Heterocycles in Organic Synthesis. Part 25.[1] Reagents for the Conversion of Halides into Aldehydes and Ketones

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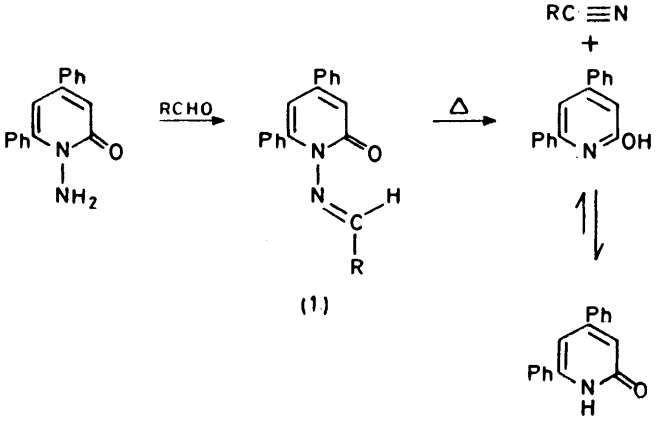
The sodium salts of 1-hydroxy-4,6-diphenyl-2-pyridone, 3-hydroxy-2-phenyl-4(3*H*)-quinazolinone, and 2-benzenesulphonamidopyridine 1-oxide react with alkyl and benzyl halides to give crystalline *N*-alkoxy- and *N*-benzyloxy-derivatives. The latter undergo thermolysis and photolysis to aromatic aldehydes and ketones in high yields. *N*-Alkoxy-analogues similarly yield aliphatic carbonyl compounds but these are contaminated by significant amounts of the corresponding alcohol.

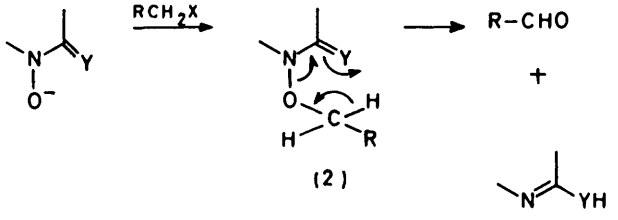
THE conversion of an alkyl halide into a non-chain-extended aldehyde or ketone involves a change in oxidation level. Routes, other than the one through the alcohol, are fairly numerous and include pathways *via* the amine (Sommelet reaction), *via* a nitrone (Kröhnke reaction), and *via* oxygen transfer agents which involve initial attack by an oxygen nucleophile followed by a base-catalysed elimination step. In the Sommelet reaction,[2,3] reaction of the halide with hexamethylenetetramine gives the formaldehyde imine of the corresponding primary amine which tautomerises into the methyl imine of the desired carbonyl compound. While satisfactory for many benzaldehydes having neither electron-deficient nor *ortho*-substituted rings, the reaction is of limited value for phenolic or aliphatic aldehydes prone to condensation.[2,3] The Kröhnke reaction[4] involves converting the halide to the pyridinium salt, which with *p*-*NN*-dimethylnitrosoaniline gives a nitrone: this is hydrolysed in aqueous acid to the carbonyl compound. The route is useful for aromatic and unsaturated aldehydes, dialdehydes, aromatic ketones, and steroid and isoprenoid carbonyl derivatives.[2] Possible



SCHEME 1

limitations arise from the use of both basic (in the nitrone-forming step) and acidic (in the hydrolysis) conditions.

The largest category of halide-to-carbonyl conversions, those involving an oxygen nucleophile, includes the well-established Kornblum method.[5,6] Normally the iodide is treated with dimethyl sulphoxide and the sulphoxonium salt decomposed to the carbonyl compound and dimethyl sulphide. The reaction is particularly convenient for benzyl bromides or iodides, but for aldehydes containing α-protons the basic conditions may cause unwanted condensations. Analogues of the Kornblum method include the use of *N*-oxides (in particular of trimethylamine,[7] pyridine,[8] and α-picoline[9]): the derived *N*-alkoxy-compounds decompose

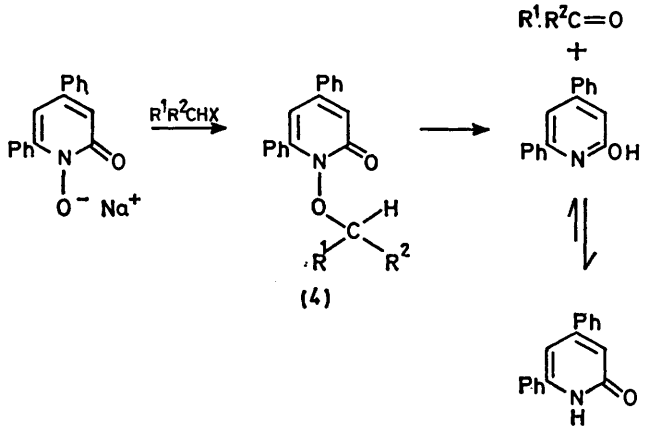


SCHEME 2

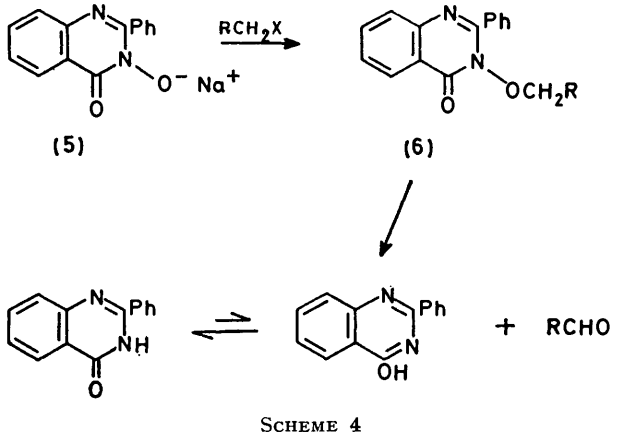
in base to give carbonyl compound and amine. Overall yields are moderate for both aromatic and aliphatic ketones but the recently observed E_2 decomposition[10] of certain *N*-alkoxypyridines to alkenes may limit the generality of this approach. The Hass–Bender reaction[11,12] involves *O*-alkylation of salts of nitroalkanes giving intermediates which, with strong base, decompose to the carbonyl compound and oxime. Yields are moderate to high, but some *C*-alkylation occurs[13] and use of strong base is again a potential drawback. Alkyl halides and metal nitrates give nitrate esters which in base decompose to aldehydes,[14–16] in some instances, notably involving mercuric salts,[16] in high yield. The reaction appears to be limited, however, to benzyl halides with non-oxidisable and non-hydrolysable substituents.

