Nucleophilic Displacement with Heterocycles as Leaving Groups. Part 16.[1] Reactions of Secondary Alkyl Primary Amines with 5,6,8,9-Tetrahydro-7-phenyldibenzo[*c,h*]xanthylium Trifluoromethanesulphonate to give Intermediates Solvolysing without Rearrangement

Alan R. Katritzky,* Maria L. Lopez-Rodriguez, James G. Keay, and Roy W. King
Department of Chemistry, University of Florida, Gainesville, Florida 32611, U.S.A.

Representative secondary alkyl primary amines $R^1R^2CHNH_2$ react with the title pyrylium cation in acetic acid, alcohols, phenols, and *NN*-dimethylaniline acting as nucleophilic solvents to give *O*- and *C*-(secondary alkyl) products. Absence of carbenium ion rearrangements is consistent with reaction *via* intimate ion–molecule pairs formed rapidly from the corresponding pyridinium cations.

This series of papers has investigated the kinetics and mechanism of the nucleophilic development of *N*-primary alkyl and *N*-secondary alkyl groups from pyridinium compounds. As recently summarized,[2] cogent evidence has been obtained for discrete mechanisms: classical S_N2, classical S_N1 *via* free carbenium ions, and both first- and second-order reactions of intimate ion–molecule pairs. The identification of reaction products, and particularly the presence or absence of rearrangement, has played an important part in the interpretation.

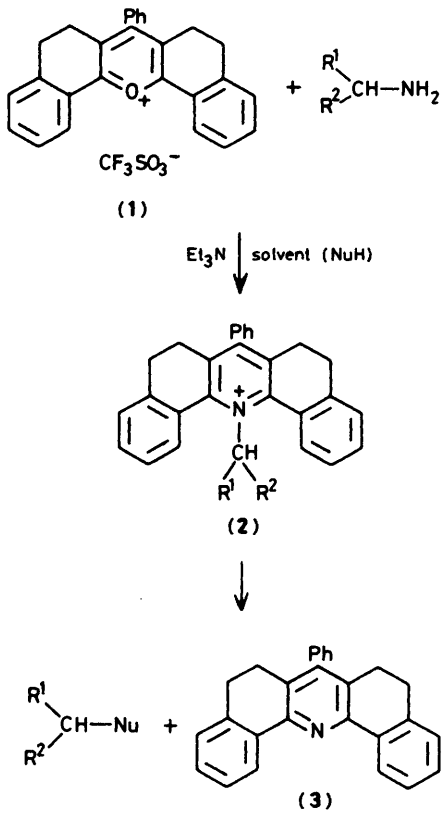
N-n-Octyl- and *N*-n-dodecyl-acridinium ions are solvolysed[3] in phenol at 140 °C to give a mixture of the n-alkyl phenyl ethers and all the isomeric secondary straight-chain *o*- and *p*-alkylphenols, probably *via* carbenium ion intermediates. Studies[1] of the solvolysis reactions of 1-(1-methylbutyl)- and 1-(1-ethylpropyl)-5,6-dihydro-2,4-diphenylbenzo[*h*]quinolinium salts have revealed that these reactions proceed *via* free carbenium ions with rearrangement in trifluoroacetic acid and 1,1,1,3,3,3-hexafluoropropan-2-ol, yet in acetic acid solvolysis occurred without any rearrangement.

We recently reported reactions of 2,4,6-triphenylpyrylium salts with the secondary alkyl primary amines 1-phenylethylamine and (diphenylmethyl)amine. Spontaneous further reaction of the intermediate pyridinium cations led to the room-temperature conversion of these amines into ethers, esters, and *C*-alkylated products.[4] Chiral 1-phenylethylamine (in acetic acid) gave 1-phenylethyl acetate with complete inversion of configuration,[5] indicating solvolysis *via* a tight ion–molecule pair.

