0[l]	127.0[l]	126.2[l]
4-m	129.9	129.6	116.6	127.4[m]	114.3[m]	128.7[m]	129.0[m]
4-p	135.2	132.3	164.8	129.0[n]	162.2[n]	129.4[n]	129.0[n]
6-i	129.0	133.1	129.4	143.3[j]	139.6[j]	138.0[j]	142.4[j]
6-o	128.8	129.1[k]	132.0	129.2[l]	131.7[l]	128.1[l]	126.2[l]
6-m	129.9	129.2[k]	116.2	128.4[m]	115.2[m]	128.7[m]	129.0[m]
6-p	135.1	130.9	163.4	130.8[n]	163.9[n]	132.9[n]	129.5[n]

[a]Chemical shifts in ppm relative to TMS, calculated by adding 39.6 ppm to the shift measured relative to the centre peak of DMSO-d_6, see G.C. Levy and J.D. Cargioli, J. Magn. Res. 6, 143 (1972). [b]Ref. 5. [c]The n-butyl shifts are:- 54.1 (α), 30.7 (β), 18.8 (γ) and 12.5 (δ). [d]The n-butyl shifts are 54.2 (α), 30.7 (β), 18.8 (γ), 12.5 (δ). [e]The C-F coupling constants in Hz are ipso- 244.5-253.0, o- 22.1, m- 8.8, p- 2.9. [f]The n-butyl shifts are 44.0 (α), 30.2 (β), 20.1 (γ), 13.9 (δ). [g]The n-butyl shifts are 44.0 (α), 30.0 (β), 19.3 (γ), 13.6 (δ). [h]The OCH_3 shift is 49.5 ppm. [i]Assignments for C-2 and C-4 are interchangeable. [j]Assignments for 2-i, 4-i, 6-i are interchangeable. [k]Assignments for 2-o, 2-m, 6-o, 6-m are interchangeable. [l]Assignments for 2-o, 4-o, 6-o are interchangeable. [m]Assignments for 2-m, 4-m, 6-m are interchangeable. [n]Assignments for 2-p, 4-p, 6-p are interchangeable.



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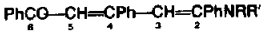
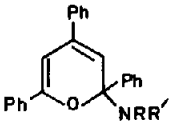
Scheme II to a pyridinium salt is not possible, and the interpretation is correspondingly simplied.

(a) *Pyrrolidine.* Reaction of 2,4,6-triphenylpyrylium tetrafluoroborate with 2 mole equivalents of pyrrolidine produces immediately a C-13 spectrum (Table 2) showing a carbonyl and two highfield signals which are consistent with that expected for the vinylogous amide **11a**: all five 'ring' shifts are very similar to those of the amide **8a** (R = nBu). Although several conformers are possible for **11a**, no evidence of line broadening is seen. Attempts to observe the corresponding 2H-pyran intermediate **12a** by adding the pyrrolidine to a solution of the pyrylium salt dissolved in acetonitrile at low temperature (−40°) were unsuccessful: the addition, deprotonation, and electrocyclic ring opening (*cf* **2**→**6**→**7**→**8**) through to the vinylogous amide are evidently all fast steps.



11a: R, R′ = $(CH_2)_4$
b: R, R′ = $(CH_2)_5$



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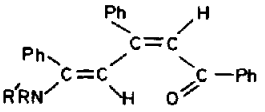
(b) *Piperidine.* Reaction of the pyrylium salt with 2 mole equivalents of piperidine gives the vinylogous amide **11b**. Here however there is evidence of a dynamic conformational process. At room temperature all the "ring" carbon signals (but not those of the phenyl rings) are broad and difficult to observe. At 80°, these signals (except the peak assigned to C2 at 146.2 ppm) are sharp and comparison with the other vinylogous amides provides positive identification (Table 2). Significant

Table 2. Chemical shifts and assignments for the divinylogous amides and pyridinium salts derived from the amine reactions with 2,4,6-triarylpyrylium tetrafluoroborates

