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A NOVEL METHOD OF THE SYNTHESIS OF HIGHER POLYMETHINIUM SALTS

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Abstract—A novel synthesis of higher polymethinium salts is based on the condensation of glutaconic aldehyde acetals (II) with vinyl alkyl ethers and alkoxydienes followed by the acidic hydrolysis of the intermediate adducts (III, V, VI and VII) in the presence of primary or secondary amines.

Higher polymethinium salts (I) containing over 5 C atoms in the chain are of great theoretical and practical interest.

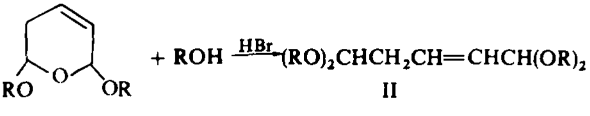
$$>N-(CH=CH)_nCH=\overset{+}{N}< \quad \bar{X}$$

I

The majority of known methods of synthesis have little practical value[1–7] or can be applied only to unbranched chain compounds.[8–9] The method based on acidic hydrolysis of some 2-alkoxy-Δ^3-dihydropyran derivatives[10] has been used only for the preparation of some heptamethinium salts.

The new method of synthesis of higher polymethinium salts, both straight-chained and branched, was expanded by the condensation of glutaconic aldehyde acetals with vinyl alkyl ethers and 1-alkoxydienes.

Glutaconic aldehyde acetals (II) were obtained by the reaction of 2,6-dialkoxy-Δ^3-dihydropyrans[11] with alcohols in the presence of hydrogen bromide.[12, 13]

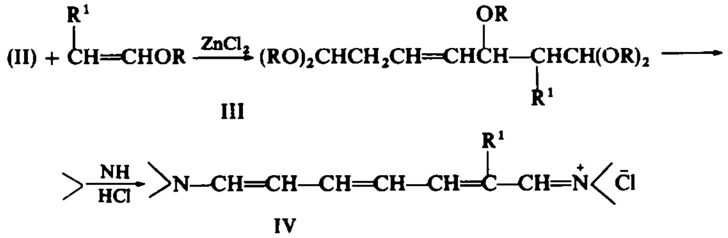


Heptamethinium salts

The condensation of equimolecular proportions of vinyl and propenyl alkyl ethers with glutaconic aldehyde tetraalkylacetals proceed specifically with the α,β-unsaturated acetal end of the molecule, the principal product being 1,1,3,7,7,-pentaalkoxyhept-4-ene derivatives (III), without telomer production.[15] This is in accordance with the mechanism of the condensation of acetals with vinyl alkyl ethers.[14]

The hydrolysis of the resulting products (III) in the presence of primary or secondary amines (aniline, methyl anyline, tetrahydroquinoline) occurs with the elimination of alcohol and the formation of heptamethinium salts (IV).

The reaction proceeds under very mild conditions and is complete in 20–30 min at



$$\text{(II)} + \underset{\text{III}}{\overset{R^1}{\overset{|}{C}}H{=}CHOR} \xrightarrow{ZnCl_2} (RO)_2CHCH_2CH{=}CH\overset{OR}{\overset{|}{C}}H{-}\underset{R^1}{\underset{|}{C}}HCH(OR)_2 \longrightarrow$$

$$\xrightarrow[HCl]{>NH} {>}N{-}CH{=}CH{-}CH{=}CH{-}CH{=}\overset{R^1}{\overset{|}{C}}{-}CH{=}\overset{+}{N}{<}\ \bar{C}l \quad \text{IV}$$

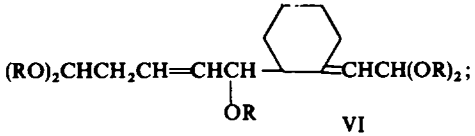
R = CH_3, C_2H_5

room temperature to produce blue-green crystals with a metallic glitter.[16] The heptamethinium salts obtained are given in Table 1.