We now report that aliphatic secondary alkyl primary amines react at ambient temperature with the xanthylium salt (**1**) to give solvolysis products of cations (**2**) without rearrangement. Use of 5,6,8,9-tetrahydro-8-phenyldibenzo[*c,h*]acridine (**3**) as a leaving group is known[6] to promote N–C bond heterolysis by steric compression and gives rates enhanced over the 2,4,6-triphenylpyridine analogues.[6]

The xanthylium salt (**1**) was treated at 25 °C with a variety of secondary alkylamines in nucleophilic solvents (Scheme 1) and the products analysed by ^1H and ^{13}C n.m.r. spectroscopy and gas chromatography–mass spectrometry. ^{13}C Peak assignments were made by considerations of chemical shift and off-resonance decoupling.

With acetic acid as nucleophile, the corresponding secondary alkyl acetates (see Table 1) were formed without any rearrangement. Thus, gas chromatography–mass spectrometry of the solvolysis reaction of 1-methylhexylamine with (**1**) in acetic acid showed only the presence of 1-methylhexyl acetate. Similar results were obtained with cycloheptyl-, 1-methylbutyl-, and 1-ethylpropyl-, giving the corresponding cycloheptyl, 1-methylbutyl, and 1-ethylpropyl acetates, respectively. Products were identified by their ^1H and ^{13}C n.m.r. spectra (Tables 2 and 3).



Scheme 1. R^1R^2CH = cycloheptyl, $Me[CH_2]_4CHMe$, Pr^nCHMe, or Et_2CH; solvent = AcOH, MeOH, EtOH, PhOH, *p*-MeC_6H_4OH, or $PhNMe_2$

Use of primary alcohols as reaction solvent at 25 °C led to the isolation in moderate yield (Table 1) of 1-methylbutyl methyl and ethyl ethers from the reaction of 1-methylbutylamine in methanol and ethanol, and, similarly, 1-ethylpropyl methyl and ethyl ethers from 1-ethylpropylamine. Structures were confirmed by ^1H and ^{13}C n.m.r. spectroscopy (Tables 2 and 3).

Use of phenol and *p*-cresol gave mixtures of *O*- and *C*-alkylated compounds. Gas chromatography–mass spectrometry

Table 1. Solvent trapping of carbenium ions formed from amines and 5,6,8,9-tetrahydro-7-phenyldibenzo[*c,h*]xanthylium trifluoromethanesulphonate (**1**)

Solvent	Amine R in RNH_2	Product	Yield %	B.p., *t*/°C (*p*/mmHg)	Lit. b.p., *t*/°C (*p*/mmHg)
AcOH	Cycloheptyl	Cycloheptyl acetate	35	96—97 (33)	76—78 (11)[a]
AcOH	$Me[CH_2]_4CHMe$	$Me[CH_2]_4CHMeOAc$	50	170—172	171—173[b]
					71 (17)[c]
					60.0—60.5 (12)[d]
AcOH	Pr^nCHMe	$Pr^nCHMeOAc$	60	134—135	131.8—132 (746)[e]
AcOH	Et_2CH	Et_2CHOAc	62	133.5—134	133.8[d]
					132.5—133 (748)[e]
MeOH	Pr^nCHMe	$Pr^nCHMeOMe$	30	90—91	91—92[f]
MeOH	Et_2CH	Et_2CHOMe	31	88—89	*g*
EtOH	Pr^nCHMe	$Pr^nCHMeOEt$	35	105—106	104[h]
EtOH	Et_2CH	Et_2CHOEt	37	104—105	106[i]

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Table 2. ^1H N.m.r. data (δ values[a]) for solvolysis products in acetic acid, methanol, and ethanol

