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1,2-DIHYDROISOQUINOLINES X[1]

THE CYCLIZATION OF BENZYLAMINOACETALDEHYDE DIALKYLACETALS

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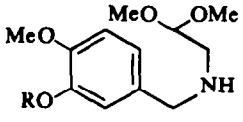
Abstract—The cyclization of some benzylaminoacetaldehyde dialkyl acetals has been examined and their utilization for the preparation of various isoquinoline derivatives studied. Some observations on the mechanism of cyclization of these acetals have also been made.

THE Pomeranz–Fritsch synthesis of isoquinolines involves[2] the cyclization of N-benzalaminoacetaldehyde dialkyl acetals with sulphuric acid, and the method has the great attractions that the fully aromatic isoquinoline is formed directly, and that the orientation of substituents in the product can differ from that obtained by the more common Bischler–Napieralski[3] reaction. There are serious disadvantages, however, and the method is very sensitive to experimental conditions. Various modifications of the synthesis have been studied but with very limited success until the recent work by Bobbitt *et al.*[4] in which reduced amino acetals (e.g. **1**, R = H) having a C_3 oxygen substituent were shown to form 1,2,3,4-tetrahydroisoquinolines (**3**) when treated with 6N HCl and the solution subsequently hydrogenated.



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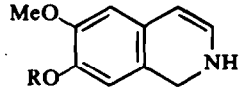

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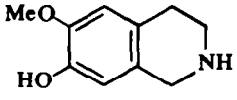

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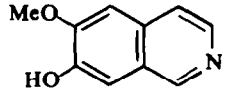

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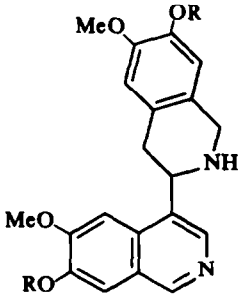
It was postulated[4] that a 1,2-dihydroisoquinoline (**2**, R = H) is an intermediate in the reductive cyclization, and although several attempts to isolate it were unsuccessful, support for this postulate was obtained by examining the products resulting from the treatment of the reduced aminoacetals of type (**1**, R = H) with 6N HCl *without* catalytic reduction. After 80 min at room temperature the 1,2,3,4-tetrahydroisoquinoline (**3**), the corresponding aromatic derivative (**4**), a dimer (**5**, R = H) and a trimer were isolated. Compounds **3** and **4** are the typical[5] products resulting from the disproportionation of a 1,2-dihydroisoquinoline in acid solution (although they

could be a function of the method of work-up used), and the dimer is most easily formulated[6] as an enamine reaction of a 1,2-dihydroisoquinoline. Further support for a 1,2-dihydroisoquinoline intermediate was provided by Bobbitt *et al.*[7] who showed that by boiling a solution of the reduced aminoacetal (**1**, R = H) with benzaldehyde and ethanolic HCl* for 30 min, a good yield of the 4-benzylisoquinoline (**6**, R = H) was obtained. A mechanism has been proposed by us[8] for this condensation reaction and some support for it is available by the isolation of intermediates such as **7** or **8**.



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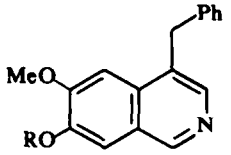

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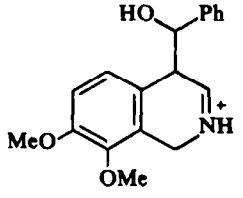
Bobbitt and Sih have now shown[9] that the treatment of reduced acetals such as **9** with 6N HCl at room temperature for 18 hr gives, not the 1,2-dihydroisoquinoline but the 4-hydroxy-1,2,3,4-tetrahydroisoquinoline (**10**).



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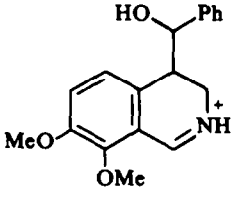

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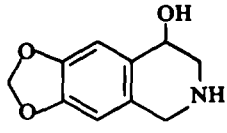

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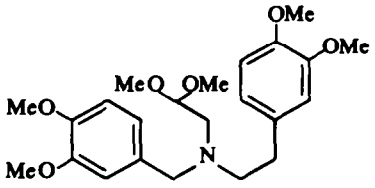
We have found by NMR studies that the aminoacetal derivative **11** is hydrolysed to the aldehyde **12** very rapidly by conc HCl, at room temperature, and that in a slower reaction[10] the doubly cyclized material **14** is formed in 80% yield. The aldehyde **12** was also prepared by Bobbitt's method using glycidol[11] and it also cyclized in good yield to **14**. The formation of **14** can be interpreted in terms of the initial formation of

* In all cases a 1:1 ethanolic concentrated hydrochloric acid solution was used.

the 4-hydroxy-1,2,3,4-tetrahydroisoquinoline (**13**) followed by nucleophilic attack at C_4 by the dimethoxyphenyl ring.

Bobbitt and Sih[9] seem to conclude that 1,2-dihydroisoquinolines are not involved in ANY of their previously described reactions of benzylaminoacetaldehyde dialkylacetals, but we suggest, however, that 1,2-dihydroisoquinolines are reactive intermediates in condensation reactions involving aldehydes. Thus, for example, benzaldehyde apparently fails to react with the tetrahydroalcohol (**15**) at RT (Experimental), whereas at higher temperatures, where dehydration of **15** to the corresponding 1,2-dihydroisoquinoline is rapid, condensation to form either **6** (R = CH_3) or **16** occurs.



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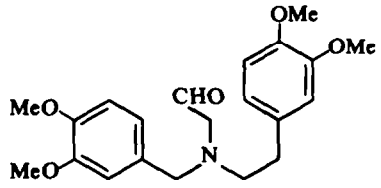

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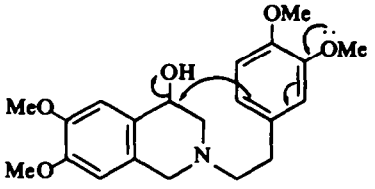

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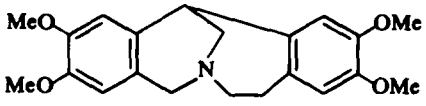

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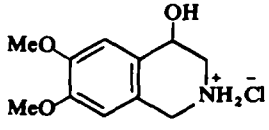
When a 1-benzyl-2-methyl-1,2-dihydroisoquinoline (**17**, R = Ar) is warmed with 2N HCl it rearranges[12,13] to the 2-methyl-3-benzyl-3,4-dihydroisoquinolinium salt (**18**, R = Ar), and we have recently shown[14] that 1-allyl-2-methyl-1,2-dihydroisoquinoline (**17**, R = —CH=CH_2) likewise rearranges to form **18** (R = —CH=CH_2). Although the mechanisms for benzyl and allyl migrations may not be identical,* each does involve a 1,2-dihydroisoquinoline as an intermediate. We have now found that when the aminoacetal (**20**, R = H), prepared[15] by the addition of allyl magnesium bromide to the Schiff's base (**19**), is warmed with ethanolic HCl the product, isolated in 80% yield, is the 3-allyl-3,4-dihydroisoquinolinium salt (**21**, R = H). The UV spectrum of the free base is typically that of a 3,4-dihydroisoquinoline (Experimental) and the NMR spectrum (in $CDCl_3$) is characteristic for the proposed structure; in particular the signal for the C_1 proton, at 8·2 ppm, appears as a doublet (J = 2 c/s)



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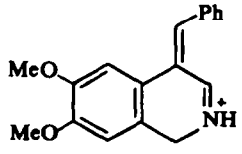

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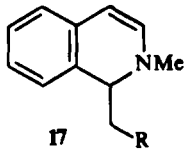
* The benzyl rearrangement may be viewed as a sigmatropic [1,3] migration, and as such is "forbidden"; the allyl migration, on the other hand, is an example of a suprafacial sigmatropic [3,3] reaction analogous to the Cope rearrangement, and may occur in a concerted manner under thermal conditions.