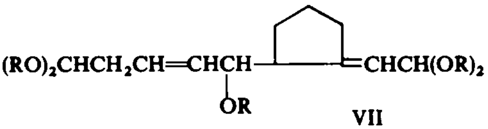
Nonamethinium salts

Polymethinium salts containing over 9 C atoms in a chain result from the condensation of glutaconic aldehyde acetals with 1-alkoxydienes,[17, 18] The α,β-unsaturated alkoxyacetals formed react with another molecule of 1-alkoxydiene to produce a mixture of unsaturated dialdehydes alkoxyacetals (V). The composition of the mixture depends upon the initial molar ratio of reagents. Twofold excess of the acetal is required to increase the percentage conversion in the first condensation.

Glutaconic aldehyde acetals react with cyclic 1-alkoxydienes such as 1-β-(ethoxyvinyl)-cyclohex-1-ene, and 1-β-(ethoxyvinyl)-cyclopent-1-ene, to afford the corresponding products (VI and VII).

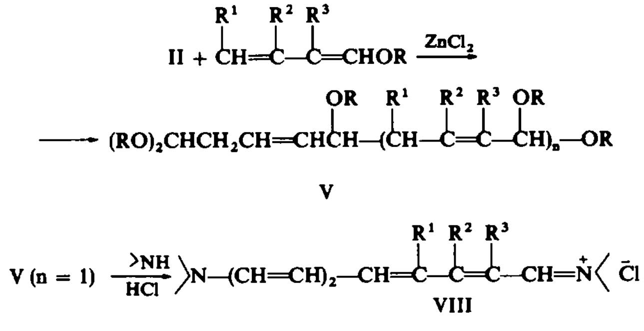


VI



VII

1,1,5,9,9-Pentaalkoxynona-2,6-diene derivatives (V, n = 1) similar to the lower homologs were converted into nonamethinium salts (VIII). All the reactions occur at room temperature or under mild cooling, to produce high yields of the required compounds. Aniline, *p*-toluidine, *p*-chloroaniline, *m*-trifluoromethylaniline, N-methylaniline, N-ethylaniline or tetrahydroquinoline were used as a base. The compounds, produced in this way, are listed in Table 2.



$$\text{II} + \overset{R^1}{\overset{|}{C}}H{=}\overset{R^2}{\overset{|}{C}}{-}\overset{R^3}{\overset{|}{C}}{=}CHOR \xrightarrow{ZnCl_2}$$

$$\longrightarrow (RO)_2CHCH_2CH{=}CH\overset{OR}{\overset{|}{C}}H{-}(\overset{R^1}{\overset{|}{C}}H{-}\overset{R^2}{\overset{|}{C}}{=}\overset{R^3}{\overset{|}{C}}{-}\overset{OR}{\overset{|}{C}}H)_n{-}OR \quad \text{V}$$

$$\text{V}\ (n = 1) \xrightarrow[HCl]{>NH} {>}N{-}(CH{=}CH)_2{-}CH{=}\overset{R^1}{\overset{|}{C}}{-}\overset{R^2}{\overset{|}{C}}{=}\overset{R^3}{\overset{|}{C}}{-}CH{=}\overset{+}{N}{<}\ \bar{C}l \quad \text{VIII}$$

R=Me, Et; R^1, R^2, R^3=H, Me; n = 1, 2, 3

TABLE 1. HEPTAMETHINIUM SALTS (IV)