Structure	Me	CH_2 (m)	>CH– (m)	OCH_2CH_3 (3 H, t)	OCH_2CH_3 (2 H, q)	CH_3CO_2 or CH_3O (s)
Cycloheptyl acetate		1.42—1.63 (8 H) 1.73 (4 H)	4.9			2.0
$Me[CH_2]_4CHMeOAc$	0.90[b], 1.10[c]	1.40	5.0			2.1
$Pr^nCHMeOAc$	0.90[b]	1.50	5.0			2.1
Et_2CHOAc	0.90[d]	1.60[e]	4.8[f]			2.1
$Pr^nCHMeOMe$	0.90[b]	1.40	3.1			3.3
Et_2CHOMe	0.90[d]	1.50[e]	3.1[f]			3.4
$Pr^nCHMeOEt$	0.90[b]	1.45	3.1	1.2	3.5	
Et_2CHOEt	0.90[d]	1.50[e]	3.0[f]	1.2	3.5	

[a] In $CDCl_3$. [b] Multiplet. [c] Doublet. [d] Triplet. [e] Quartet. [f] Quintet.

Table 3. ^{13}C Chemical shifts[a] (p.p.m.) for solvolysis products in acetic acid, methanol, and ethanol

						Other signals	
Structure	C-1	C-2	C-3	C-4	C-5	Ester or ether Me	Ester CO or ether CH_2
$Me[CH_2]_4CHMeOAc$[b]	19.6	71.0	35.6	24.8	31.4	20.5	170.5
$Pr^nCHMeOAc$	20.9	71.2	37.7	18.3	13.5	20.4	170.5
Et_2CHOAc	9.0	26.0	76.0			20.4	170.1
$Pr^nCHMeOMe$	20.1	77.2	39.7	19.6	15.1	56.3	
Et_2CHOMe	9.2	25.2	83.1			56.1	
$Pr^nCHMeOEt$	19.9	76.5	39.7	19.5	14.9	15.1	63.7
Et_2CHOEt	9.4	25.9	81.6			15.3	63.8

[a] In $CDCl_3$, referred to $^{13}CDCl_3$ at 77.0 p.p.m. [b] C-6, 22.3; C-7, 13.7.

of the reaction of (**1**) with 1-ethylbutylamine in phenol showed three peaks. Peak areas (Table 4) were determined from the total ion content for all ions above *m/z* 32. The mass spectrum of each component exhibited a molecular ion of *m/z* 164. The fragmentation patterns were distinctive and characteristic, proving that the three components are 1-methylbutyl phenyl ether (A), *p*-(1-methylbutyl)phenol (B), and *o*-(1-methylbutyl)-phenol (C) (Table 4).

The ether (A) (*O*-alkylated product) exhibited a base peak at *m/z* 94, produced by the loss of pentene accompanied by hydrogen migration to the ring (a characteristic fragmentation of an aromatic alkyl ether[7]). By contrast, the *C*-alkylated compounds (B) and (C) each displayed the base peak at *m/z* 121 corresponding to $M^+ - C_3H_7$, a characteristic fragmentation for a *C*-(α-propylalkyl)phenol.[7] The *meta*-orientation for the benzene ring substitution was eliminated for both the *C*-alkyl products as *m*-(n-alkyl)phenols show an intense peak at *m/z* 108 for loss of alkene to give C_7H_7O and only a very weak signal at *m/z* 107, in contrast to the *ortho*- and *para*-isomers.[8] We find no such alkene loss. The *ortho*- and *para*-(1-methylbutyl)phenols were clearly distinguished; loss of H_2O to give a distinct *m/z* 146 ($M^+ - 18$) occurs only in *ortho*-isomers.[8]

Gas chromatographic–mass spectrometric analysis of the reaction products from 1-ethylpropylamine with (**1**) in phenol

Table 4. Mass spectral peak intensities for g.l.c. peaks (A), (B), and (C) for the solvolysis products derived from 1-methylbutyl- and 1-ethylpropyl-amine with (**1**) in phenol