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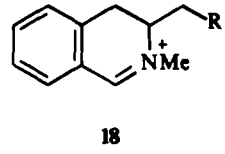

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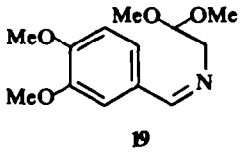

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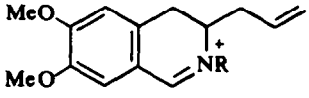
due to long range coupling with the methine proton at C_3. In the NMR spectrum of 6,7-dimethoxy-3,4-dihydroisoquinoline (**22**), in the same solvent, the C_1 proton appears as a triplet (J = 2 c/s) at 8·2 ppm and the two protons at C_3 form half of an A_2X_2 triplet at 3·7 ppm, further split (J = 2 c/s) into six lines. When the product **21** (R = H) was reacted with dimethyl sulphate and alkali a nitrogen-free *aldehyde* was obtained and characterized as its oxime. Structure **23** for this aldehyde is supported by its NMR spectrum which, in $CDCl_3$ solution, exhibits a 1 proton singlet at 10·3 ppm (—CHO); one hydrogen singlets at 7·4 and 6·95 ppm (C_2—H and C_5—H); one



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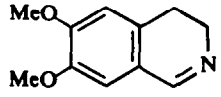

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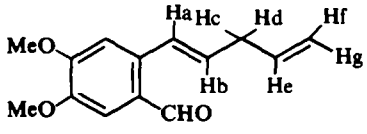

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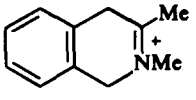
hydrogen doublet centred at 7·2 ppm (J = 15 c/s) (proton "a"); two hydrogen complex 6·4–5·7 ppm (protons "b" and "e"); two hydrogen complex 5·4–5·0 ppm (protons "f" and "g"); two three hydrogen singlets at 4·0 and 3·95 (2 × OCH_3) and a two hydrogen complex at 3·0 ppm (protons "c" and "d"). When the acetal **20** (R = Me), prepared by methylation of **20** (R = H) was treated with acids, the product, also isolated in 80% yield, proved to be **21** (R = Me); degradation with alkaline methyl sulphate produced the same aldehyde **23**. A 1-substituted -3,4-dihydroisoquinoline when degraded by this method[16] is converted into a ketone. The formation of **21** (R = H or Me) must surely involve the formation, from **20** (R = H or Me) of the 1-allyl-1,2-dihydroisoquinoline which then rearranges, and this reaction provides

very strong supporting evidence for the formation of 1,2-dihydroisoquinolines as intermediates in the cyclization and subsequent reactions of benzylaminoacetaldehyde dialkylacetals.

We have found that 2-methyl-1,2-dihydroisoquinoline (**24**) reacts in alcoholic hydrochloric acid solution with a variety of aldehydes to form 4-substituted-2-methylisoquinolinium salts (**25**); the results are summarised in Table 1, where yields are based upon 2-methyl-isoquinolinium iodide. The structures of the products follow from

24 **25**

their UV and diagnostic NMR spectra (Table 1A). but in addition the compound **25** (R = C_6H_5) was shown to be identical with authentic[17] 2-methyl-4-benzylisoquinolinium iodide. No identifiable isoquinoline derivatives were isolated when the enamine (**24**) was reacted with aliphatic aldehydes. We have also briefly examined the reaction of 2,3-dimethyl-1,2-dihydroisoquinoline with some aldehydes. In our preliminary experiments with this 1,2-dihydroisoquinoline the main product was the iminium salt (**26**), which is unusually stable; by a slight modification of procedure, however, the formation of this compound was suppressed. Under certain conditions a



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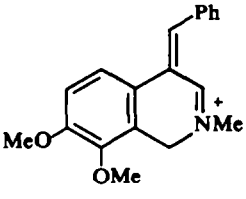

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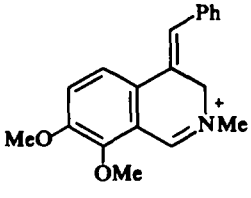

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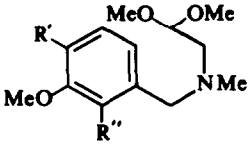

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product, which may be formulated as **27** or **28**, can be isolated from the reaction of the acetal **29** (*R'* = H, R'' = OMe) and benzaldehyde. When attempts were made to recrystallize this compound a tautomeric change to the corresponding isoquinolinium salt (**30**) occurred, whereas reduction with sodium borohydride in aqueous ethanol gave the stilbene derivative (**31**), characterized as the methiodide.