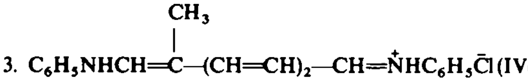
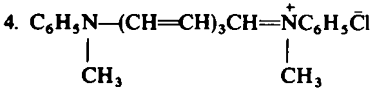
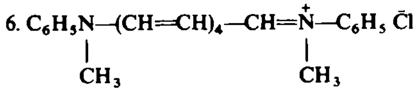
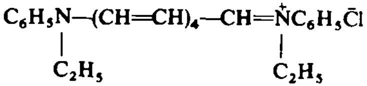
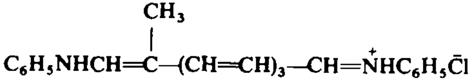
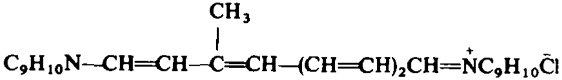
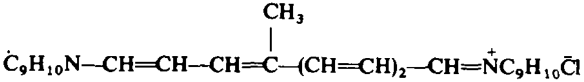
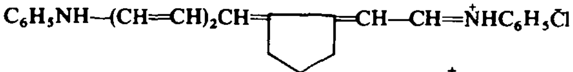
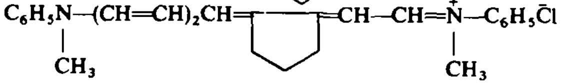
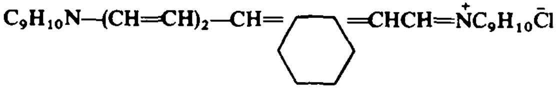
Formula	Yield %	M.p. in °C	λ_{max} (alcohol) in mμ	Found		Formula	Calc	
				Cl	N		Cl	N
1. $C_6H_5NH{-}(CH{=}CH)_3CH{=}\overset{+}{N}HC_6H_5\bar{Cl}$ (IVa)	61	162–163	592	11·43	8·72	$C_{19}H_{19}ClN_2$	11·41	9·01
2. $C_9H_{10}N{-}(CH{=}CH)_3CH{=}\overset{+}{N}C_9H_{10}\bar{Cl}$ (IVb)	80	140–142 (dec)	597	9·86	6·65	$C_{25}H_{27}ClN_2$	9·07	7·16
3.  $C_6H_5NHCH{=}\overset{CH_3}{C}{-}(CH{=}CH)_2{-}CH{=}\overset{+}{N}HC_6H_5\bar{Cl}$ (IVc)	71	124–125 (dec)	590	10·98	8·03	$C_{20}H_{21}ClN_2$	10·92	8·62
4.  $C_6H_5\underset{CH_3}{N}{-}(CH{=}CH)_3CH{=}\underset{CH_3}{\overset{+}{N}}C_6H_5\bar{Cl}$ (IVd)	67	110–111 (dec)	552	10·29	—	$C_{21}H_{23}ClN_2$	10·46	—

TABLE 2. NONAMETHINIUM SALTS (VIII, IX, X, XI)

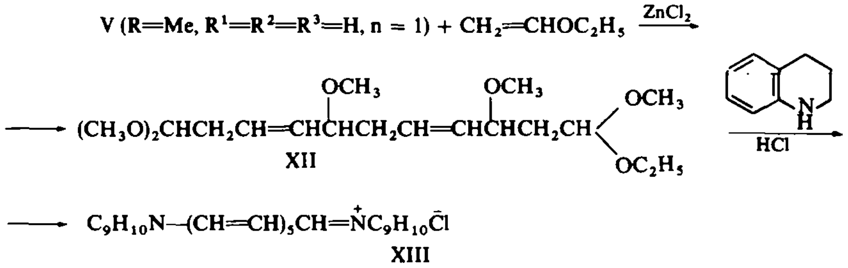
Formula		Yield %	M.p. in °C	λ_{max} (alcohol) in mμ	Found		Formula	Calc	
					Cl	N		Cl	N
1. $C_6H_5NH{-}(CH{=}CH)_4{-}CH{=}\overset{+}{N}HC_6H_5\bar{C}l$	(VIIIa)	83	141–142 (dec)	691	10·40	—	$C_{21}H_{21}ClN_2$	10·52	—
2. $C_9H_{10}N{-}(CH{=}CH)_4{-}CH{=}\overset{+}{N}C_9H_{10}\bar{C}l$	(VIIIb)	73	123–124	696	8·25	6·39	$C_{27}H_{19}ClN_2$	8·50	6·71
3. n-$CH_3C_6H_4NH{-}(CH{=}CH)_4{-}CH{=}NHC_6H_4CH_3$-n $\bar{C}l$	(VIIIc)	66	143–146 (dec)	700	9·61	—	$C_{23}H_{25}ClN_2$	9·71	—
4. n-$ClC_6H_4NH{-}(CH{=}CH)_4{-}CH{=}\overset{+}{N}HC_6H_4Cl$-n $\bar{C}l$	(VIIId)	84	145–146 (dec)	676	26·17	—	$C_{21}H_{19}Cl_3N_2$	26·21	—
5. m-$CF_3C_6H_4NH{-}(CH{=}CH)_4{-}CH{=}\overset{+}{N}HC_6H_4CF_3$-m $\bar{C}l$	(VIIIe)	68	128 (dec)	683	7·31	—	$C_{23}H_{19}F_6ClN_2$	7·50	—
6.  $C_6H_5\underset{\underset{CH_3}{\mid}}{N}{-}(CH{=}CH)_4{-}CH{=}\underset{\underset{CH_3}{\mid}}{\overset{+}{N}}{-}C_6H_5\ \bar{C}l$	(VIIIf)	60	102–103 (dec)	657	9·54	—	$C_{23}H_{25}ClN_2$	9·71	—

