The Reaction of Some 4-Pyrones with Activated Isocyanates

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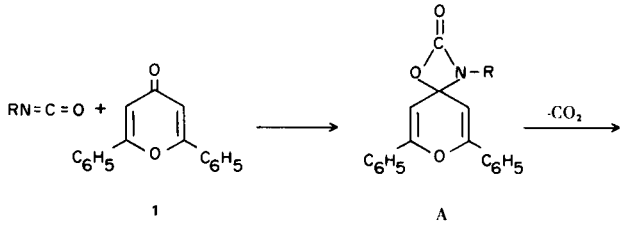
The pyrones, 2,6-diphenyl-4*H*-pyran-4-one, flavone, and 2-phenyl-4*H*-naphtho[2,1-*b*]pyran-4-one reacted with activated isocyanates, such as trichloroacetyl isocyanate, giving 4-trichloroacetylimino derivatives. These acylimino compounds underwent a slow reaction with a second mole of isocyanate to give a bisiminopyran.

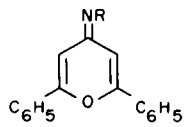
It is shown that carbonyl groups that are conjugated with electron-releasing groups will react with activated isocyanates.

In continuation of our study of the chemistry of 4-pyrones (1), we have investigated the reactions of 2,6-diphenyl-4*H*-pyran-4-one (**1**), flavone (**2**), and 2-phenyl-4*H*-naphtho[2,1-*b*]pyran-4-one (**3**) with trichloroacetyl isocyanate (**4**), chlorosulfonyl isocyanate (**5**), *p*-toluenesulfonyl isocyanate (**6**), and benzoyl isocyanate (**7**). The only work involving the reactions of isocyanates with a keto group that has come to our attention is that of Paquette (2), who described the reactions of diphenylcyclopropenone with activated isocyanates.

The isocyanates **4-7** reacted with **1** in acetonitrile at room temperature to give products that were assigned structures **8-11**, respectively. These were formed presumably *via* the unstable adduct A, formally produced by a $2\pi s$ - $2\pi a$ cycloaddition (3), followed by the loss of carbon dioxide to give the iminopyrans.

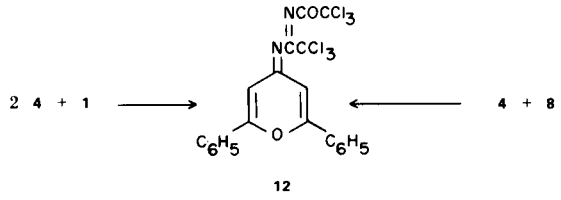


1 A



8 (R = $COCCl_3$)
9 (R = SO_2Cl)
10 (R = $SO_2C_6H_4CH_3$)
11 (R = COC_6H_5)

The reaction of two equivalents of **4** with one equivalent of **1** in acetonitrile at 90° gave **12**, which was also obtained by the reaction of **4** with **8**. Compound **13** was formed by the reaction of **4** with **10**. The apparent



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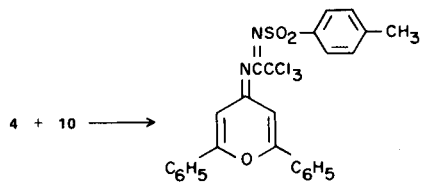

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rearrangement that took place during the formation of **13** from **10** and **4** can be explained on the basis of an addition of the isocyanate **4** to the imine bond (4) to give an adduct B, which, in turn, eliminated the less reactive isocyanate (5) giving **6** and **8**. The latter compounds reacted slowly to give the final product **13**, which was also demonstrated in a separate experiment. This reaction course is not without precedent, since Richter (4) reported that *p*-nitrophenyl isocyanate displaced the anil group of 4,4′-dimethylaminobenzophenone anil yielding phenyl isocyanate. We have also found that a benzoyl group was displaced by a trichloroacetyl group in the reaction of **11** with **4** to give **8**.

The acid hydrolysis of **8-13** with perchloric acid in acetic acid gave 4-amino-2,6-diphenylpyrylium perchlorate (**14**) in good yield; in fact, this is the preferred method for preparing **14**. Compounds **8** and **9** were regenerated by treating **14** with the appropriate acid chloride in pyridine solution.