TABLE 1 2-METHYL-4-ALKYLISOQUINOLINIUM SALTS

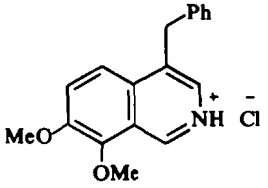
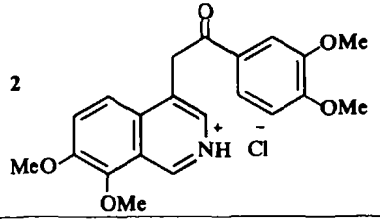
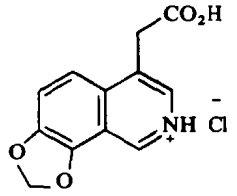
No.	R	% yield	m.p.	Molecular formula	Analysis								Solvent for recrystallization
					Required				Found				
					C	H	N	Cl	C	H	N	Cl	
1	C_6H_5—	38*	170–171°	$C_{17}H_{16}NO_4Cl$	61·15	4·8	4·2	—	61·2	4·75	4·4	—	EtOH
2	p-$MeOC_6H_4$—	39*	210–211°	$C_{18}H_{18}NO_5Cl$	58·4	5·0	3·8	—	58·8	5·0	3·8	—	EtOH
3	3,4-$(MeO)_2C_6H_3$—	20*	176–177°	$C_{19}H_{20}NO_6Cl$	58·0	5·2	3·6	—	58·4	5·2	3·8	—	EtOH
4	p-O_2N—C_6H_4—	39*	191–192°	$C_{17}H_{15}N_2O_6Cl$	53·9	4·0	7·4	—	53·9	3·8	7·6	—	EtOH
5	o-O_2N—C_6H_4—	46*	180–182°	$C_{17}H_{15}N_2O_6Cl$	53·9	4·0	7·4	9·4	54·2	3·7	7·2	9·5	EtOH
6	C_6H_5CO—	62*	185–186°	$C_{18}H_{16}NO_5Cl$	59·5	4·4	3·9	—	59·5	4·4	3·9	—	EtOH
7	CH_3CO—	27*	170–171°	$C_{13}H_{14}NO_5Cl$	52·2	4·7	4·7	—	52·2	4·9	4·7	—	EtOH
8	C_6H_5CH=CH—	33†	130–135°	$C_{19}H_{18}NCl$	77·2	6·1	4·7	—	67·3	6·3	5·1	—	aq. Acetone
9	2-Furfuryl	46*	269–270°	$C_{15}H_{14}NClO_5$	55·7	4·3	4·3	—	55·6	4·1	4·4	—	EtOH
10	3,4-Methylenedioxyphenyl	20†	126–128°	$C_{18}H_{16}NO_2Cl$	68·4	5·1	4·4	11·2	68·5	5·3	4·6	11·3	EtOH
11	—CO_2H	71*	191–192° (dec)	$C_{12}H_{12}NO_6Cl$	47·9	3·9	4·7	—	47·9	4·0	4·0	—	aq. Acetone
12		67·5*	224–225°	$C_{16}H_{15}N_2(ClO_4)_2$	44·2	3·7	6·6	—	44·3	3·9	6·5	—	MeOH

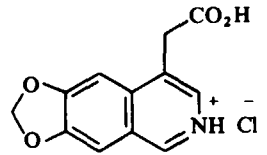
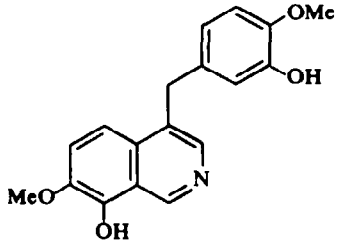
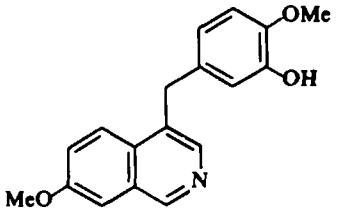
* As perchlorate. † As chloride.

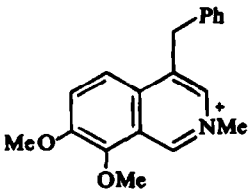
TABLE 1A. SPECTRAL DATA 2-METHYL-4-ALKYLISOQUINOLINIUM SALTS

Compound No. (from Table 1)	Solvent	NMR ppm							UV	IR
		C_1—H	C_3—H		Aromatic protons C_4-Substituent	C_4—CH_2	$\overset{+}{N}CH_3$	Miscellaneous	λ_{max} (ε) mμ	$\bar{\nu}_{max}$ cm^{-1}
1	CF_3CO_2H	S 9·2	Complex ~7·9 [5]		S 6·1	S 4·45	S 4·35			1635, 1615
2	CF_3CO_2H	S 9·1	S 8·0	Complex ~7·85 [4]	AB quartet (J = 9·5 c/s, 7·1, 6·7	S 4·45	S 4·4	MeO—		1640, 1615
3	CF_3CO_2H	S 9·1	S 8·1	Complex ~7·9 [4]	Broad singlet [3] 6·75	S 4·45	S 4·3	2x MeO—		1635, 1610
4	CF_3CO_2H	S 9·35	Complex ~8·0 [5]		AB quartet (J = 8 c/s, 8·1, 7·3	S 4·7	S 4·6		232 (17,000) 270 (4130) 340 (2350)	1640, 1615
5	CF_3CO_2H	S 9·1	Complex 8·4 – 7·2 [9]			S 4·85	S 4·3			1635, 1615
6	CF_3CO_2H	S 9·2	S 8·2	Complex 8·3 – 7·3 [9]		S 5·0	S 4·4			1660, 1635, 1610, 1605
7	CD_3SOCD_3	S 9·6	S 8·3	Complex ~7·9 [4]		S 4·45	S 4·4	S 2·35 [3] CH_3—CO		1710, 1640, 1605
8	CF_3CO_2H	S 8·9	S 7·65	Complex 7·5 – 7·2 [11] aromatic and olefinic		Broad singlet 4·8	S 3·7		208 (19,400) 230 (14,700) 305 (9500)	1635, 1605
9	CF_3CO_2H	S 9·1	Complex ~8·0 [5]			S 4·45	S 4·3			1625, 1615
10	CF_3CO_2H	S 8·8	S 8·5	Complex 7·7 [4]	Broad singlet 7·15 [3]	S 5·2	S 3·95	S 6·0 [2] —O—CH_2—O—		1640, 1600
11	CF_3CO_2H	S 9·25	Complex ~8·1 [5]			S 4·45	S 4·5			1730, 1635 1600
12	CD_3SOCD_3	S 9·55	Complex 8·7 – 7·3 [9]			S 4·8	S 4·3			2800, 1635, 1610.

TABLE 2. MISCELLANEOUS 4-SUBSTITUTED ISOQUINOLINES FROM REDUCED AMINOACETALS

No.	Compound	% yield	m.p.	Molecular formula	Analysis								Solvent for Recrystallization
					Required				Found				
					C	H	N	Cl	C	H	N	Cl	
1		30	178–179°	$C_{18}H_{13}NO_2Cl$	68·4	5·7	4·4	11·2	68·5	5·4	4·7	11·8	EtOH
2		20	212–214°	$C_{21}H_{22}NO_5Cl$	62·3	5·5	3·5	—	62·2	5·6	3·6	—	EtOH
3		46	209° (dec)	$C_{12}H_{10}NO_4Cl$	53·9	3·8	5·2	—	54·1	3·7	5·5	—	2N HCl

4		68	274° (dec)	$C_{12}H_{10}NO_4Cl$	53·9	3·8	5·2	—	53·7	3·8	5·4	—	2N HCl
5		60	206–207°	$C_{18}H_{17}NO_4$	69·4	5·5	4·5	—	69·0	5·9	4·4	—	Ethylacetate
6		60	138°	$C_{18}H_{17}NO_3$	73·2	5·8	4·7	—	72·8	6·0	4·7	—	EtOH



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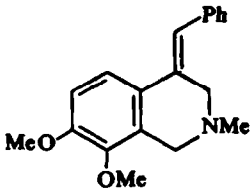

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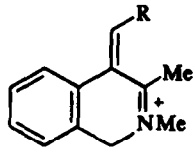
Similarly the products from the reaction of certain aromatic aldehydes (Experimental) with 2,3-dimethyl-1,2-dihydroisoquinoline were not the anticipated isoquinolinium salts, but rather of the type (32), in which one of the double bonds is exocyclic to the heterocycle. The NMR spectrum of these compounds, in trifluoroacetic acid, shows a one proton singlet at approx 8·0 ppm due to the H atom of the exocyclic double bond (the chemical shift of C_1—H of an isoquinolinium salt is normally ~9·2 ppm), a broad two proton singlet at 5·0–5·2 ppm, characteristic of a benzylic methylene function adjacent to a quaternary N atom (it is noteworthy that the chemical shift of the benzylic methylene protons of a 4-benzylisoquinolinium salt, in the same solvent, is 4·0–4·5 ppm) and a broad three proton singlet at 3·0 ppm, due to the Me group at C_3. The broadening of the signals associated with the Me and methylene groups presumably arises through long range coupling across 5 bonds,



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a phenomenon observed in many heterocyclic systems.[18] Surprisingly, these compounds (e.g. 32, R = Ph) are not readily isomerized to the corresponding isoquinolinium salts; this may in part be due to the hyperconjugative stabilization of the imminium system by the Me group at C_3.