Compound no. R	3a $PhCH_2$	3a Ph	8a $PhCH_2$	8a cyclohexyl	11a pyrrolidino	11b piperidino
Ring carbons[a]						
C2	156.6	156.3	157.6*	158.4*	158.4*	146.2*
C3	126.3	125.2	98.7	98.0	101.3	106.6
C4	155.0	155.6	159.3*	160.0*	159.9*	153.2*
C5	126.3	125.2	112.7	112.1	111.1	111.2
C6	156.6	156.3	186.8	187.1	186.2	181.1
Other carbon shifts and assignments[b]						
i	134.0	139.5	143.2	143.3	143.3	141.7
	133.1	133.5	141.2	141.6	141.5	139.3
	133.0	133.1	138.8	137.9	136.6	138.4
			139.7			
p	132.6	133.1	131.1	130.9	130.8	130.3
	130.8	132.5	129.3		128.2	128.2
	129.7		128.0			127.7
			127.1			
o	129.0	129.8	128.6	129.4	129.3	128.6
	128.0	128.8	128.5	128.8	128.7	127.9
		128.1		127.5	128.4	126.5
m	128.6	128.8	127.5	128.4	127.9	127.5
	128.5			127.5	127.1	127.3
				127.3		127.2
Other	57.8 (CH_2)		47.6 (CH_2)	52.9 (α)	49.8 (α)	49.1 (α)
				32.1 (β)	25.0 (β)	25.2 (β)
				24.7 (γ)		23.7 (γ)
				25.5 (δ)		

[a]Chemical shifts in ppm relative to TMS. *Alternative assignments. [b]The assignment of the o and m carbons is not considered reliable and assignments may be reversed.

differences in chemical shifts between the piperidine and pyrrolidine vinylogous amides **11a** and **11b** especially those of C2 and C3, suggest that the piperidine compound **11b** adopts the more open structure **13** rather than **14** because of the larger size of the piperidine group.



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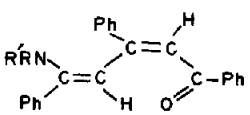

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Reaction of pyrylium salts with primary amines

(a) *n-Butylamine.* The reaction of two mole equivalents of n-butylamine at 20° in DMSO-d_6 with the triphenylpyrylium salt **2a** results in the immediate formation of the vinylogous amide **8a** (R = n-Bu) which is easily recognised from the carbonyl chemical shift. Intermediate **8a** (R = n-Bu) is converted into the pyridinium cation **3a** (R = n-Bu) with a half-life of about 5 h; after 25 h only the spectrum of the pyridinium salt **3a** (R = n-Bu) was observed. [Complete assignments for **8a** and **3a** (R = n-Bu) are discussed later.]

The use of less than 2 mole equivalents of amine results in the formation of increasing amounts of the diketone **9a** as a byproduct. Thus, one mole equivalent of n-butylamine gives immediately the spectrum for a mixture of 50% of the diketone **9a** and 50% of the vinylogous amide **8a** (R = n-Bu). The vinylogous amide **8a** (R = n-Bu) is converted as described above into the pyridinium ion product **3a** (R = n-Bu), such that after 25 hr the reaction mixture contains 50% pyridinium ion **3a** (R = n-Bu) and 50% diketone **9a**. Under these reaction conditions the diketone (**9a**) is itself also converted to the pyridinium salt **3a** (R = n-Bu) but at a much slower rate (over about 5 days). Thus production of a quantitative yield of the pyridinium salt **3a** (R = n-Bu) does occur eventually with one mole of the amine, but the use of 2 mole equivalents gives a faster and more efficient conversion of the pyrylium salt. Similar behaviour is found in the other reactions described in this paper.

We believe that the role of the second mole of amine is to accept the proton from the inital intermediate **6a**, thus producing the 2H-pyran **7a** and the amine salt. If only one mole of amine is used, one half forms the 2H-pyran **7a** (which is immediately converted into the more stable vinylogous amide **8a**), while the other half is protonated. The remainder of the pyrylium salt is efficiently converted by traces of water, catalysed by the amide **8a** into the diketone **9a**. In support of this hypothesis, the pure vinylogous amide **8a** (R = n-Bu) was produced using 2 moles of n-butylamine and when another mole of pyrylium salt (**2a**) was subsequently added it was immediately and completely converted into the diketone **9a** as was evident from the C-13 spectrum.

Since the conversion of amines into other functional groups via the pyrylium salt route is a synthetically useful procedure it is desirable to use a reaction which proceeds efficiently using only *one* mole equivalent of amine. Since the purpose of the 2nd mole is to deprotonate an intermediate, it should be possible to substitute a tertiary amine for it. We have shown (from C-13 spectra) that the reaction of **2a** with (a) two moles of n-butylamine, or (b) one mole of n-butylamine and one mole of triethylamine in each case produced the pyridinium salt product **3a** (R = n-Bu) in quantitative yield at 20°, at approximately the same rate.