Novel alkyl halide-to-carbonyl conversions, which do not suffer limitations imposed by the pH of the media or by oxidising conditions, would provide useful alternatives to the methods outlined above. Following work from these laboratories[17] on the conversion of aldehydes into nitriles *via* intermediate (1) (Scheme 1) we now report investigations of conceptually similar pathways for 'non-oxidative' and neutral pH conversions of a halide into a carbonyl compound. The key steps (Scheme 2) are the formation of intermediates of type (2) and their subsequent thermal or photochemical decomposition. Three series have been investigated (Schemes 3—5) and an assessment is made of their synthetic utility. The base-catalysed decomposition of *N*-alkoxypicolinium[9] and *N*-alkoxylutidinium[18] salts are obviously

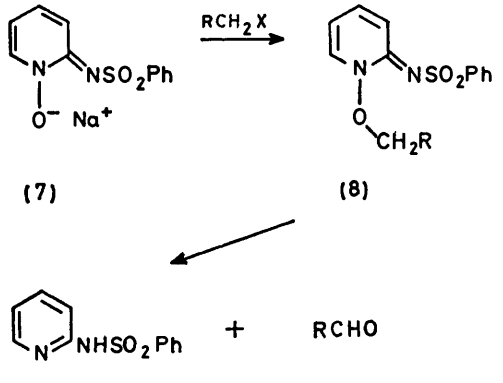
related to the decomposition step of Scheme 2. Prior to the present work a communication appeared concerning the photochemical decomposition of 1-alkoxy-4,6-dimethyl-2-pyridones to aldehydes,[19] and during the course of this investigation the thermal decomposition of a pyridinethione (Scheme 6) was also reported.[20]



SCHEME 3

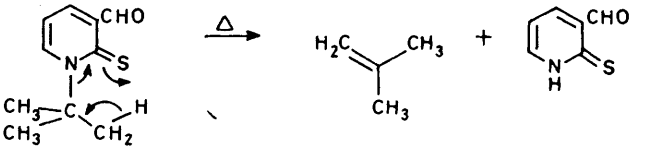


SCHEME 4



SCHEME 5

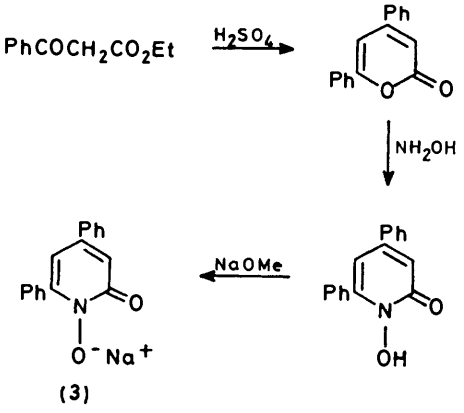
In selecting precursors for the reaction sequence of Scheme 2, those leading to non-volatile by-products were deemed to have greatest potential for synthetic work. Of the systems fulfilling this criterion, (3) was a natural choice, being the analogue of the precursor in the earlier work depicted in Scheme 1, while (5) and (7) added variety and were conveniently prepared.



SCHEME 6

Reactions using Sodium 1-Oxido-4,6-diphenyl-2-pyridone (Scheme 3).—The synthesis of (3) (Scheme 7) commenced with the acid-catalysed cyclisation of ethyl benzoylacetate into 4,6-diphenyl-2-pyrone in 30—35% yield using the conditions of Arndt and Eistert (3 weeks at room temperature).[21] Variation of these conditions did not significantly improve the yield. The pyrone with hydroxylamine hydrochloride gave 1-hydroxy-4,6-diphenyl-2-pyridone [22] which with sodium methoxide in methanol was converted into (3) in high yield. The salt (3) is a stable, colourless, mildly hygroscopic powder. In early experiments, some of which were reported in a preliminary communication,[1a] (3) was treated with alkyl halides in either dry methanol or ethanol, at 0 °C or under reflux, for 2—20 h depending upon the reactivity of the halide. *N*-Alkoxy-derivatives (4) precipitated on cooling and a further crop was obtained upon evaporation of the mother liquors. In later experiments dimethylformamide was shown to be a superior solvent for the reaction, leading to comparable or improved yields in shorter reaction times (*cf.* Table 1 with data in ref. 1*a*).

Results for the fragmentation of the *N*-benzyloxy-4,6-diphenyl-2-pyridones to the aromatic aldehydes are summarised in Table 2. With one exception, thermolytic decomposition was achieved in 2—5 h at 180—200 °C under vacuum using a distillation or sublimation unit as appropriate. The aromatic aldehydes were collected pure, free from the involatile 4,6-diphenyl-2-pyridone. Decomposition of the 2,4,6-trinitrobenzyloxy-compound occurred smoothly in refluxing xylene (140 °C), presumably because fragmentation is facilitated by the electron-withdrawing groups.



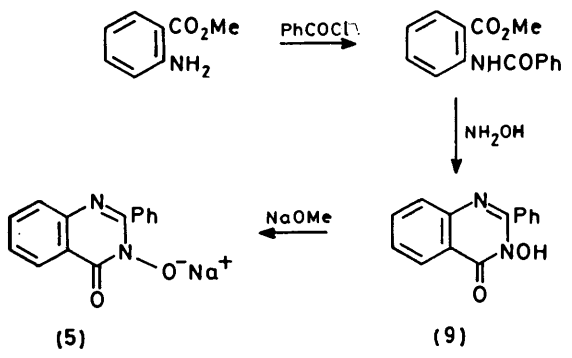
SCHEME 7

The photolytic decomposition of the *N*-benzyloxy-derivatives of (4) was investigated in various solvents but reactions in ethyl acetate and benzene proceeded most cleanly (Table 2). These solvents were also readily separated from the aldehydes by evaporation; several aldehydes co-distilled with methanol and ethanol. Steam distillation of the residue effected separation of the aldehyde from the by-product.