Our results with 3,4-dimethoxybenzylaminoacetaldehyde dimethyl acetal (1, R = Me) are summarized in the Experimental. In some cases concomitant formation of N-alkylisoquinolinium salts and C_4-alkylated products was observed,[8] but under the conditions we now employ N-alkylation is only a very minor side reaction. Reaction between the aminoacetal (1, R = Me) and various *o*-nitrobenzaldehydes results in the formation of products which lack the methylene function at C_4 (as indicated by their NMR spectra) and the structures of these products, which are not yet assigned, are actively being examined. Similar products are obtained by the reaction of the same aldehydes with 2-methyl-1,2-dihydroisoquinoline in acid solution.

Into Table 2 have been collected the miscellaneous compounds prepared during the course of this work. Failure to achieve condensation between the aminoacetal (1, R = Me) and formaldehyde or butyraldehyde was observed, and the nitrogen

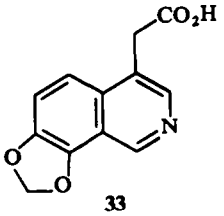
TABLE 2A. SPECTRAL DATA ON MISCELLANEOUS COMPOUNDS LISTED IN TABLE 2

Compound No. from Table 2	Solvent	NMR ppm							UV	IR
		C_1—H	C_3—H	Aromatic protons of isoquinoline nucleus	Aromatic protons of C-4 substituent	C_4—CH_2	OMe's	—OCH_2O—	λ_{max} (ε) mμ	$\bar{\nu}_{max}$ cm^{-1}
1*	$CDCl_3$*	S 9·5	S 8·25	AB quartet (J = 10 c/s) 7·5 (C_5—H), 7·15 (C_6—H)	S 7·05 [4]	S 4·2	S 3·95		236 (13,500), 255 (8360) 2801 (1650)	1630, 1605
2	CD_3SOCD_3	S 9·6	S 8·5	Complex 8·0–7·0 [7]		S 5·1	4·15 4·05 3·9 3·8		233 (40,500), 275 (14,400) 360 (3300)	1700, 1645, 1618
3	CF_3CO_2H	S 9·6	S 8·4	Singlet 7·99 [2] C_6—H, C_5—H)	—	S 4·45		S 6·5 (—OCH_2O—)	240 (23,720) 302 (2210) 379 (2480)	1700
4	CF_3CO_2H	Doublet 8·9 (J = 6 c/s)	Doublet 8·2 (J = 6 c/s)	Two singlets 7·45, 7·4 (C_8—H, C_5—H)	—	S 4·25	—	S 6·2 (—OCH_2O—)	246 (41,400)	1700
5	CD_3SOCD_3	S 9·5	S 8·3	Broad singlet 7·5 (C_6—H, C_5—H)	Complex 6·7	S 4·2	3·9 3·7			1640, 1610
6	CF_3CO_2H	Doublet 9·5 (J = 6 c/s)	Doublet 8·25 (J = 6 c/s)	AB quartet (J = 10 c/s) 8·35 (C_5—H), 7·9 (C_6—H)	Complex 7·0 [3]	4·5	4·15 4·0			*1630, 1600

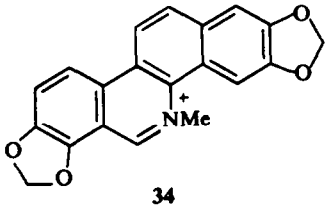
* As free base.

containing products resulting from the interaction of this acetal and acrolein, crotonaldehyde and salicylaldehyde resisted all attempts at characterization.

One of the most attractive features of this method for the preparation of 4-substituted isoquinolines in the relative ease with which 7,8-dioxygenated isoquinolines can be obtained, and we have used this approach to prepare **33**, which was required as a starting material for the first synthesis of the alkaloid sanguinarine (**34**).[19]



33



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EXPERIMENTAL

All m.ps are uncorrected. UV spectra were determined as EtOH solns and IR spectra as Nujol mulls. NMR spectra were recorded using a Varian A-60 spectrometer and chemical shifts are measured in ppm downfield from TMS as an internal standard.

N-[4-(3,4-Dimethoxyphenyl)butenyl]aminoacetaldehyde dimethylacetal (**20**, R = H).

N-(3,4-dimethoxybenzylidene)aminoacetaldehydedimethylacetal (25·3 g) was dissolved in dry ether (50 ml) and cooled to 0°, allyl magnesium bromide (0·17 mole) in ether (200 ml) was then added slowly, under a protective atmosphere of N_2. After stirring overnight at room temp, the reaction mixture was heated under reflux for a further 1 hr, and then cooled. 10% NH_4Cl aq (200 ml) was added to destroy the excess Grignard reagent; the aqueous phase was separated and washed with ether (2 × 100 ml). The combined ether extracts were dried and evaporated, to yield a pale yellow oil (24·5 g), distillation of which gave a fraction b.p. 140–144°/5 mm (23·8 g, 81%) of **20** (R = H). $\bar{\nu}_{max}$ cm^{-1}, 3340, 3080, 1645; NMR ($CDCl_3$) ppm, 7·0 s* [1] and 6·8 s [2] (aromatic protons); 5·6, 5·2, 5·0 complex [3] (—C<u>H</u>=C<u>H</u>$_2$); 4·4 tr [1], J = 6·5 c/s [—C<u>H</u>$_2$—C<u>H</u>(OMe)$_2$]; 3·9 s [6] (2 × —OC<u>H</u>$_3$); 3·6 tr, J = 7·75 c/s (Ar—C<u>H</u>—C<u>H</u>$_2$—); 3·2 s [6] (2 × —OC<u>H</u>$_3$); 2·6 d [2], J = 6·5 c/s (—C<u>H</u>$_2$—CH(OMe)$_2$); 2·4 d [2], J = 7·75 c/s (—C<u>H</u>$_2$—C<u>H</u>—Ar); 1·7 broad s [1], removed with D_2O (=N<u>H</u>). (Found: C, 65·3; H, 8·3; N, 4·7. $C_{16}H_{25}NO_4$ requires: C, 65·0; H, 8·5; N, 4·7%).