7.  $\underset{C_2H_5}{C_6H_5N}-(CH{=}CH)_4-CH{=}\underset{C_2H_5}{\overset{+}{N}}C_6H_5\bar{Cl}$	(VIIIg)	46	87–88 (dec)	647	8·91	—	$C_{25}H_{29}ClN_2$	9·02	—
8.  $C_6H_5NHCH{=}\overset{CH_3}{C}-(CH{=}CH)_3-CH{=}\overset{+}{N}HC_6H_5\bar{Cl}$	(VIIIh)	82	127–129	690	10·23	—	$C_{22}H_{23}ClN_2$	10·12	—
9.  $C_9H_{10}N-CH{=}CH-\overset{CH_3}{C}{=}CH-(CH{=}CH)_2CH{=}\overset{+}{N}C_9H_{10}\bar{Cl}$	(VIIIi)	58	86–89	713	—	5·73	$C_{28}H_{31}ClN_2$	—	6·51
10.  $\dot{C}_9H_{10}N-CH{=}CH-CH{=}\overset{CH_3}{C}-(CH{=}CH)_2-CH{=}\overset{+}{N}C_9H_{10}\bar{Cl}$	(VIIIj)	77	107–109	694	—	6·73	$C_{28}H_{31}ClN_2$	—	6·51
11. 	(IX)	85	fusion	728	—	7·24	$C_{24}H_{25}ClN_2$	—	7·43
12. 	(X)	63	63–65 (dec)	693	8·23	—	$C_{26}H_{31}ClN_2$	8·71	—
13. 	(XI)	26	93–95	730	7·41	6·03	$C_{31}H_{35}ClN_2$	7·52	5·94

The above method is convenient for the synthesis of both straight chain nonamethinium salts and those with alkyl substituents in different positions of the polyene chain, as well as alicyclic compounds containing five (IX and X) or six (XI) numbered cycles in a conjugated chain (obtained from compounds VI and VII (Table 2).

Undecamethinium salts[15]

The condensation of 1,1,5,9,9-pentamethoxynona-3,6-diene (V, R = Me, R^1 = R^2 = R^3 = H, n = 1) with vinyl ethyl ether affords 1,3,7,11-pentamethoxy-1-ethoxyundeca-4,8-diene XII, which on treatment with dilute hydrochloric acid in the presence of tetrahydroquinoline yields undecamethinium salts (XIII; λ_{max} 800 mμ) in good yield.



$$\mathrm{V\ (R{=}Me,\ R^1{=}R^2{=}R^3{=}H,\ n = 1) + CH_2{=}CHOC_2H_5 \xrightarrow{ZnCl_2}}$$

$$\longrightarrow \underset{\mathrm{XII}}{\mathrm{(CH_3O)_2CHCH_2CH{=}CH\overset{OCH_3}{C}HCH_2CH{=}CH\overset{OCH_3}{C}HCH_2CH\begin{smallmatrix}OCH_3\\OC_2H_5\end{smallmatrix}}} \xrightarrow[\mathrm{HCl}]{}$$

$$\longrightarrow \underset{\mathrm{XIII}}{\mathrm{C_9H_{10}N{-}(CH{=}CH)_5CH{=}\overset{+}{N}C_9H_{10}\overset{-}{Cl}}}$$