The *N*-alkoxy-derivatives (4; R^1 = alkyl, R^2 = H or alkyl) destined to give aliphatic aldehydes and ketones underwent thermal decomposition with varying degrees of success (Table 3). Yields of aldehydes were in the range 37—65 and of ketones, 32—66%. In some instances, the corresponding alcohol was also obtained and this side product was presumably the precursor to the 30% yield of styrene recovered during acetophenone preparation. Formation of alcohol finds analogy in the photochemical decomposition of *N*-decyloxy-4,6-dimethyl-2-pyridone.[19] In the decomposition of (4; $R^1 = C_7H_{15}$, R^2 = H), a rearrangement product was isolated and for (4; R = $PhCH_2$, R^2 = H) and (4; $R^1 = CH_2{=}CHCH_2$, R^2 = H) a by-product analysing for starting material less H_2CO was isolated. These products appear to be 2-pyridones with free NH groups but substituted at the 3-position. Further investigations of these and related products are in progress.

Three examples of photochemical decomposition to ketones and aliphatic aldehydes were investigated (Table 3). Acetophenone was obtained in higher yield than in the thermolysis experiments, but aliphatic aldehydes were contaminated by significant quantities of the corresponding alcohol (*cf.* ref. 19).

Reactions using Sodium 3-Oxido-2-phenyl-4(3H)-quinazolinone (5) (*Scheme* 4).[1b]—The salt (5) was readily prepared following the pathway in Scheme 8. The *N*-hydroxyquinazolinone (9),[23] obtained in 70% overall yield, was converted into the salt (5) using sodium methoxide in methanol. In dimethylformamide, reaction of (5) with alkyl halides generally began at room temperature and in the case of benzyl halides bearing electron-withdrawing groups was complete within 10 min. Other halides required gentle heating but in



SCHEME 8

TABLE 1

Preparation and characterisation of intermediates (4), (6), and (8)