Methylation of this product with MeI (molar equiv) in acetone at room temp over Na_2CO_3 gave the corresponding **20** (R = Me); $\bar{\nu}_{max}$ cm^{-1}, 2800. (Found: C, 66·1; H, 8·1. $C_{17}H_{27}NO_4$ requires: 66·0; H, 8·0%).

Acid treatment of **20** (R=H). The secondary base (2·5 g) was dissolved in EtOH and conc HCl (1:1) and heated on a steam-bath for 3 hr, then set aside to cool. The following morning the soln was diluted with water (50 ml) and washed with ether (3 × 25 ml); basification of the aqueous phase with dil NH_4OH, followed by ether extraction gave, after evaporation of the solvent, a pink oil; $\bar{\nu}_{max}$ cm^{-1}, 1645, 1630; λ_{max} 234, 285, 316 (almost identical with the UV spectrum of 6,7-dimethoxy-3,4-dihydroisoquinoline) NMR ($CDCl_3$) ppm 8·2 d [1], J = 2 c/s (Ar—C<u>H</u>=N—CH(R^2)—R); 6·8 s [1] (C_8—<u>H</u>); 6·7 s [1] (C_5—<u>H</u>); 5·8–4·1 complex [3] (C<u>H</u>$_2$—C<u>H</u>—); 3·9 broad peak [7] (2 × —OC<u>H</u>$_3$ and Ar CH$_2$—C<u>H</u>—CH$_2$—) ~2·5 complex (Ar C<u>H</u>$_2$—CH—C<u>H</u>$_2$—CH=C<u>H</u>$_2$). The NMR spectrum of **22** in $CDCl_3$ shows a 1H

* s = singlet; tr = triplet; d = doublet; m = multiplet.

triplet at 8·2 ppm J = 2 c/s and a pair of 2H triplets at 3 and 2·6, J = 7 c/s, the lower field triplet being further split into six lines, J = 2 c/s; this is indicative of the Ar—C<u>H</u>$_2$—C<u>H</u>$_2$—N=C<u>H</u>— unit of structure. Reduction of this oil, which could not be distilled unchanged, with $NaBH_4$ in aqueous EtOH, afforded a gum, $\bar{\nu}_{max}$ cm^{-1}, 3320, 3075, 1645, from which a solid hydrochloride salt was prepared. Recrystallization from EtOH yielded pale yellow prisms m.p. 222–225°; $\bar{\nu}_{max}$ cm^{-1}, 3080, 2690, 2600, 2510, 2490, 1645; λ_{max} (ε) mμ 232 (7700), 285 (4400). (Found: C, 62·6; H, 7·5; N, 5·3; Cl, 12·9. $C_{14}H_{20}NO_2Cl$ requires: C, 62·3; H, 7·5; N, 5·2; Cl, 13·1%).

Acid treatment of **20**, R = Me). The tertiary base (3·09 g) in 6N HCl (25 ml) was diluted with EtOH (10 ml) and heated on a steam-bath for 3 hr and then allowed to cool overnight. After dilution with water (50 ml) the soln was washed with ether (3 × 50 ml) and neutralized by the addition of Na_2CO_3 aq. It was again washed with ether and treated with 10% KCNaq, which caused the separation of oily droplets. These were extracted into ether, and after removal of the solvent gave the pseudocyanide of **21** (R = Me) as colourless crystals (2·1 g, 78%), m.p. 68–70°; $\bar{\nu}_{max}$ cm^{-1}, 2815, 1645, 1610; λ_{max} (ε) mμ, 235 (8900), 286 (4200), 315 (2500), 372 (2100); NMR ($CDCl_3$) ppm s 6·75 [1] (C_8—<u>H</u>), s 6·65 [1] (C_5—<u>H</u>), complex 6·1–4·9 [3] (—C<u>H</u>=C<u>H</u>$_2$), s 4·7 [1] (C_1—<u>H</u>), 3·9 s [6] (2 × —OC<u>H</u>$_3$), 2·7 m (Ar C<u>H</u>$_2$—C<u>H</u>—C<u>H</u>$_2$—), s 2·6 [3] (=NC<u>H</u>$_3$). (Found: C, 70·3; H, 7·4; N, 10·2. $C_{16}H_{20}N_2O_2$ requires: C, 70·6; H, 7·4; N, 10·3%).

Degradation of the rearranged product **21**, R = Me

Regeneration of the 3,4-dihydroisoquinolinium salt from the above pseudocyanide was not facile, being incomplete after heating under reflux with 2N HCl for 3 hr. Accordingly the above procedure was repeated up to the stage where the KCN soln was to be added, instead Me_2SO_4 (10 ml) and 2N NaOH (100 ml) were introduced. The reaction mixture was heated at 100° with stirring and, after 30 min, more Me_2SO_4 (5 × 2 ml) was added portionwise at 10 min intervals. After the last addition, and a further 30 min period of heating, the soln was cooled and extracted with ether (3 × 25 ml). The combined ethereal extracts were washed with 2N HCl (2 × 25 ml), dried and evaporated to give a greenish oil (0·98 g). TLC on SiO_2, developing the plate with benzene, AcOH, MeOH (45:4:8) solvent mixture, showed two components to be present, R_f 0·52 and R_f 0·33. The spot at R_f 0·52 being due to the major component. Column chromatography on SiO_2 eluting with $CHCl_3$ afforded a lemon coloured oil (0·9 g); $\bar{\nu}_{max}$ (ε) mμ 203 (11,400), 252 (21,200), 288 (9300), 323 (7000); NMR see page 6. (Found: C, 72·0; H, 6·8. $C_{14}H_{16}O_3$ requires: C, 72·4; H, 6·9%). This aldehyde (**23**) was converted into the corresponding oxime, a sticky solid, which was purified by chromatography on silica, $\bar{\nu}_{max}$ (ε) mμ, 249 (22,200), 285 (15,200). NMR ($CDCl_3$) ppm, 8·6 broad s [1], removed by deuteration (=N—O<u>H</u>); 8·5 s [1] (Ar—C<u>H</u>=NOH); singlet 7·3 [1] (C_8—<u>H</u>); s 6·95 [1] (C_5—<u>H</u>); d 6·65, J = 16 c/s [1] (Ar C<u>H</u>=CH—); complex 6·25–5·6 [2] (=C<u>H</u>—CH$_2$—C<u>H</u>=); complex 5·3–4·9 [2] (—CH=C<u>H</u>$_2$); s 3·9 [6] (2 × OC<u>H</u>$_3$); finely split tr 3·0 [2] J = 7 c/s (=CH—C<u>H</u>$_2$—CH=). (Found: C, 68·7; H, 6·4; N, 5·0. $C_{14}H_{17}NO_3$ requires: C, 68·0; H, 6·9; N, 5·7%).