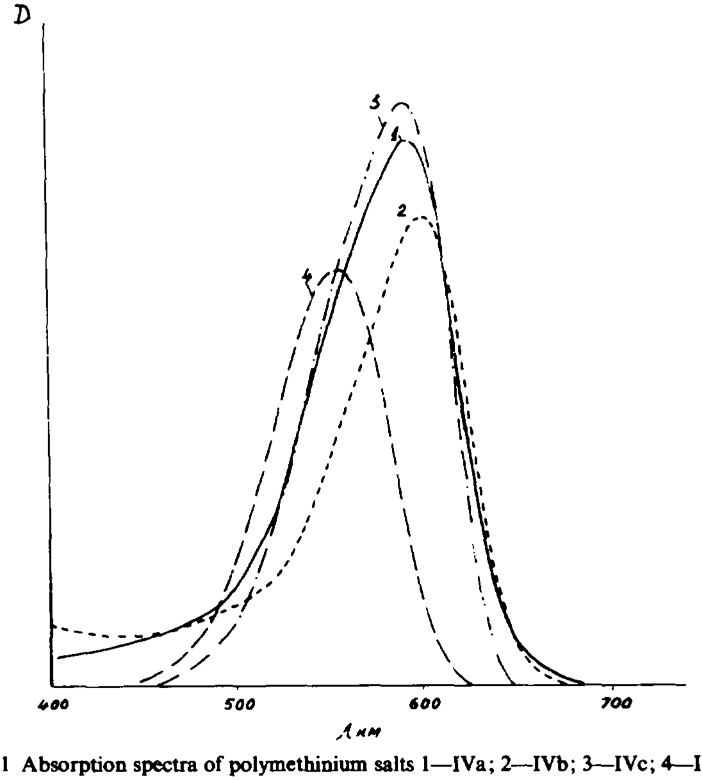


Fig. 1 Absorption spectra of polymethinium salts 1—IVa; 2—IVb; 3—IVc; 4—IVd.

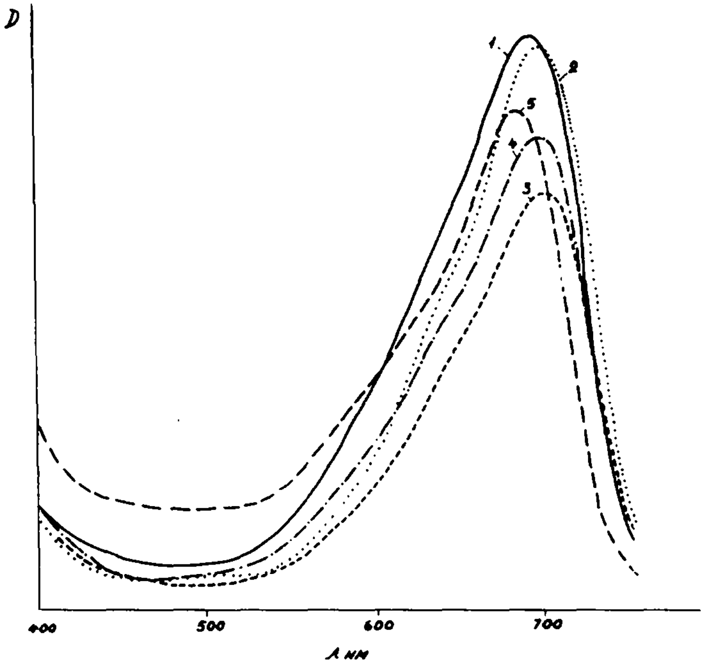


FIG. 2 Absorption spectra of polymethinium salts 1—VIIIa; 2—VIIIb; 3—VIIIc; 4—VIIIe; 5—VIIId.