	Structure R^1	R^2	Alkyl halide	Preparation: Solvent	Temp. (°C)	Time	Recryst. solvent	Crystal form	M.p.(°C)	Yield(%)	Elemental analysis: Found (%) C	H	N	Molecular formula	Required (%) C	H	N
(4)	C_6H_5	H	$C_6H_5CH_2Br$	DMF	20	2 h	EtOH	needles	127—129	94	81.3	5.45	4.2	$C_{24}H_{19}NO_2$	81.6	5.4	4.0
	2-ClC_6H_4	H	2-$ClC_6H_4CH_2Cl$	MeOH	66	7 h	C_6H_{12}	prisms	114—116	92	74.1	4.7	3.6	$C_{24}H_{18}ClNO_2$	74.3	4.7	3.6
	4-ClC_6H_4	H	4-$ClC_6H_4CH_2Cl$	DMF	20	2 h	EtOH	prisms	162—164	95	74.5	4.6	3.6	$C_{24}H_{18}ClNO_2$	74.3	4.7	3.6
	3-$NO_2C_6H_4$	H	3-$NO_2C_6H_4CH_2Br$	MeOH	66	3 h	MeOH	needles	120—121	94	72.2	4.75	6.9	$C_{24}H_{18}N_2O_4$	72.35	4.55	7.0
	4-$NO_2C_6H_4$	H	4-$NO_2C_6H_4CH_2Br$	DMF	20	1 h	$CHCl_3$–MeOH	needles	140—141	99	72.3	4.7	7.15	$C_{24}H_{18}N_2O_4$	72.35	4.55	7.0
	2,4,6-$(NO_2)_3C_6H_2$	H	2,4,6-$(NO_2)_3C_6H_2CH_2Cl$	MeOH	0	6 h	C_6H_6–MeOH	yellow needles	168—170	72	58.7	3.4	11.4	$C_{24}H_{16}N_4O_8$	59.0	3.3	11.5
	2-CNC_6H_4	H	2-$CNC_6H_4CH_2Br$	DMF	20	2 h	MeOH	needles	165—167	97	79.1	4.9	7.45	$C_{25}H_{18}N_2O_2$	79.35	4.8	7.4
	3-CNC_6H_4	H	3-$CNC_6H_4CH_2Br$	MeOH	66	1.5 h	MeOH	needles	140—142	97	79.4	4.7	7.4	$C_{25}H_{18}N_2O_2$	79.35	4.8	7.4
	2-$MeOC_6H_4$	H	2-$MeOC_6H_4CH_2Br$	MeOH	66	2.5 h	light petroleum–$CHCl_3$	needles	124—126	90	78.2	5.4	3.6	$C_{25}H_{21}NO_3$	78.3	5.5	3.65
	n-C_3H_7	H	n-C_4H_9Br	EtOH	78	20 h	EtOH	needles	109—111	94	78.85	6.7	4.6	$C_{21}H_{21}NO_2$	79.0	6.6	4.4
	n-C_6H_{13}	H	n-$C_7H_{15}Br$	EtOH	78	20 h	EtOH	needles	67—69	97	79.4	7.4	3.7	$C_{26}H_{27}NO_2$	79.7	7.5	3.9
	n-C_7H_{15}	H	n-$C_7H_{15}I$	DMF	70	3 h	EtOH	needles	80—82	94	79.6	7.6	3.7	$C_{28}H_{29}NO_2$	80.0	7.8	3.7
	$C_6H_5CH_2$	H	$C_6H_5(CH_2)_2Br$	DMF	70	3 h	EtOH	needles	128—130	99	81.5	5.7	3.9	$C_{25}H_{21}NO_2$	81.7	5.8	3.8
	$CH_2{:}CHCH_2$	H	$CH_2{:}CH(CH_2)_2Br$	DMF	50	4 h	C_6H_{12}	needles	67—69	90	79.6	6.1	4.5	$C_{21}H_{19}NO_2$	79.5	6.0	4.4
	$CH_2{:}CH$	H	$CH_2{:}CHCH_2Br$	DMF	40	3 h	light petroleum	needles	63—66	98	79.2	5.9	4.6	$C_{20}H_{17}NO_2$	79.2	5.65	4.6
	$CH_3CH{:}CH$	H	$CH_3CH{:}CHCH_2Cl$	DMF	50	4 h	C_6H_{12}–$CHCl_3$	prisms	105—106	96	79.1	6.0	4.4	$C_{21}H_{19}NO_2$	79.5	6.0	4.4
	CH_3	CH_3	$CH_3CHBrCH_3$	DMF	50	4 h	EtOH	needles	118—120	94	78.7	6.2	4.5	$C_{26}H_{19}NO_2$	78.7	6.3	4.6
	C_6H_5	CH_3	$C_6H_5CHBrCH_3$	DMF	50	1 h	EtOH	needles	129—131	93	81.6	6.0	3.9	$C_{25}H_{21}NO_2$	81.7	5.8	3.8
	C_6H_5	C_6H_5	$(C_6H_5)_2CHBr$	DMF	20	5 h	EtOH	needles	173—175	99	84.2	5.5	3.7	$C_{30}H_{23}NO_2$	83.9	5.4	3.3
(6)	C_6H_5		$C_6H_5CH_2Br$	DMF	85	15 min	MeOH	prisms	125—127	86	76.7	4.9	8.6	$C_{21}H_{16}N_2O_2$	76.8	4.9	8.5
	4-MeC_6H_4		4-$MeC_6H_4CH_2Cl$	DMF	90	15 min	MeOH	needles	126—127	78	77.3	5.5	8.0	$C_{22}H_{18}N_2O_2$	77.2	5.3	8.2
	2-ClC_6H_4		2-$ClC_6H_4CH_2Cl$	DMF	75	30 min	MeOH	needles	145—147	84	69.4	4.2	7.8	$C_{21}H_{15}ClN_2O_2$	69.5	4.2	7.7
	4-ClC_6H_4		4-$ClC_6H_4CH_2Cl$	DMF	90	20 min	MeOH	needles	130—131	77	69.1	4.4	7.5	$C_{21}H_{15}ClN_2O_2$	69.5	4.2	7.7
	4-CNC_6H_4		4-$CNC_6H_4CH_2Br$	DMF	20	10 min	MeOH	needles	153—155	83	74.5	4.3	11.6	$C_{22}H_{15}N_3O_2$	74.8	4.3	11.9
	3-CNC_6H_4		3-$CNC_6H_4CH_2Br$	DMF	20	10 min	MeOH	needles	147—149	75	75.0	4.6	11.5	$C_{22}H_{15}N_3O_2$	74.8	4.3	11.9
	n-C_3H_7		C_4H_9Br	DMF	95	45 min	MeOH	prisms	93—94	75	73.35	6.0	9.4	$C_{18}H_{18}N_2O_2$	73.4	6.2	9.5
	n-C_7H_{15}		$C_8H_{17}I$	MeOH	66	8 h	MeOH	prisms	42—43	28 [a]	75.2	7.55	8.0	$C_{23}H_{26}N_2O_2$	75.4	7.5	8.0
(8)	C_6H_5		$C_6H_5CH_2Br$	DMF	100	30 min	$CHCl_3$	prisms	134	82	63.4	4.8	8.5 [b]	$C_{18}H_{16}N_2O_3S$	63.5	4.7	8.2
	4-MeC_6H_4		4-$MeC_6H_4CH_2Cl$	DMF	100	30 min	EtOH	prisms	144—145	84	64.3	5.3	7.8 [c]	$C_{19}H_{18}N_2O_3S$	64.4	5.1	7.9
	4-ClC_6H_4		4-$ClC_6H_4CH_2Cl$	DMF	100	1.5 h	MeOH	prisms	143	91	57.65	4.3	7.6 [d]	$C_{18}H_{15}ClN_2O_3S$	57.7	4.0	7.5
	2-CNC_6H_4		2-$CNC_6H_4CH_2Br$	DMF	20	12 h	MeOH	prisms	135—137	92	62.6	4.4	11.3 [e]	$C_{19}H_{13}N_3O_3S$	62.45	4.1	11.5
	4-CNC_6H_4		4-$CNC_6H_4CH_2Br$	DMF	60	30 min	EtOH	prisms	177—178	94	62.4	4.3	11.5 [f]	$C_{19}H_{13}N_3O_3S$	62.45	4.1	11.5
	4-$NO_2C_6H_4$		4-$NO_2C_6H_4CH_2Br$	DMF	20	12 h	MeOH	plates	185	80	55.9	3.8	10.7 [g]	$C_{18}H_{13}N_3O_5S$	56.0	3.9	10.9
	n-C_3H_7		n-C_4H_9Br	DMF	60	3 h	MeOH	prisms	129—130	98	58.5	5.95	9.2 [h]	$C_{15}H_{18}N_2O_3S$	58.8	5.9	9.1
	n-C_7H_{15}		n-$C_8H_{17}I$	DMF	20	12 h	EtOH	plates	79	85	62.8	7.1	7.6 [i]	$C_{19}H_{26}N_2O_3S$	63.0	7.2	7.7

[a] Yield reduced during recrystallisation. [b] S found 9.4, required 9.4%. [c] S found 8.9, required 9.05%. [d] S found 8.5, required 8.55%. Cl found 9.7, required 9.5%. [e] S found 8.8, required 8.8%. [f] S found 8.8, required 8.8%. [g] S found 8.4, required 8.3%. [h] S found 10.4, required 10.5%. [i] S found 8.8, required 8.8%.