			1-Methylbutylamine			1-Ethylpropylamine		
m/z of peak	Corresponding fragment	Fragment loss	(A)	(B)	(C)	(A)	(B)	(C)
164	*M*		3	13	8	3	17	13
146	$C_{11}H_{14}$	H_2O			2			4
135	$C_9H_{11}O$	C_2H_5				1	53	100
121	C_8H_9O	C_3H_7	1	100	100			
107	C_7H_7O			14	11		100	78
94	C_6H_6O	C_5H_{10}	100			100		
91	C_7H_7			8	6		10	7
77	C_6H_5	$C_5H_{11}O$	6	13	9	6	8	9
Retention time/s			548	729	782	540	700	766
Substitution pattern			*o*	*p*	*o*	*o*	*p*	*o*
% Relative yield			54	35	11	50	30	20

Table 5. Mass spectral peak intensities for g.l.c. peaks (A), (B), and (C) for the solvolysis products derived from 1-methylbutyl- and 1-ethylpropyl-amine with (**1**) in *p*-cresol

			1-Methylbutylamine			1-Ethylpropylamine		
m/z of peak	Corresponding fragment	Fragment loss	(A)	(B)	(C)	(A)	(B)	(C)
178	*M*		6	15	6	4	27	36
149	$C_{10}H_{13}O$	C_2H_5				1	82	100
135	$C_9H_{11}O$	C_3H_7	1	100	24			
121	C_8H_9O			12	6		100	98
108	C_7H_8O	C_5H_{10}	100	1	100	100	3	
107	C_7H_7O	C_5H_{11}	19	3	20	19	5	
91	C_7H_7		3	8	6	3	11	
77	C_6H_5	$C_6H_{13}O$	3	4	8	3	8	
Retention time/s			601	741	801	593	713	799
Substitution pattern			*o*	*o*	*m*	*o*	*o*	*m*
% Relative yield			57	41	2	55	44	1

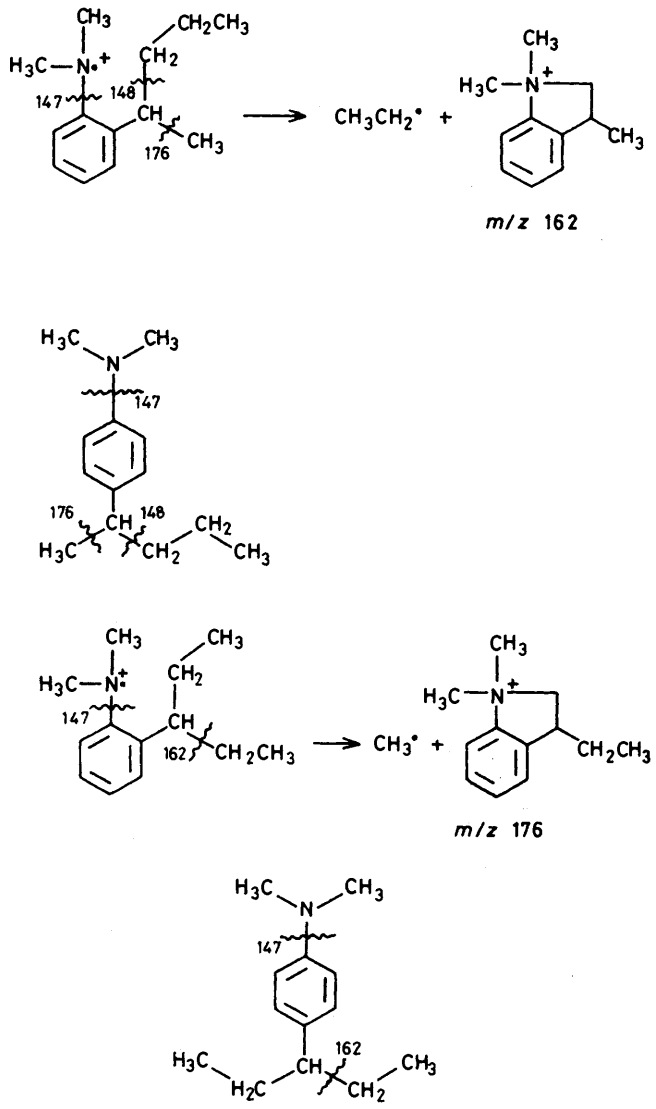
Table 6. Mass spectral peak intensities for g.l.c. peaks (A) and (B) for the solvolysis products derived from 1-methylbutyl- and 1-ethylpropyl-amine with (**1**) in *NN*-dimethylaniline