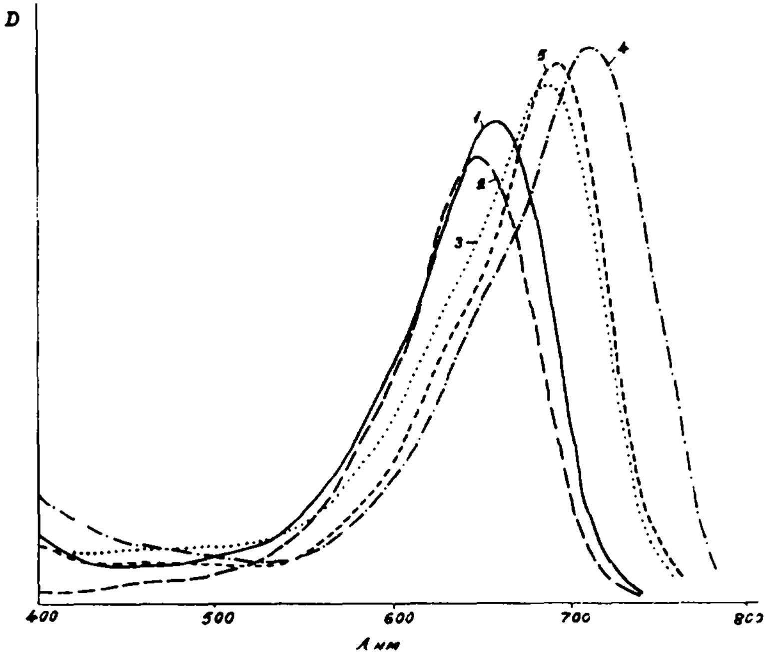


FIG. 3 Absorption spectra of polymethinium salts 1—VIIIf; 2—VIIIg; 3—VIIIh; 4—VIIIi; 5—VIIIj.

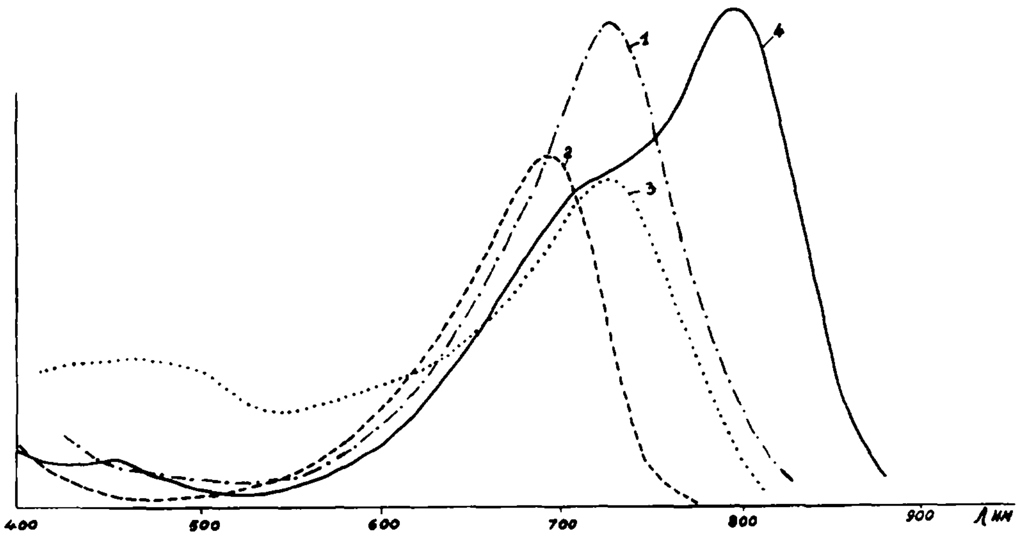


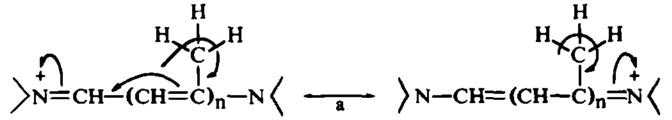
Fig. 4 Absorption spectra of polymethinium salts 1—IX; 2—X; 3—XI; 4—XIII.

UV and visible spectra of polymethinium salts

All polymethinium salts are characterized by a single narrow band in the visible region of the absorption spectra (Figs. 1–4). The extention of the polymethinium chain results in the usual bathochromic shift.

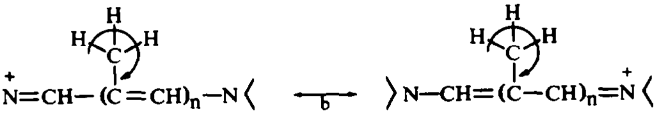
N-Methylaniline derivatives exhibit their max 35–40 mμ shorter than aniline derivatives (e.g. IVa and IVd, or VIIIa and VIIIf), and tetrahydroquinoline compounds shift the absorption 5 mμ to longer wavelengths as compared with their aniline analogues (e.g. IVa and IVb, VIIIa and VIIIb).