TABLE 2

Preparation of aromatic aldehydes [a]

Precursor		Thermolytic decomposition				Photolytic decomposition				
No.	R^1	Time/h	Temp./°C	Work-up	Yield (%)	Solvent	Time/h	Temp./°C	Work-up	Yield (%)
(4; R^2 = H)	C_6H_5	4	200	*b*	73	EtOAc	4	20	*c*	80
						C_6H_6	4	20	*c*	73
	2-ClC_6H_4	5	195	*b*	77					
	4-ClC_6H_4	3	180	*d*	85	EtOAc	4	20	*c*	95
						C_6H_6	4	20	*c*	86
	3-$NO_2C_6H_4$	2	190	*d*	71					
	4-$NO_2C_6H_4$	4	190	*d*	79	EtOAc	4	20	*c*	53
	2,4,6-$(NO_2)_3C_6H_2$ [e]	4	140	*c*	93					
	2-CNC_6H_4	5	190	*d*	86					
	3-CNC_6H_4	3	200	*d*	70	EtOAc	4	20	*c*	46
						C_6H_6	4	20	*c*	50
	2-$MeOC_6H_4$	8	200	*b*	79					
	R									
(6)	C_6H_5	4	240	*b*	62	CH_2Cl_2	8	20	*f*	66
	4-MeC_6H_4					CH_2Cl_2	9	20	*f*	63
	2-ClC_6H_4	4	240	*b*	65	C_6H_6	4	20	*f*	69
	4-ClC_6H_4					C_6H_6	4	20	*f*	67
	4-CNC_6H_4					C_6H_6	5	20	*c*	53
	3-CNC_6H_4					C_6H_6	5	20	*c*	46
(8)	C_6H_5	3	205	*b*	75	$(CH_3)_2CO$	0.5	20	*g*	81
	4-MeC_6H_4	3	205	*b*	37	$(CH_3)_2CO$	0.5	20	*g*	86
	4-ClC_6H_4	3	205	*d*	61	$(CH_3)_2CO$	0.5	20	*g*	93
	2-CNC_6H_4	3	205	*d*	67	$(CH_3)_2CO$	0.5	20	*g*	63
	4-CNC_6H_4	4	205	*d*	86	$(CH_3)_2CO$	0.5	20	*g*	78
	4-$NO_2C_6H_4$	1	225	*d*	78					

[a] Products were identified by spectroscopic (i.r. and n.m.r.) comparison with authentic samples. They were further characterised on the basis of m.p. (for solids) and the m.p. of the 2,4-DNP derivative. All m.p.s were in agreement with those reported in standard tables. [b] Aldehyde isolated by vacuum-distillation of thermolysis products. [c] Aldehyde obtained by steam-distillation after removal of solvent under vacuum. [d] As *b* but aldehyde collected as a solid ('cold finger'). [e] Reaction performed in hot xylene solution. Product isolated by precipitation on addition of light petroleum to cooled solution. [f] Residue, after evaporation of solvent, treated with 5M-H_2SO_4 and extracted into $CHCl_3$. Extracted material vacuum-distilled. [g] Solution evaporated to dryness and aldehyde extracted, free of contaminants, into ether–light petroleum (9 : 1).

TABLE 3

Preparation of ketones and aliphatic aldehydes [a]

Precursor			Thermal decomposition					Photolytic decomposition					
						Yield (%)						Yield (%)	
No.	R^1	R^2	Time/h	Temp./°C	Work-up	Carbonyl	Alcohol	Solvent	Time/h	Temp./°C	Work-up	Carbonyl	Alcohol
(4)	Pr^n	H	3	240	*b*	59	10						
	n-C_6H_{13}	H	3	240	*b*	62	4						
	n-C_7H_{15}	H	4	240	*b*	37	13 [c]	EtOAc	5	20	*d*	47	23
	$C_6H_5CH_2$	H	4	220	*b*	49	0 [e]	EtOAc	5	20	*d*	30	20
	$CH_2{:}CHCH_2$	H	3	230	*b*	50	0 [e]						
	$CH_2{:}CH$	H	4	200	*b*	65	0						
	$CH_3CH{:}CH$	H	4.5	200	*b*	53	0						
	CH_3	CH_3	3.5	220	*f*	32	0						
	C_6H_5	CH_3	3.5	210	*b*	66	4 [g]	EtOAc	4	20	*d*	85	5
	C_6H_5	C_6H_5	3	200	*b*	54	0						
	R												
(6)	Pr^n		4	230	*h*			MeOH	8	20	*i*		
	n-C_7H_{15}							C_6H_6	7.5	20	*i*		
(8)	Pr^n		6	170	*b*	14	32						
	n-C_7H_{15}		24	170	*b*	23	23	C_6H_6	0.5	20	*j*		

[a] Products were identified by spectroscopic (i.r. and n.m.r.) comparison with authentic samples, and by physical constants either of the material or of the 2,4-DNP derivative. Unless where otherwise stated, yield refers to isolated carbonyl compound or carbonyl–alcohol mixture as appropriate, the composition of mixtures being determined by g.l.c. analysis. [b] Vacuum distillation of thermolysis products. [c] Small yield of a rearrangement product also isolated. [d] Evaporation of solvent under reduced pressure and steam-distillation of the residue. [e] Low yield of product isolated analysing for precursor less H_2CO. [f] Distillation under nitrogen using a solution of Brady's reagent to trap acetone as the 2,4-DNP derivative: yield assessed on the basis of the yield of 2,4-DNP. [g] Styrene (30% yield) was also isolated. [h] Precursor distilled over largely undecomposed at 230 °C and 15 mmHg. [i] Solvent removed under vacuum, and residue steam-distilled to afford negligible product: i.r. spectrum shows alcohol as principal product. [j] Solvent removed under vacuum to afford sticky residue containing at least four components. A similar result was obtained using acetone as solvent.

all instances reaction was complete within 45 min. Reactions were monitored conveniently either by t.l.c. or by colour change (yellow to colourless, with precipitation of sodium halide). In isolated cases the organic product (6), precipitated. High yields were also obtained using methanol as solvent but much longer reaction times were required, as illustrated by the example in Table 1.

Generation of the intermediate (6) was also attempted in tetrahydrofuran by alkylation of (9) in the presence of sodium hydride. However, yields were consistently lower, *e.g.* (6; R = phenyl, yield 55%; R = *o*-chlorophenyl, 51%). An excess of sodium hydride appeared to cause decomposition, most probably to the desired aldehyde (see later) but the process was not investigated further because of its relative inefficiency.