Treatment of **8** with ammonium acetate in acetic acid gave 4-amino-2,6-diphenylpyridine (**15**). Compounds **9-11** did not react under these conditions. However, **11**

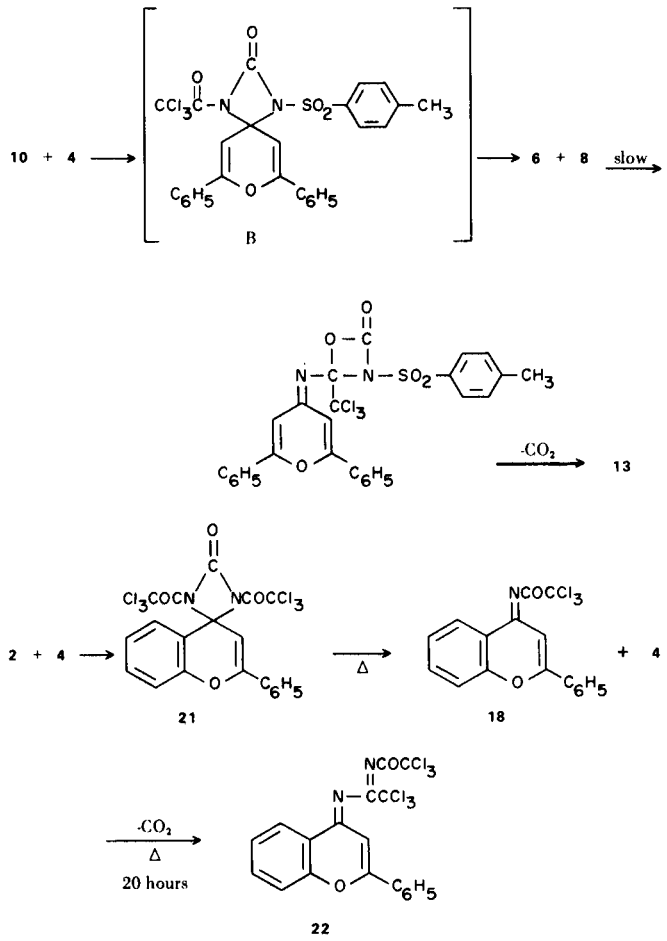
TABLE I

Physical Data

Compound Number	Empirical formula	Anal. Calcd./Found C	H	N	Cl or S	M.p., °C	Yield, %	Method of preparation	Crystn. solvent
8	$C_{19}H_{12}Cl_3NO_2$	58.1	3.1	3.6	27.1	144-145	97	A	CH_3CN
		58.1	3.2	3.9	26.8				
9	$C_{17}H_{12}ClNO_3S$	59.0	3.5		(S) 9.3	157-158	72	A	CH_3CN
		59.1	3.6		9.5				
10	$C_{24}H_{19}NO_3S$	71.8	4.8	3.5	(S) 8.0	177-178	87	A	CH_3NO_2
		72.0	4.5	3.3	8.0				
11	$C_{24}H_{17}NO_2$	82.0	4.9	4.0		159-160	35	A	CH_3NO_2
		82.1	4.9	4.0					
12	$C_{21}H_{12}Cl_6N_2O_2$	46.9	2.2	5.2	39.6	175-176	97	B	CH_3CN
		47.1	2.4	5.0	39.6				
13	$C_{26}H_{19}Cl_3N_2O_3S$	57.2	3.5	5.1	19.5	189-190	58	B	CH_3CN
		57.1	3.2	4.9	19.6				
14	$C_{17}H_{14}ClNO_5$	58.7	4.1	4.0	10.2	187-188	70-90	C	CH_3CO_2H
		58.9	3.9	3.9	10.4				
15	$C_{17}H_{14}N_2$	82.9	5.2	11.4		131-132	64	Exptl.	Ligroin (b.p. 100-115°)
		82.7	5.5	11.1					
16	$C_{24}H_{18}N_2O$	82.3	5.2	8.0		156-157	82	Exptl.	CH_3CN
		82.5	5.3	8.3					
17	$C_{17}H_{14}N_2O_3S$	62.6	4.3		(S) 9.8	187-188	67	Exptl.	C_2H_5OH
		62.9	4.1		9.8				
18	$C_{17}H_{10}Cl_3NO_2$	55.7	2.7		29.0	125-126	71	A	CH_3CN
		55.9	2.7		28.9				
19	$C_{15}H_{10}ClNO_3S$	56.3	3.2		(S) 10.0	202-203	85	A	CH_3CN
		56.4	3.1		10.3				
20	$C_{22}H_{17}NO_3S$	70.4	4.6		(S) 8.5	172-173	97	A	CH_3NO_2
		70.4	4.7		8.6				
21	$C_{20}H_{10}Cl_6N_2O_4$	43.3	1.8		38.3	92-93	78	A	Ligroin (b.p. 63-75°)
		43.5	2.1		38.6				
22	$C_{19}H_{10}Cl_6N_2O_2$	44.7	2.0		41.6	187-188	73	B	CH_3NO_2
		44.8	2.1		41.4				
23	$C_{15}H_{12}ClNO_5$	56.0	3.8	4.4		219-220	80	C	C_2H_5OH
		55.8	3.9	4.6					
24	$C_{15}H_{11}NO$	81.4	5.0	6.3		66-67	85	Exptl.	C_2H_5OH
		81.5	5.2	6.2					
25	$C_{21}H_{12}Cl_3NO_2$	60.5	2.9	3.4		249-250	94	A	$HCON(CH_3)_2$
		60.6	2.9	3.6					
26	$C_{19}H_{12}ClNO_3S$	61.7	3.2	3.8		220-221	92	A	CH_3CN
		62.0	3.5	3.8					