			1-Methylbutylamine		1-Ethylpropylamine	
m/z of peak	Corresponding fragment	Fragment loss	(A)	(B)	(A)	(B)
191	*M*		62	14	48	13
176	$C_{12}H_{18}N$	CH_3	13	4	36	
162	$C_{11}H_{16}N$	C_2H_5	97		100	100
148	$C_{10}H_{14}N$	C_3H_7	100	100		
147	$C_{11}H_{15}$	C_2H_6N	11	11	23	13
Retention time/s			518	815	500	770
Substitution pattern			*o*	*p*	*o*	*p*
% Relative yield			51	49	45	55

gave similar results. Three peaks in the ratio 50:30:20 were assigned to 1-ethylpropyl phenyl ether (A), *p*-1-ethylpropyl-phenol (B), and *o*-1-ethylpropylphenol (C). The ether (A) exhibited characteristic fragmentations at *m/z* 135 and 94 corresponding to $M^+ - C_2H_5$ and $M^+ - C_5H_{10}$ while the phenols (B) and (C) showed ions at *m/z* 146 ($M^+ - H_2O$, *ortho*-isomer only), 135 ($M^+ - C_2H_5$), and 107 ($M^+ - C_4H_9$) (see Table 4).

The gas chromatographic-mass spectrometric study of the reaction of 1-methylbutylamine with the xanthylium ion (**1**) in *p*-cresol again revealed the presence of three components in the ratio 57:41:2 (Table 5), each with molecular ions of *m/z* 178. Component (A) showed a base peak at *m/z* 108 for olefin loss accompanied by hydrogen migration (characteristic of an aromatic alkyl ether), and an ion of *m/z* 135 corresponding to $M^+ - C_3H_7$; hence component (A) is 1-methylbutyl *p*-tolyl ether. Components (B) and (C) were identified as 4-methyl-2-(1-methylbutyl)- and 4-methyl-3-(1-methylbutyl)-phenol, respectively. The distinction between these two isomers utilised the intensity ratio of the alkene loss peaks as described above.[8] The structures of the products, 1-ethylpropyl *p*-tolyl ether, 4-methyl-2-(1-ethylpropyl)phenol, and 4-methyl-3-(1-ethylpropyl)phenol, from the solvolysis of 3-(1-ethylpropyl)amine with (**1**) in *p*-cresol (Table 5) were assigned by the same criteria as those used for 1-methylbutylamine.

We have also investigated reactions in *NN*-dimethylaniline. The xanthylium ion (**1**) with 1-methylbutylamine gave a mixture of *o*- and *p*-(1-methylbutyl)-*NN*-dimethylaniline, which



Scheme 2.

where shown by gas chromatography–mass spectrometry (Table 6) to be formed in the ratio 51:49. Both components (A) and (B) showed peaks at *m/z* 191 (M^+), 176 ($M^+ - CH_3$), 148 ($M^+ - C_3H_7$), and 147 ($M^+ - C_2H_6N$), consistent with isomeric compounds. However, fragmentation to give the *m/z* 162 ion was shown only by component (A) and was used to differentiate between the two isomers. Loss of C_2H_5 by displacement reaction [7] at nitrogen is favourable only from *o*-(1-methylbutyl)-*NN*-dimethylaniline (Scheme 2). Hence, components (A) and (B) are *o*- and *p*-(1-methylbutyl)-*NN*-dimethylaniline, respectively.