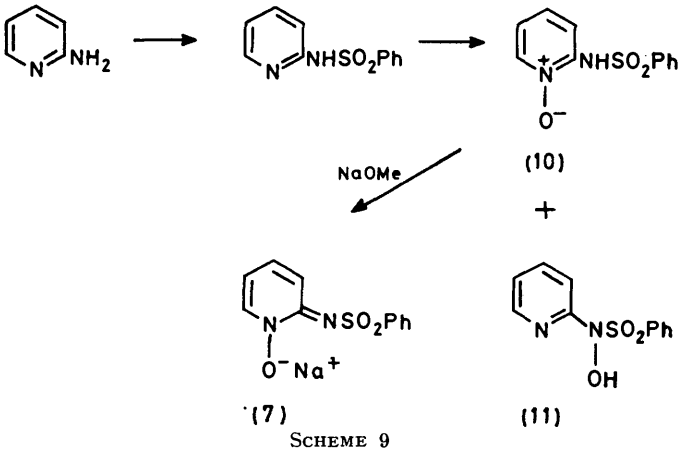
The results of solid-state thermolyses of the *N*-benzyloxy-derivatives are reported in Table 2. Reactions were performed as for the decomposition of series (4) above. Isolated yields of the two aromatic aldehydes which were prepared appeared to be proportional to the pyrolysis temperature, reaching 62 and 65% at 240 °C. Attempts were also made to decompose (6; R = Ph) in solution. However after 3.5 days in refluxing xylene, starting material was recovered in >70% yield. Similarly, no decomposition was apparent after 4.5 days in refluxing dimethylformamide. However addition of an equivalent of a halide salt to the latter solution catalysed partial decomposition to benzaldehyde. Yields of benzaldehyde, as the 2,4-dinitrophenyl derivative, were 32% after 20 h with potassium iodide, 13% after 2 days with lithium chloride, and 11% after 14 h with sodium bromide.

N-Benzyloxy-derivatives (6; R = aryl) were more conveniently decomposed to the aromatic aldehyde under photolytic conditions. Aldehydes were recovered by evaporation of the solvent, followed by steam distillation or extraction of a solution of the residue in acid. Photolyses in benzene solution afforded good yields of aromatic aldehyde within 4 or 5 h, and the isolated materials were essentially pure (g.l.c.), containing no more than trace amounts of the corresponding alcohol. Photolyses in methylene chloride afforded aldehydes in comparable yield and purity but reaction times were about twice as long. In acetone solution yields were slightly lower and there were small amounts of unidentified side products.

Attempts to prepare aliphatic aldehydes by either thermolysis or photolysis were disappointing. Under thermolysis conditions, (6; R = n-propyl) merely distilled largely undecomposed, and on photolysis the same compound and its homologue (6; R = n-heptyl) decomposed to give the alcohol as the major product.

Reactions using Sodium 2-Benzenesulphonylimino-1-oxidopyridine (7) (*Scheme* 5).—The salt (7) was prepared readily from 2-aminopyridine according to Scheme 9. Oxidation of 2-benzenesulphonamidopyridine afforded a readily separable mixture of the desired 1-oxide (10) and the isomeric *N*-hydroxy-compound (11). Reaction of (10) with sodium methoxide gave the salt (7) which precipitated out of solution in near quantitative yield and was dried and used without further purification. Alkylation of (7) to give the intermediate (8) was achieved by treatment of a halide with a suspension of (7) in dimethylformamide at either ambient or elevated temperature. As the reaction proceeded the solution became clear. The products (8) prepared in this way are reported in Table 1.

N-Benzyloxy-derivatives were thermolysed using the same procedure as above and aromatic aldehydes were obtained in moderate to good yield at temperatures in excess of 200 °C. Reaction times were in the range 1—4 h. This series, however, decomposed extremely readily under photochemical conditions. Indeed, a solid sample of (8; R = Ph) gave off benzaldehyde when



SCHEME 9

stood on the bench in sunlight. Under u.v. irradiation in acetone solution, the five examples investigated all decomposed to the aldehyde in <30 min and samples obtained were free of side-products.

However, as with Schemes 3 and 4, attempts to decompose the intermediates to aliphatic aldehydes were largely unsuccessful. Thermolysis of (8; R = n-propyl) and (8; R = n-heptyl) gave mixtures containing both aldehyde and alcohol, and photolysis of the latter in both acetone and benzene solution afforded a sticky product containing at least four components (t.l.c.).

Schemes (3)—(5) *as Synthetic Methods.*—The present Schemes provide access to aromatic aldehydes and aromatic ketones from benzyl halides under neutral and non-oxidative conditions, and thus offer advantages over existing methods. However, the Schemes do not provide synthetically useful routes to carbonyl compounds of the aliphatic series because of the formation of side-products, notably the corresponding alcohol.

The precursors (3), (5), and (7) are all readily prepared but the synthesis of (3) involves a lengthy (3 week) step. The salts are stable and easy to handle and their alkylation proceeds readily in dimethylformamide, the conversion of (5) into (6) being the most rapid. The intermediates (4), (6), and (8) are again easy to handle and provide useful crystalline products for characterisation, particularly for benzyl halides. From the practical viewpoint their decomposition to aldehydes is

more conveniently achieved by thermolysis because the product simply volatilises out of the reaction vessel. Of the three, fragmentation of (4) requires the lowest temperatures. Photolytic cleavage, though requiring separation of product from solvent, should be a useful alternative for heat sensitive aldehydes; here decomposition of (8) is particularly facile offering high yields after short reaction times.

EXPERIMENTAL

M.p.s were determined using a Reichert hot stage microscope. I.r. spectra were recorded using a Perkin-Elmer 257 spectrophotometer. N.m.r. spectra were obtained using a Varian HA 100 or a Perkin-Elmer R 12 spectrometer.

Materials.—Alkyl and benzyl halides were obtained as commercial samples or generously donated by Mr. J. E. Arrowsmith, and were used either as such or after distillation. Solvents were dried by standard methods. The following were prepared by literature methods: 4,6-diphenyl-2-pyridone,[21] m.p. 137—139 °C (lit.,[21] 139—140 °C); 1-hydroxy-4,6-diphenyl-2-pyridone,[22] m.p. 160—162 °C (lit.,[22] 162 °C); 2-carboxymethylbenzanilide (used as the crude material, see ref. 1*b*); 3-hydroxy-2-phenyl-4(3*H*)-quinazolininone,[23] m.p. 176—180 °C (lit.,[23] 176—177 °C); and 2-benzenesulphonamidopyridine,[24] m.p. 172 °C (lit.,[24] 171—172 °C).