27	$C_{26}H_{19}NO_3S$	73.4	4.5	3.3		223-224	90	A	CH_3CN
		73.6	4.5	3.1					
28	$C_{19}H_{14}ClNO_5$	61.4	3.8		9.5	319-320	45	C	CH_3CO_2H
		61.6	4.1		9.6				
29	$C_{11}H_{11}Cl_3N_2O$	45.0	3.8		36.2	99-100	83	A	CH_3CN
		45.3	4.0		36.0				
30	$C_9H_{11}ClN_2SO_2$	43.8	4.5		14.4	134-135	80	A	CH_3CN
		44.0	4.4		14.7				

and ammonium hydroxide in pyridine gave 4-benzamido-2,6-diphenylpyridine (**16**); **9** gave 2,6-diphenyl-4-sulfonamidimino-4*H*-pyran (**17**), and **10** again did not react.

The reactions of flavone (**2**) with the isocyanates **4**, **5**, and **6** paralleled those of **1**, and 2-phenyl-4-trichloroacetylimino-4*H*-1-benzopyran (**18**), 4-chlorosulfonylimino-2-phenyl-4*H*-1-benzopyran (**19**), and 2-phenyl-4-(*p*-toluenesulfonyl)imino-4*H*-1-benzopyran (**20**) were obtained. We were able to isolate an adduct containing two equivalents of **4** and one equivalent of **2** to which we assign the sturcture **21**. This adduct is similar to the proposed adduct B and can be isolated because it possesses some stability; recrystallization of **21** resulted in the formation of **18**. When **21** or two equivalents of **4** and one equivalent of **2**

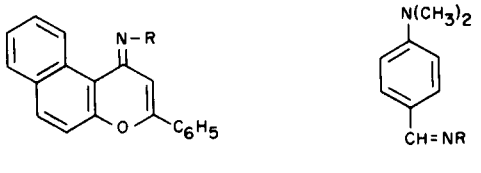


were refluxed for 20 hours in toluene, compound **22** was obtained. There is evidently a fast reversible addition of the isocyanate **4** to the imino bond of **18** and a very slow addition of **4** to the carbonyl bond of **18**, which is irreversible because of a decarboxylation step.

The imino compounds **18-20** were hydrolyzed with perchloric acid in acetic acid to 4-aminoflavylium perchlorate (**23**), which gave 4-imino-2-phenyl-4*H*-1-benzopyran (**24**) on treatment with methanolic potassium hydroxide.

The naphthopyrone derivative **3** reacted with **4**, **5**, and **6** to give the corresponding imino derivatives **25**, **26**, and **27**. The hydrolysis of **27** with perchloric acid gave 4-amino-2-phenylnaphtho[2,1-*b*]pyrylium perchlorate (**28**).