4-Benzyl-6,7-dimethoxyisoquinolinium chloride (**6**, R = Me). 3,4-Dimethoxybenzylaminoacetaldehyde dimethylacetal (10·2 g) was dissolved with cooling in 1:1 conc HCl–EtOH (150 ml) and the soln allowed to stand at room temp for 20 hr. Benzaldehyde (5·1 g) was added and the reaction mixture heated upon a steam-bath for 30 min. Water was then added and the soln cooled to 0°. After 48 hr the orange red needles which had separated were collected, this material (6·3 g) melted at 192–195°. The mother-liquor was extracted with benzene, to remove unchanged benzaldehyde, and evaporated to yield a residue which, upon trituration with acetone, afforded an orange crystalline solid (3·0 g), m.p. 193–195°. The two crops of product were combined and recrystallized from MeOH to yield **16** as orange needles m.p. 193–195°; λ_{max} (ε) mμ, 211 (22,100), 280 (10,300), 300 (9700), 412 (4000); $\bar{\nu}_{max}$ cm^{-1} 2560, 1653, 1603; NMR (CF_3CO_2H) ppm 9·0 doublet [1], J = 8 c/s (C_3—<u>H</u>), 8·5 s [1] (>C=C<u>H</u>—Ph) 7·6 s [5] (aromatic protons); 7·5 s [1] (C_5—<u>H</u>); 6·9 s [1] (C_8—<u>H</u>); 5·2 s [2] (Ar—C<u>H</u>$_2$—$\overset{+}{N}$<). This material was readily isomerized to the aromatic isoquinolinium salt by heating with MeOH under reflux for 1 hr; upon evaporation of the solvent to low volume and cooling, pale yellow cubes of **6** (R = Me) separated m.p. 194–196° (for analytical and spectroscopic data see Tables 1 and 1a).

6,7-Dimethoxy-4-hydroxy-1,2,3,4-tetrahydroisoquinolinium chloride (**15**). A soln of 3,4-dimethoxybenzylaminoacetaldehyde dimethylacetal (20·4 g) in 6N HCl (400 ml) was allowed to stand at room temp for 17 hr. The solvent was carefully removed at 40° under reduced press to give an oily residue, trituration of which with acetone effected crystallization. The product (18·9 g) m.p. 177° (dec) was washed several times

with cold acetone–EtOH mixtures. (Found: C, 53·3; H, 6·6; N, 6·1; Cl, 15·1. $C_{11}H_{16}NO_3Cl$ requires: C, 53·8; H, 6·6; N, 5·7; Cl, 14·4%). Further recrystallization proved to be difficult.

Reaction of 6,7-*dimethoxy*-4-*hydroxy*-1,2,3,4-*tetrahydroisoquinolinium chloride with benzaldehyde*

A. 6,7-Dimethoxy-4-hydroxy-1,2,3,4-tetrahydroisoquinolinium chloride (2·5 g) and benzaldehyde (1·26 g) were dissolved in 1:1 EtOH–conc HCl (25 ml) and the soln stirred at room temp for 72 hr, then diluted with water (25 ml) and cooled to 0° for 48 hr. Since after this time no product had separated, the unreacted benzaldehyde was recovered by extraction with benzene (6 × 10 ml); recovery 84%. In a control experiment 92% benzaldehyde was recovered from an identical procedure in which the addition of the tetrahydroisoquinolinium salt was omitted. Evaporation of the aqueous phase at 40° under reduced press gave a sticky residue (2·24 g) which crystallized on trituration with acetone to yield the unchanged tetrahydroisoquinolinium chloride (92%). After filtration, the acetone mother liquor, from which this compound was obtained, was evaporated to give a yellow oil (0·2 g), the NMR spectrum of which showed it not to be a 6,7-dimethoxy-4-benzylisoquinoline derivative (ratio of methoxyl to aromatic hydrogen atoms).

B. *Scale as above.* A soln of the tetrahydroisoquinolinium salt in ethanolic HCl was warmed on a steam-bath for 30 min, cooled to room temp and benzaldehyde added. This mixture was stored at room temp for 30 hr and then diluted with water. Unchanged benzaldehyde was removed by benzene extraction and the aqueous phase cooled to 0°. Later (48 hr) the orange crystalline product m.p. 193–195°, shown to be 4-benzylidene-6,7-dimethoxy 1,4-dihydroisoquinolinium chloride, was collected (0·26, 7·2%). The filtrate was basified with ammonia and then extracted first with ether (4 × 15 ml), then chloroform (4 × 15 ml). Evaporation of the combined ether extracts and crystallization of the residue from acetone afforded **5** (R = Me) as colourless prisms (0·26 g, 13·7%), m.p. 218–219°; λ_{max} mμ, 206, 248, 283, 312 and 327; $\bar{\nu}_{max}$ cm^{-1}, 1620, 1610. NMR ($CDCl_3$) ppm, 8·7 s [1] (C_1—H); 8·25 s [1] (C_3—H); 7·35 s [1] (C_8—H); 6·95 s [1] (C_5—H); 6·4 s [2] (C_5—H, C_8—H); 4·4 complex [1] (C_3—H); 4·1 s [2] (C_1—H_2); 3·95, 3·85 two s [3] (2 × OCH_3); 3·7 s [6] (2 × —OCH_3); 3·0 complex [2] (C_4—H_2); 2·0 broad s [1], removed by deuteration (=NH). (Found: C, 69·5; H, 6·4; N, 7·4. $C_{22}H_{24}N_2O_4$ requires: C, 69·5; H, 6·4; N, 7·4%). The hydrochloride salt of this dimer was also prepared white prisms m.p. 231–232°. (Found: C, 63·0; H, 6·0; N, 6·6. $C_{22}H_{25}N_2O_4Cl$ requires: C, 63·2; H, 6·05; N, 6·7%).

Removal of the solvent from the combined chloroform extracts yielded a small quantity of uncharacterized resinous material.

C. *Scale as in A above.* A soln of the tetrahydroisoquinolinium chloride in ethanolic HCl containing benzaldehyde was heated upon a steam-bath for 30 min. diluted with water and extracted with benzene (recovery of unreacted benzaldehyde 28%). After cooling at 0° for 48 hr the orange-red needles of 4-benzylidene-6,7-dimethoxy-1,4-dihydroisoquinolinium chloride (0·97 g, 31%), m.p. 192–195°, which had separated were collected, and the filtrate made basic with ammonia. Extraction with ether gave, after removal of the solvent, a gum which, when dissolved in benzene and saturated with HCl, yielded a crystalline ppt of **5** (R = Me) as the hydrochloride salt (0·4 g 17·7%). The filtrate from which this product separated was then evaporated to give 4-benzyl-6,7-dimethoxyisoquinolinium chloride (0·32 g, 10·1%). Extraction of the initial aqueous filtrate with chloroform afforded an uncharacterized resinous material (0·15 g).