Sodium 1-Oxido-4,6-diphenyl-2-pyridone (3).—1-Hydroxy-4,6-diphenyl-2-pyridone (39.5 g) and dry MeOH (500 ml) were heated under reflux, and sodium (3.45 g) in dry MeOH (150 ml) was added during 0.5 h. After 1 h, the mixture was cooled and the *salt* (3) separated as white needles. The MeOH was evaporated off and a second crop collected. The combined precipitates (40.1 g, 94%) were dried *in vacuo* over P_2O_5 and used without crystallisation, m.p. 299—301 °C (Found: C, 72.4; H, 4.2; N, 4.7. $C_{17}H_{12}NaNO_2$ requires C, 71.6; H, 4.2; N, 4.9%); $\nu_{max.}$ ($CHBr_3$) 1 630 cm^{-1} (C=O); δ[$(CD_3)_2SO$] 6.4 (1 H, s), 6.5 (1 H, s), and 7.5 (10 H, m).

Sodium 3-Oxido-2-phenyl-4(3H)-quinazolinone (5).—Recrystallised 3-hydroxy-2-phenyl-4(3*H*)-quinazolinone (16.4 g) was added to a solution resulting from the reaction of sodium (1.60 g) with MeOH (150 ml). The resulting solution was stirred 1 h. The reaction mixture was evaporated to dryness and the residue dried over P_2O_5 to yield the crude sodium salt which was used without further purification.

2-Benzenesulphonamidopyridine 1-Oxide (10).—To 2-benzenesulphonamidopyridine (14.0 g) in 98% formic acid (25 ml) was added 30% (100 vol) hydrogen peroxide (10 ml) and the solution warmed to 55—60 °C. After 3 h, further hydrogen peroxide (15 ml) was added and the solution left overnight. The solvent was removed under reduced pressure and the residue recrystallised from 10% v/v aqueous AcOH (20 ml), washed with water, and stirred in a solution of $NaHCO_3$ (5 g) in water (35 ml) for 2 h. The undissolved *N-hydroxy-compound* (11) (2.9 g, 20%), m.p. 168—170 °C, was recrystallised as needles from EtOH (Found: C, 52.7; H, 4.1; N, 11.2; S, 12.9. $C_{11}H_{10}N_2O_3S$ requires C, 52.8; H, 4.0; N, 11.2; S, 12.8%); $\nu_{max.}$ (Nujol) 3 200—2 500, 1 590, and 1 070 cm^{-1}. The alkaline solution was acidified (conc. HCl) and the precipitated *2-benzenesulphonamidopyridine 1-oxide* (10) (4.0 g, 27%), m.p. 155 °C, recrystallised as needles from EtOH (Found: C, 52.8; H, 4.1; N, 11.1; S, 12.9. $C_{11}H_{10}N_2O_3S$ requires C, 52.8; H, 4.0; N, 11.2; S, 12.8%); $\nu_{max.}$ (Nujol) 1 600, 1 560, 1 500, 1 260, 1 210, 1 170, and 1 090 cm^{-1}.

Sodium 2-Benzenesulphonylimino-1-oxidopyridine (7).—To a solution of sodium (278 mg) in dry MeOH (20 ml) was added 2-benzenesulphonamidopyridine 1-oxide (3.00 g) and the mixture stirred for 1 h. The precipitated salt (7) was collected by filtration, washed (MeOH and $CHCl_3$), dried under vacuum, and used without further purification.

General Procedures for Alkylation Reactions.—Alkylation of (3) *in alcohols.* The halide (0.8 g) and (3) (1.1 mol. equiv.) in dry MeOH or EtOH (40 ml) were allowed to react at 0 °C or under reflux for 2—20 h, depending upon the reactivity of the halide. The cooled solution was filtered and evaporated to dryness. The intermediate (4) was separated from the excess of (3) and sodium halide by extraction into $CHCl_3$, and subsequent recrystallisation from aqueous EtOH.

Alkylation of (3) *in dimethylformamide.* The halide (1.0 g), (3) (1.1 mol. equiv.) and dry $HCONMe_2$ (15 ml) were stirred at 20 or 60 °C for 2—12 h, depending on the reactivity of the halide. The cooled solution was diluted with water (150 ml) and extracted with $CHCl_3$ (3 × 75 ml). The combined extracts were washed with water (2 × 75 ml), dried ($MgSO_4$), filtered, evaporated *in vacuo*, and the residue was crystallised from the appropriate solvent.

Alkylation of (5) *in methanol.* To a solution of the sodium salt of (5) (5.20 g, 20 mmol) in MeOH (50 ml) was added one equivalent of the appropriate alkyl halide and the solution was refluxed and stirred until t.l.c. (silica gel–$CHCl_3$) indicated virtually complete reaction (6—10 h). The cooled reaction mixture was poured into saturated aqueous NH_4Cl and extracted with $CHCl_3$. The $CHCl_3$ extracts were dried ($MgSO_4$) and evaporated *in vacuo* and the residue recrystallised from the appropriate solvent.

Alkylation of (5) *in dimethylformamide.* 3-Hydroxy-2-phenyl-4(3*H*)-quinazolinone sodium salt (2.6 g; 10 mmol) was dissolved in $HCONMe_2$ (10 ml). The appropriate halide (10 mmol) was added and the solution stirred at room temperature for 10 min or warmed at 70—80 °C for 15—20 min. The reaction mixture was poured into water (50 ml) and extracted with $CHCl_3$ (3 × 20 ml). The extracts were dried ($MgSO_4$), evaporated *in vacuo*, and the residue recrystallised from the appropriate solvent. ^1H N.m.r. spectra of all esters showed a doublet at δ 8.38 and a complex multiplet in the region δ 6.8—8.0 for the other aromatic protons.