(b) *Benzylamine, cyclohexylamine and aniline.* The reaction of benzylamine (2 moles or 1 mole with 1 mole of triethylamine) with the pyrylium salt **2a** follows the same course as the reaction of n-butylamine discussed above. The vinylogous amide **8a** (R = $PhCH_2$) spectrum appears on mixing the solutions, and after 4 days the C-13 spectrum is that of the pyridinium salt (**3a**, R = $PhCH_2$) (for assignments see Table 2).

Reaction of 2 moles of cyclohexylamine with **2a** produces the vinylogous amide (**8a**, R = C_6H_{11}) (for spectral assignment see Table 2). At 20° ring closure to the pyridinium salt does not occur in DMSO.†

By contrast, reaction of two moles of aniline with the pyrylium salt **2a** gives (in < 40 min) the spectrum of the pyridinium salt **3a** (R = Ph). Here the conversion of the initially formed vinylogous amide (**8a**, R = Ph) into the pyridinium salt is too fast to obtain a C-13 spectrum under the conditions employed. The C-13 assignment for **3a**, R = Ph is shown in Table 2.

C-13 *Assignments*

The identification and assignments of the C-13 shifts of the intermediates and products is essential to the establishment of the reaction sequences. We now discuss the full C-13 assignments for the compounds in Table 1: those of Table 2 follow from intensity considerations, ORD measurements, and by comparison with Table 1. In Table 2 the assignment for the *o* and *m* carbons could well be reversed.

The assignment for the triphenylpyrylium salt **2a** and the 2-methoxy-2H-pyran **10** have been discussed previously.[5] The diketone **9a**, which is produced immediately by reaction of the pyrylium salt with hydroxide is easily recognisable from the two carbonyl signals. The non-conjugated carbonyl is assigned to the low field peak at 195.9 ppm by comparison with acetophenone.[6] Assignment of the other non-phenyl carbons, and the identification of the *ipso*- and *para*-carbons in the phenyl rings have been made from intensity considerations, chemical shifts and ORD spectra. However, assignments of carbon shifts to particular phenyl rings are very tentative. The *meta*-carbons are all assigned to the same peak at 128.7 ppm and the three remaining peaks assigned to the *ortho*-carbons.

Assignment of the chemical shifts for both the vinylogous amides **8** and the pyridinium salts **3** have been made from a comparison of the chemical shifts in the triphenyl- and tri((*p*-fluorophenyl)-compounds (**8a,b** and **5a,b** R = n-Bu), a technique previously used for the corresponding triarylpyrylium salts.[5]

For the pyridinium salts **3a,b** (R = n-Bu) the pyridinium ring carbons may be identified from ORD spectra, and from the small substituent chemical shifts induced by the *para*-fluoro substituent in the phenyl rings. The characteristic carbon-fluorine coupling constants[7] of the phenyl ring carbons allow complete assignment of the *para*-fluoro compound **3b** (R = n-Bu): we used known substituent chemical shifts for the fluorine substituent[7] to estimate the actual chemical shifts in the unsubstituted compound **3a** (R = n-Bu), comparison with the actual spectrum gave excellent agreement. Only the unique assignment of the 2,6-*ortho* and the 2,6-*meta* carbons to peaks at 129.1 and 129.2 remained uncertain.

The assignment for the vinylogous amide **8a** (R = n-

†In other solvent systems such as $CDCl_3$ the amide **8a**, R = C_6H_{11} does ring close.

Bu) similarly utilised the assignments of the fluorine compound **8b** (R = n-Bu), and the known substituent chemical shifts. In **8a** and **8b** (R = n-Bu) the differentiation between the phenyl ring carbons from those in the conjugated backbone of the molecule are readily made, as are the identification of the *ipso-*, *ortho-*, *meta-* and *para*-carbons in the phenyl rings, but the unique assignment of the phenyl carbons to a particular ring is arbitrary.

EXPERIMENTAL

The pyrylium salts were known compounds prepared by literature methods,[8] and were vacuum dried. The amines were distilled, and kept over molecular sieves. The DMSO-d_6 was standard spectral grade. In a typical experiment 0.2 g of pyrylium salt was dissolved in the DMSO (1.4 ml), and the calculated quantity of amine (usually 2 mole equivalents) was added rapidly from a microsyringe.

Spectroscopic measurements. The spectra were recorded at 28°C on a JEOL FX-100 spectrometer at 25.05 MHz. DMSO-d_6 was used as the internal reference and lock. Typical spectrometer conditions were 6 KHz width, 8 K data, giving a digital resolution of 0.05 ppm; pulse width 5 μsec (30°); repetition time 1 sec. Under these conditions spectra with sufficient signal to noise to detect the carbon signals for components >5% are obtained in *ca.* 15 min of accumulation.

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