The introduction of the alkyl groups conjugated with positive charged N atom of



$$\rangle\overset{+}{N}{=}CH{-}(CH{=}\overset{CH_3}{C})_n{-}N\langle \xrightarrow{a} \rangle N{-}CH{=}(CH{-}\overset{CH_3}{C})_n{=}\overset{+}{N}\langle$$

the polymethinium salts (compounds a) causes a bathochromic shift (15–17 mμ) (e.g. VIIIb and VIIIi) but no shift was observed for nonconjugated derivatives (compounds b) (e.g. VIIIa and VIIIh, VIIIb and f).



$$\rangle\overset{+}{N}{=}CH{-}(\overset{CH_3}{C}{=}CH)_n{-}N\langle \xrightarrow{b} \rangle N{-}CH{=}(\overset{CH_3}{C}{-}CH)_n{=}\overset{+}{N}\langle$$

Products with alicyclic substituents in the conjugated chain exhibit a bathochromic shift (35–39 mμ) as compared with unsubstituted compounds (e.g. VIIIa and IX, XI; VIIIf and X).

EXPERIMENTAL

Condensation of glutaconic aldehyde tetramethyl acetal (II, R=Me) *with methylpropenyl ether, and conversion of* III *into heptamethinium salts* (Table 1)

Glutaconic aldehyde tetramethyl acetal (II, R=Me). 2,6-Dimethoxy-Δ^3-dihydropyrane (113·6 g) was added to anhyd MeOH (420 ml) saturated with HBr (71 g) at −30°. The mixture was kept at −10° for 2hr, then cooled to −30°, and dry ammonia added to pH 8. The mixture was treated with water and ether. The ether extract was dried (K_2CO_3), evaporated and the residue distilled *in vacuo* to yield II (R = Me; 129·5 g, 86·5%), b.p. 105°/10 mm, n_D^{20} 1·4330. (Found: C, 56·81; 56·51; H, 9·52, 9·45. $C_9H_{18}O_4$ requires: C, 56·82; H, 9·54%).

1,1,3,7,7-*Pentamethoxy-2-methylhept-4-ene* (III, R = R^1 = Me). Methyl propenyl ether (7·2 g) was added dropwise during 15 min to a stirred mixture of glutaconic aldehyde tetramethyl acetal (19 g), 10% soln of $ZnCl_2$ in EtOAc (0·5 ml) adn two drops of BF_3-Et_2O at 35°. The mixture was stirred for 2 hr at 20°, diluted with ether and washed with 5% soln K_2CO_3aq. The ether soln (dried with K_2CO_3) was evaporated and twofold distillation of the residue afforded 63% of III (R = R^1 = Me; 16·5 g), b.p. 105–108°/2 mm, n_D^{20} 1·4413. (Found: C, 59·43, 59·88; H, 10·14, 10·20. $C_{13}H_{26}O_5$ requires: C, 59·51; H 9·99%).

7-*Anilinohepta-2,4,6-trienylidene) aniliniumchloride* IVa). Dil HCl (18%, 0·6 ml) was added to an ice-cold stirred mixture of III (R = Me, R^1 = H, 0·64 g) and aniline (0·65 g). After 40 min the ppt of IV was filtrated off, thoroughly washed with water, ether and benzene to produce after drying in a vacuum dessicator 61% of IVa (0·8 g) (Table 1).

[7-(N-*Methylanilino)hepta-2,4,6-trieneylidene*] *methylanilinium chloride* (IVd). Dil HCl (6%, 4 ml) was added to a mixture of III (R = Et, R^1 = H, 0·64 g) and N-methylaniline hydrochloride (0·58 g). The mixture was kept in an ice-bath for 30 min then the crystalline ppt (IVd) was collected, washed with cold water, ether benzene and dried in vacuum-dessicator, yield 0·45 g (67%) (Table 1).

Condensation of glutaconic aldehyde tetramethyl acetal (II, R = Me) *with* 1-*methoxybuta*-1,3-*diene, and and conversion of* V (n = 1) *into nonamethinium salts* (Table 2)

Condensation of glutaconic aldehyde tetramethyl acetal with 1-*methoxybutadiene*. 1-Methoxybuta-1,3-diene (30·1 g) was added dropwise to a mixture of glutaconic aldehyde tetramethyl acetal (136 g), 10% soln of $ZnCl_2$ in EtOAc (25 ml) at 33–35° for 30 min. The soln was allowed to stand overnight at 20°, diluted with 5% NaOHaq (3 × 100 ml), water (2 × 100 ml) and dried with $MgSO_4$. Twofold distillation gave

(i) Starting glutaconic aldehyde tetramethyl acetal (79·1 g), b.p. 50–62°/0·1 mm, n_D^{20} 1·4345.