Similarly, the solvolysis of 1-ethylpropylamine with the xanthylium ion (**1**) in *NN*-dimethylaniline showed the presence of two components, *o*- and *p*-(1-ethylpropyl)-*NN*-dimethylaniline. Their structures were assigned by the same criteria as used for 1-methylbutylamine (see Table 6 and Scheme 2).

The present results are consistent with reaction of intimate ion–molecule pairs derived from (**2**) with the solvent as nucleophile or (less likely in view of other evidence [2]) with a classical S_N2 reaction. That no rearrangement products were observed confirms that free carbenium ions are not involved.

Experimental

^1H and ^{13}C N.m.r. spectra were measured with Varian EM 360L and JEOL FX100 spectrometers (Me_4Si as internal standard). Gas chromatographic–mass spectrometric measurements were recorded by using an AEI MS-30 mass spectrometer (using a Kratos DS-55 data system) interfaced *via* a jet separator to a Pye 104 gas chromatograph. The column packings employed were DEGS-PS on 70—200 mesh Supelcoport, 10% DEGS-PS on 40—200 mesh Supelcoport, 3% SP-2100 on 100—250 mesh Supelcoport, or 3% SP-2250 DB on 100—250 mesh Supelcoport (2 m × 0.25 in glass columns; helium as the carrier gas at flow rate 30 ml min^{-1}).

Solvolyses in Acetic Acid.—To a stirred suspension of the xanthylium salt (**1**)[9] (2.55 g, 5 mmol) in acetic acid (9.0 g, 150 mmol) and triethylamine (5.0 g, 50 mmol) at 25 °C was added the secondary alkyl primary amine (7.5 mmol). After 120 h, the acridine (**2**) (85—90%) was filtered off; it crystallized from acetic acid as needles, m.p. 192—194 °C (previously reported [9] as plates, m.p. 166—167 °C) (Found: C, 90.0; H, 5.9; N, 3.9. $C_{27}H_{21}N$ requires C, 90.2; H, 5.9; N, 3.9%). Water (50 ml) was added and the mixture extracted with ether (3 × 25 ml). The extracts were washed with water (2 × 20 ml) and dried ($MgSO_4$), and then dry HCl was passed in. Filtration, evaporation *in vacuo*, and distillation and/or column chromatography (silica; 5% EtOAc–hexane) gave the products (see Tables 1—3).

Solvolyses in Methanol or Ethanol.—To a stirred suspension of the xanthylium salt (**1**) (2.55 g, 5 mmol) in the alcohol (25 ml) was added the secondary alkyl primary amine (0.65 g, 7.5 mmol) and triethylamine (2.5 g, 25 mmol). After 96 h at 25 °C, the acridine (**2**) (80—85%) was filtered off. Solvent was removed (25 °C; 15 mmHg) and the residue extracted with ether (3 × 50 ml). The extracts were dried ($MgSO_4$), and HCl gas passed through until precipitation of amine hydrochlorides was complete. Filtration, evaporation *in vacuo*, distillation, and/or column chromatography (silica; 5% EtOAc–hexane) gave the products (see Tables 1—3).

Solvolyses in Phenol or p-*Cresol.*—The xanthylium salt (**1**) (2.55 g, 5 mmol) and secondary alkyl primary amine (0.65 g, 7.5 mmol) were stirred in triethylamine (5.0 g, 50 mmol) and dried phenol or *p*-cresol (75 mmol) for 72 h at 25 °C. The acridine (**2**) (90—95%) was filtered off and the mixture analysed by gas chromatography–mass spectrometry (3% SP-2100 column) (see Tables 4 and 5).

Solvolyses in NN-*Dimethylaniline.*—The xanthylium salt (**1**) (2.55 g, mmol) and secondary alkyl primary amine (0.69 g, 8 mmol) in *NN*-dimethylaniline (30 ml) were stirred for 72 h at 25 °C. The mixture was analysed by gas chromatography–mass spectrometry (3% SP-2250 DB column) (see Table 6).

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