2,3-*Dimethyl*-1,4-*dihydroisoquinolinium perchlorate* (**26**). 2,3-Dimethyl-1,2-dihydroisoquinoline (prepared by the LAH reduction of 10 g of 2,3-dimethylisoquinolinium iodide) in ether (100 ml) was treated with conc HCl (25 ml) in EtOH (50 ml). After heating at 100° for 1 hr the solvents were removed to yield a yellow oil, to which a little perchloric acid was added. Crystallization was initiated by scratching and cooling, thus yielding **26** as pale yellow prisms which were recrystallized from EtOH (1·5 g) m.p. 116–117°; ν_{max} cm^{-1}. 1695, 1090; NMR (CF_3CO_2H) ppm; 7·3 broad s [4] (aromatic protons), 5·0 broad s [2] (protons at C_1), 4·2 broad s [2] (protons at C_4) 3·8 s [3] ($\equiv\overset{+}{N}$—CH_3), 2·65 s [3] ($\equiv C_3$—CH_3). (Found: C, 50·8; H, 5·2; N, 5·35; Cl, 14·0. $C_{11}H_{14}NClO_4$ requires: C, 51·0; H, 5·0; N, 5·4; Cl, 13·7%).

This product was also obtained when aromatic aldehydes were introduced prior to heating, under reaction conditions similar to the above. In such cases little or no condensation products, formed by interaction of aldehyde and 1,2-dihydroisoquinoline, were isolated.

General reaction between 2,3-*dimethyl*-1,2-*dihydroisoquinoline and aromatic aldehydes*

The 1,2-dihydroisoquinoline, from LAH reduction of the corresponding isoquinolinium iodide (10 g) in ether, was freed of solvent by continuous pumping at 10 mm press for 2 hr, and the aldehyde (molar equiv, assuming total conversion of isoquinolinium salt to dihydroisoquinoline) in EtOH (50 ml) containing

conc HCl (25 ml) was then added. After heating under reflux for 4 hr, the solvent was removed under reduced press, and the residual oil treated with perchloric acid to give the crystalline perchlorate salt.

Benzaldehyde. 28% yield, m.p. 196–197° (aqueous EtOH), λ_{max} (ε) mμ, 232 (31,200), 350 (9000); $\bar{\nu}_{max}$ cm^{-1}, 1640, 1100; NMR (CF_3CO_2H) ppm, 7·9 singlet [1] (exocyclic olefinic proton), 7·3 complex [9] (aromatics), 5·0 broad s [2] (Ar—$C\underline{H}_2$—$\overset{+}{N}\equiv$), 3·9 s [3] ($\equiv\overset{+}{N}$—$C\underline{H}_3$), 2·9 broad s [3] (C_3—$C\underline{H}_3$). (Found: C, 62·0; H, 5·0; N, 4·1. $C_{18}H_{18}NO_4Cl$ requires: C, 62·2; H, 5·2; N, 4·0%).

p-Nitrobenzaldehyde, 65% yield, m.p. 256–257° (water), $^{N}_{max}$ (ε) mμ, 232 (31,200), 350 (9000); ν_{max} cm^{-1}, 1640, 1100; NMR (CF_3CO_2H) ppm 7·9 s [1] (exocyclic olefinic proton), 7·3 complex [9] (aromatics), 5·0 broad s [2] (Ar—$C\underline{H}_2$—$\overset{+}{N}\equiv$), 3·9 s [3] ($\equiv\overset{+}{N}$—$C\underline{H}_3$) 3·0 broad s [3] (C_3—$C\underline{H}_3$). (Found: C, 55·0; H, 4·3; N, 7·35; Cl, 9·3. $C_{18}H_{17}N_2ClO_6$ requires: C, 55·2; H, 4·1; N, 7·15; Cl, 9·1%).

m-Nitrobenzaldehyde. 43% yield, m.p. 243–246° (aqueous EtOH), λ_{max} (ε) mμ, 245 (39,150), 265 (4940), 350 (3120); NMR (CF_3CO_2H ppm 8·2 s [1] (exocyclic olefinic proton), 7·9 finely split s [1] (C_2—$\underline{H}$), 7·5 complex [7] (aromatics), 5·2 broad s [2] (Ar—$C\underline{H}_2$—$\overset{+}{N}\equiv$), 3·9 s [3] ($=\overset{+}{N}$—$C\underline{H}_3$), 3·0 broad s [3] (C_3—$C\underline{H}_3$). (Found: C, 55·35; H, 4·25; N, 7·15; Cl, 9·25. $C_{18}H_{17}N_2ClO_6$ requires: C, 55·2; H, 4·1; N, 7·15; Cl, 9·1%).

p-Dimethylaminobenzaldehyde: 10% yield, m.p. 236–238° (EtOH), λ_{max} (ε) mμ, 240 (7420), 280 (8200), $\bar{\nu}_{max}$ cm^{-1}, 1649, 1090; NMR (CF_3CO_2H), 7·9 s [1] (exocyclic olefinic proton) ~7·5 complex [8] (aromatics), 5·2 broad s [2] (Ar—$C\underline{H}_2$—$\overset{+}{N}\equiv$), 4·0 s [3] ($\equiv\overset{+}{N}$—$C\underline{H}_3$), 3·4, 3·45 two s's [6] (—$N(CH_3)_2$), 3·0 s [3] (C_3—$C\underline{H}_3$). (Found: C, 48·8; H, 5·2; N, 6·0; Cl, 14·8, $C_{20}H_{24}N_2Cl_2O_8$ requires: C, 48·9; H, 4·9; N, 5·7; Cl, 14·4%).

Reactions with veratrylaldehyde and glyoxalic acid failed to yield crystalline products.

4-Benzylidene-2-methyl-7,8-dimethoxy-1,4-dihydroisoquinolinium chloride (**27**).

The acetal **29** (R′ = H, R″ = OMe; 4·4 g) was dissolved in conc HCl (25 ml) and heated on a water-bath for 5 min. Benzaldehyde (1·7 g) was then added and the mixture heated for a further hr. After cooling at 0° for 48 hr, the orange crystalline product was collected, washed with conc HCl and EtOH and dried under vacuum. This material (3·5 g) m.p. 106–109° could not be recrystallized; ν_{max} cm^{-1}, 1650 ($\rangle C{=}\overset{+}{N}\langle$), 1608 ($\rangle C{=}C\langle$), λ_{max} (ε) mμ, 212 (22,000), 290 (17,100); NMR (CF_3CO_2H) ppm, 8·33 s [1] (C_3—H), 8·12 s [1] (exocyclic olefinic proton) 7·2 m [7] (aromatic protons), 5·0 s [2H] (Ar $C\underline{H}_2$—$\overset{+}{N}\equiv$), ~3·85 two s [6] (2 × OMe), 3·73 s [3] ($\equiv\overset{+}{N}$—CH_3).

Reduction of this product with $NaBH_4$ in aqueous EtOH gave a sticky solid, which with MeI afforded yellow prisms. Recrystallization of the latter from EtOH gave 4-benzylidene-2-methyl-7,8-dimethoxy-1,2,3,4-tetrahydroisoquinolinium methiodide, m.p. 241–242° (dec); $\bar{\nu}_{max}$ cm^{-1}, 1603 ($\rangle C{=}C\langle$); λ_{max} (ε) mμ, 223 (23,100), 312 (19,300); NMR (CF_3CO_2H) ppm, ~6·8 m [8] (aromatic and olefinic proton), 4·62 s [2] ($\equiv\overset{+}{N}$—$C\underline{H}_2$—), 4·37 s [2] (Ar—$C\underline{H}_2$—$\overset{+}{N}\equiv$), ~3·86 two s's [6] (2 × —OMe), 3·1 s [6] ($=\overset{+}{N}(CH_3)_2$). (Found: C, 55·1; H, 5·5; N, 3·4. $C_{20}H_{24}NO_2I$ requires: C, 54·9; H, 5·5; N, 3·2%).