(ii) Compound V (R = Me, R^1 = R^2 = R^3 = H, n = 1, 45·0 g), b.p. 107–110°/0·5 mm, n_D^{20} 1·4562. (Found: C, 60·88, 61·10; H, 9·48, 9·64. $C_{14}H_{26}O_5$ requires: C, 61·29; H, 9·55%).

(iii) Compound V (R = Me, R^1 = R^2 = R^3 = H, n = 2; 18·3 g), d.p. 156–160°/0·5 mm, n_D^{20} 1·4675. (Found: C, 63·27, 63·46; H, 9·75, 10·01. $C_{19}H_{34}O_6$ requires: C, 63·66; H, 9·56%).

(iv) Compound V (R = Me, R^1 = R^2 = R^3 = H, n = 3; 5·1 g), b.p. 178–180°/0·5 mm, n_D^{20} 1·4845. (Found: C, 65·33, 65·42; H, 9·43, 9·62. $C_{24}H_{42}O_7$ requires: C, 65·13; H, 9·57%).

[9-(N-*Tetrahydroquinolino)nona-2,4,6,7-tetraenylidene*]-*tetrahydroquinolinium chloride* (VIIIb). HCl (18%, 0·5 ml) was added to a mixture of tetrahydroquinoline (0·45 g) and V (R = Me, R^1 = R^2 = R^3 = H, n = 1, 0·45 g) and after 5 min stirring water (1 ml) was added dropwise. The resulting crystals of VIIIb were treated as above, yield 0·5 g (73%) (Table 2).

[9-(N-*Methylanilino)nona-2,4,6,8-tetraenylidene*]-N-*methylaniliniumchloride* (VIIIf). HCl (6%, 30 ml) was added to ice-cold mixture of V (R = Me, R^1 = R^2 = R^3 = H, n = 1; 5·5 g) and N-methylaniline hydrochloride (5·8 g). The mixture was kept in ice for 30 min, then the crystalline ppt (VIIIf) was removed and treated as above, yield 4·5 g (60%) (Table 2).

Condensation of 1,1,5,9,9-*pentamethoxynona-2,6-diene* (V, R = Me, R^1 = R^2 = R^3 = H, n = 1) *with vinyl ethyl ether, and conversion of* XII *into an undecamethinium salt* (XIII)

1,3,7,11,11-Pentamethoxy-1-ethoxyundeca-4,7-diene (XII). Vinyl ethyl ether (1·5 g) was added dropwise to a stirred mixture of 1,1,5,9,9-pentamethoxynona-2,6-diene (5·5 g), two drops of 10% soln of $ZnCl_2$ in EtOAc and one drop of BF_3-Et_2O at 40° for 20 min. After additional stirring at 40° for 1·5 hr it was treated with 5% K_2CO_3aq and ether. The organic layer was then washed with water, dried (K_2CO_3) and evaporated, to yield after distillation 42·8% of 1,3,7,11,11-pentamethoxy-1-ethoxyundeca-4,8-diene (3 g), b.p. 130–133°/0·2 mm, n_D^{20} 1·4566. (Found: C, 62·45, 62·85; H, 9·91, 10·27. $C_{18}H_{34}O_6$ requires: C, 62·40; H, 9·89%).

[1-(N-*Tetrahydroquinolino)undeca-2,4,6,8,10-pentaenylidene*]-*tetrahydroquinolinium chloride* (XIII). To a mixture of XII (0·2 g) and tetrahydroquinoline (0·2 g) cooled in ice, 12% HCl (0·3 g) was added with stirring After 30 min, the crystals were separated and treated as above, yield 0·18 g (60·8%); m.p. 110–112°. (Found: N, 6·00, 6·06; Cl, 7·57, 7·77. $C_{29}H_{31}ClN_2$ requires: N, 6·32; Cl, 9·00%) λ_{max} (CH_3OH) 800 mμ.

UV spectra were determined in MeOH soln using SF-2M Spectrophotometer. We thank Prof. I. I. Levkoev for his interest to this work.

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