In order to demonstrate that a carbonyl group that is conjugated with an electron-donating group will react with activated isocyanates, 4-dimethylaminobenzaldehyde was allowed to react with **4**, and **5** and the products **29** and **30** were isolated. Benzaldehyde did not react with **4** and **5**.



25 (R = $COCCl_3$)
26 (R = SO_2Cl)
27 (R = $SO_2C_6H_4CH_3$)

29 (R = $COCCl_3$)
30 (R = SO_2Cl)

TABLE II

Mass Spectral Data

Compound No.	m/e (relative intensity)
8	356 (1.8) [M-Cl]; 328 (68) [m/e 356-CO]; 274 (100) [M-CCl_3]; 137 (4) [m/e 274^{++}]; 105 (12.5) [C_6H_5CO]; 102 (4) [$C_6H_5C{\equiv}$CH].
9	345 (85) [M^+]; 310 (100) [M-Cl]; 248 (6.5) [310-NSO]; 247 (8); 220 (13) [248-CO]; 191 (52) [220-HCO]; 105 (57); 102 (57).
10	401 (10) [M^+]; 337 (87) [M-SO_2]; 248 (35); 247 (40); 220 (100); 105 (82); 102 (70).
11	351 (5) [M^+]; 350 (4) [M-1]; 274 (100) [M-C_6H_5]; 246 (8.8) [M-C_6H_5CO]; 105 (16); 102 (26).
12	417 (100) [M-CCl_3]; 383 (14); 272 (15) [M-2CCl_3]; 258 (10) [272-N]; 150 (16) [417-CCl_3^+]; 105 (55); 102 (12).
13	544 (0.6) [M^+]; 427 (100) [M-CCl_3]; 272 (80) [427-tosyl]; 155 (14) [tosyl]; 105 (36); 102 (10).
15	246 (100) [M^+]; 245 (58) [M-1]; 230, 219, 218, 217, 102 = 2.5%.
17	326 (60) [M^+]; 310 (100) [M-NH_2]; 247 (13) [M-SO_2NH]; 246 (9) [M-SO_2NH_2]; 219 (20); 191 (40); 105 (20); 102 (20).

EXPERIMENTAL

The physical data for the compounds are collected in Table I. The syntheses are described by general procedures when possible. Some mass spectral data showing the typical fragmentation patterns are collected in Table II.

Method A.

A mixture of 0.01 mole each of **1** or 4-dimethylaminobenzaldehyde and the isocyanate in 10 ml. of acetonitrile was allowed to stand at room temperature for 1 hour (with the exception of **11**, which required 20 hours at reflux temperature). The solid was collected and crystallized from the appropriate solvent. The pyrones **2** and **3**, with the isocyanates and acetonitrile, required 1 hour at reflux temperature for satisfactory results.

Method B.

A mixture of 0.01 mole of the pyrone, 0.02 mole of isocyanate and 30 ml. of acetonitrile or a mixture of 0.01 mole of the iminopyran derivative and 0.01 mole of isocyanate in acetonitrile was refluxed for 1 hour, chilled, and the solid was collected. Compound **22** was obtained by this procedure after 20 hours of reflux time.

Method C.

A solution of 2 g. of the iminopyran in 40 ml. of acetic acid and 3 ml. of 70% perchloric acid was heated to boiling, cooled to room temperature, and the solid was collected.

4-Amino-2,6-diphenylpyridine (**15**).

A mixture of 1 g. of **8**, 10 ml. of acetic acid, and 4 g. of ammonium acetate was refluxed for 8 hours, diluted with water, made basic by the addition of ammonium hydroxide, boiled for 5 minutes, and after being chilled, the solid was collected.

4-Benzamido-2,6-diphenylpyridine (**16**).

A solution of 1 g. of **11**, 1 ml. of ammonium hydroxide, and 20 ml. of pyridine was refluxed for 5 minutes, diluted with water, chilled, and the solid was collected.

2,6-Diphenyl-4-sulfonamidimino-4*H*-pyran (**17**).

This compound was prepared by the method described for **16**.

4-Imino-2-phenyl-4*H*-1-benzopyran (**24**).

A solution of 1 g. of **23** and 20 ml. of 10% methanolic potassium hydroxide was diluted with water and then chilled.

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