Alkylation of (7) *in dimethylformamide.* To a suspension of the sodium salt (7) (4.0 g) in dry $HCONMe_2$ (30 ml) was added one equivalent of the appropriate alkyl halide and the reaction mixture stirred at room temperature or heated until complete reaction (t.l.c.). The cooled mixture was poured into water (200 ml) and the alkylated product which precipitated was filtered off, dried, and crystallised from the appropriate solvent.

General Procedure for Solid Phase Thermolysis Reactions.—For those intermediates affording liquid thermolysis products, the material was placed in a Claisen distillation flask and heated on an oil-bath under vacuum to the temperature and for the time reported in Tables 2 and 3. The carbonyl compound was collected in a cooled (−78 °C) receiver. For solid aldehydes and ketones, the intermediate was thermolysed under vacuum in a sublimation unit, and the product collected on a cold finger.

Thermolysis of [4; R^1 = 2,4,6-$(NO_2)_3C_6H_2$, R^2 = H] *in Xylene.*—The named compound (0.49 g) in xylene (20 ml)

was heated under reflux under nitrogen for 4 h. When cool light petroleum (40—60 °C) (100 ml) was added and 4,6-diphenyl-2-pyridone (0.24 g, 99%) was collected by filtration. The solution was evaporated to dryness to afford 2,4,6-trinitrobenzaldehyde (0.22 g, 93%), m.p. 115—117 °C (from EtOH) (lit.,[25] 119—119.5 °C).

Attempted Thermolysis of (6; R = Ph) *in Xylene.*—The named compound (495 mg) in xylene (11 ml) was heated under reflux for 3.5 days. T.l.c. showed at least 3 components of which that corresponding to starting material predominated. Further experiments in the presence of an equivalent of an alkali metal salt gave the following yields of benzaldehyde (isolated as the 2,4-dinitrophenyl derivative after addition of Brady's reagent to the residue remaining after removal of the solvent): KI, 32% after 20 h; LiCl, 13% after 2 days; NaBr, 11% after 14 h.

General Procedure for Photolysis Reaction.—A solution of the intermediate (*ca.* 4.0 mmol) in the appropriate solvent (100 ml), contained in a water-cooled Pyrex cell, was degassed (dry N_2) for 1—2 h. The solution was irradiated using a Hanovia medium-pressure mercury lamp for the times reported in Tables 2 and 3. The solvent was removed under vacuum and the product isolated by the procedure indicated in the Tables.

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REFERENCES

[1] Part 24, A. R. Katritzky, P.-L. Nie, A. Dondoni, and D. Tassi, *J.C.S. Perkin I*, 1979, 1961; preliminary communications, (*a*) M. J. Cook, A. R. Katritzky, and G. H. Millet, *Heterocycles*, 1977, **7**, 227; (*b*) A. R. Katritzky and S. B. Brown, *Synthesis*, 1978, 619.

[2] S. J. Angyal, *Organic Reactions*, 1954, **8**, 197.

[3] S. J. Angyal, P. J. Morris, J. R. Tetaz, and J. G. Wilson, *J. Chem. Soc.*, 1950, 2141.

[4] F. Kröhnke and E. Borner, *Chem. Ber.*, 1936, **69**, 2006; F. Kröhnke, *ibid.*, 1938, **71**, 2583.

[5] N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, *J. Amer. Chem. Soc.*, 1957, **79**, 6562; N. Kornblum, W. J. Jones, and G. J. Anderson, *ibid.*, 1959, **81**, 4113.

[6] A. P. Johnson and A. Pelter, *J. Chem. Soc.*, 1964, 520.

[7] V. Franzen and S. Otto, *Chem. Ber.*, 1961, **94**, 1360.

[8] W. Feely, W. L. Lehn, and V. Boekelheide, *J. Org. Chem.*, 1957, **22**, 1135.

[9] V. J. Traynelis and J. P. Kimball, *J. Org. Chem.*, 1975, **40**, 2365.

[10] H. Sliwa and A. Tartar, *Tetrahedron Letters*, 1976, 1315; *Tetrahedron*, 1977, **33**, 3111.

[11] H. B. Hass and M. L. Bender, *J. Amer. Chem. Soc.*, 1949, **71**, 1767; *Org. Synth.*, Coll. Vol. IV, 1963, 932.

[12] I. N. Nazarov, S. M. Makin, V. B. Mochalin, and D. V. Nazarova, *Zhur. obshchei Khim.*, 1959, **29**, 3965 (*Chem. Abs.*, 1960, **54**, 21,170g).

[13] N. Kornblum, P. Pink, and K. V. Yorka, *J. Amer. Chem. Soc.*, 1961, **83**, 2779.

[14] J. W. Baker, W. S. Nathan, and C. W. Shoppee, *J. Chem. Soc.*, 1935, 1847.

[15] R. L. Letsinger and J. D. Jamison, *J. Amer. Chem. Soc.*, 1961, **83**, 193.

[16] A. McKillop and M. E. Ford, *Synth. Comm.*, 1974, **4**, 45.

[17] J. B. Bapat, R. J. Blade, A. J. Boulton, J. Epsztajn, A. R. Katritzky, J. Lewis, P. Molina-Buendia, P.-L. Nie, and C. A. Ramsden, *Tetrahedron Letters*, 1976, 2691.

[18] W. N. Marmer and D. Swern, *J. Amer. Chem. Soc.*, 1971, **93**, 2719.

[19] H. Furrer, *Tetrahedron Letters*, 1974, 2953.

[20] J. Becher and E. G. Frandsen, *Tetrahedron Letters*, 1976, 3347.

[21] F. Arndt and B. Eistert, *Chem. Ber.*, 1925, **58**, 2318.

[22] I. E.-S. El-Kholy, F. K. Rafla, and M. M. Mishrikey, *J. Chem. Soc.* (*C*), 1970, 1578.

[23] D. Harrison and A. C. B. Smith, *J. Chem. Soc.*, 1960, 2157.

[24] J. P. English, D. Chappell, P. H. Bell, and R. O. Roblin, jun., *J. Amer. Chem. Soc.*, 1942, **64**, 2516.

[25] A. R. Norris, *Canad. J. Chem.*, 1967, **45**, 175.