4-Benzyl-2-methyl-7,8-dimethoxyisoquinolinium perchlorate (**30**). The chloride **27** was dissolved in water and $HClO_4$ added to give the corresponding perchlorate salt (λ_{max} 209 and 286 mμ). Repeated recrystallization of this compound from EtOH gave **30** in 85% yield, as bright yellow needles m.p. 188–189°; $\bar{\nu}_{max}$ cm^{-1}, 1667 ($\rangle C{=}\overset{+}{N}\langle$), 1610 ($\rangle C{=}C\langle$). λ_{max} (ε) mμ, 219 (23,200), 258 (22,000). (Found: C, 57·6; 4, 5·2; N, 4·0. $C_{19}H_{20}NO_6Cl$ requires: C, 57·9; H, 5·1; N, 3·6%).

Reaction between 2-methyl-1,2-dihydroisoquinoline and aldehydes (Table 1)

2-Methyl-1,2-dihydroisoquinoline (0·01 mole) in ether (150 ml) was added to a soln of the aldehyde (0·01 mole) in EtOH (50 ml) and conc HCl (25 ml) protected by an atmosphere of N_2. After heating under reflux for 30 min, the soln was evaporated to yield a syrupy residue, which in the case of compounds numbered 8 and 10 (in Table 1) crystallized spontaneously; in the other examples the residue was treated with ethanolic perchloric acid to yield the crystalline perchlorate salt. Recrystallization was normally achieved from EtOH.

Reaction between 2-benzyl-1,2-dihydroisoquinoline and aldehydes

An identical procedure to that described above was carried out using 2-benzyl-1,2-dihydroisoquinoline,

prepared by the LAH reduction of 2-benzylisoquinolinium iodide. The products were characterized as the perchlorate salts.

p-*Nitrobenzaldehyde.* 4·0% yield, m.p. 180–181° (MeOH), λ_{max} (ε) mμ, 237 (31,620), 340 (5010); $\bar{\nu}_{max}$ cm^{-1} 1650, 1600; NMR (CD_3SOCD_3) 9·75 s [1] (C_1—H), 8·5 s [1] (C_3—H) ~7·5 complex [13] (aromatic protons) 5·6 s [2] (Ar—CH_2—$\overset{+}{N}\equiv$), 4·6 s [2] (—CH_2—Ar). (Found: C, 60·7; H, 3·9; N, 6·0. $C_{23}H_{19}N_2O_6Cl$ requires: C, 60·8; H, 4·2; N, 6·2%).

p-*Methoxybenzaldehyde.* 1·4% yield, m.p. 186–187° (EtOH), λ_{max} mμ, 240, 335, $\bar{\nu}_{max}$ cm^{-1}, 1650, 1615; NMR (CF_3CO_2H) ppm, 9·1 s [1] (C_1—H), 8·1–7·5 complex [5] (aromatic protons); 6·9 d [2], J = 9 c/s ($C_{2'}$—H, $C_{6'}$—H); 6·6 d [2], J = 9 c/s ($C_{3'}$—H, $C_{5'}$—H), 7·16 s [5] ($\equiv\overset{+}{N}$—CH_2—C_6H_5), 5·6 s [2] (ArCH_2—$\overset{+}{N}\equiv$); 4·4 s [2] (—CH_2—Ar); 3·8 s [3] (—OCH_3). (Found: C, 65·4; H, 4·9; N, 3·0. $C_{24}H_{22}NO_5Cl$ requires: C, 65·5; H, 5·0; N, 3·2%).

Reaction between the acetal (1, R = Me) *and aldehydes*

The reduced aminoacetal (5 g) in 6N HCl (30 ml) was stored at room temp for 12 hr; the aldehyde (5 g) was then added and the reaction mixture heated to 100° for 30 min (in the case of aldehydes which did not readily dissolve the minimum volume of EtOH necessary to effect soln was added). On cooling the hydrochloride salt normally separated slowly from the reaction medium, although in the case of *p*-methoxybenzaldehyde KI was added to precipitate the less soluble hydroiodide.

Benzaldehyde. 35% yield; m.p. 192–194° (water); λ_{max} (ε) mμ, 245 (6760), 313 (1000); $\bar{\nu}_{max}$ cm^{-1}, 1630, 1610; NMR (CF_3CO_2H) ppm, d 9·35, J = 5·5 c/s [1] (C_1—H); 8·25 d, J = 6 c/s [1] (C_3—H); 7·8 singlet [1] (C_8—H); 7·6 s [1] (C_5—H); 4·1, 4·05 two s's [6] (2 × —OCH_3) 4·55 s [2] (—CH_2Ar). (Found: C, 68·35; H, 5·8; N, 4·65. $C_{18}H_{18}NClO_2$ requires: C, 68·4; H, 5·7; N, 4·4%).

p-*Methoxybenzaldehyde.* 8% yield (as the hydroiodide), m.p. 188–189° (EtOH), λ_{max} (ε) mμ, 243 (12,200), 313 (5010); $\bar{\nu}_{max}$ cm^{-1}, 1630, 1610; NMR (CF_3CO_2H) ppm, 9·25 d, J = 6 c/s [1] (C_1—H); 8·35 d, J = 6 c/s [1] (C_3—H), 7·8 s [1] (C_8—H); 7·5 s [1] (C_5—H); 7·3 d, J = 10 c/s [2] ($C_{2'}$—H, $C_{6'}$—H); 7·1 d, J = 10 c/s [2] ($C_{3'}$—H, $C_{5'}$—H); 4·2, 4·1 two s's (2 × OCH_3). (Found: C, 52·6; H, 4·7; N, 3·2. $C_{19}H_{20}NIO_3$ requires: C, 52·3; H, 4·6; N, 3·2%).

p-*Dimethylaminobenzaldehyde.* 73% yield, m.p. 221–226° (aqueous MeOH), λ_{max} (ε) mμ 256 (64,100), 314 (10,500); $\bar{\nu}_{max}$ cm^{-1}, 1636, 1618; NMR (CF_3CO_2H) ppm, 9·4 d, J = 5·5 c/s [1] (C_1—H); 8·3 d, J = 6 c/s [1] (C_3—H); 8·0–7·6 complex [6] (aromatic protons); 4·15, 4·05 two s's [6] (2 × —OCH_3); 3·5, 3·55 two s's [6] (—$N(CH_3)_2$). (Found: C, 60·6; H, 6·1; N, 7·4; Cl, 18·1. $C_{20}H_{24}N_2Cl_2O_2$ requires: C, 60·8; H, 6·1; N, 7·1; Cl, 17·9%).

p-*Nitrobenzaldehyde.* Only a small amount of nitrogen containing compound was isolated for which satisfactory analyses were not obtained.

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