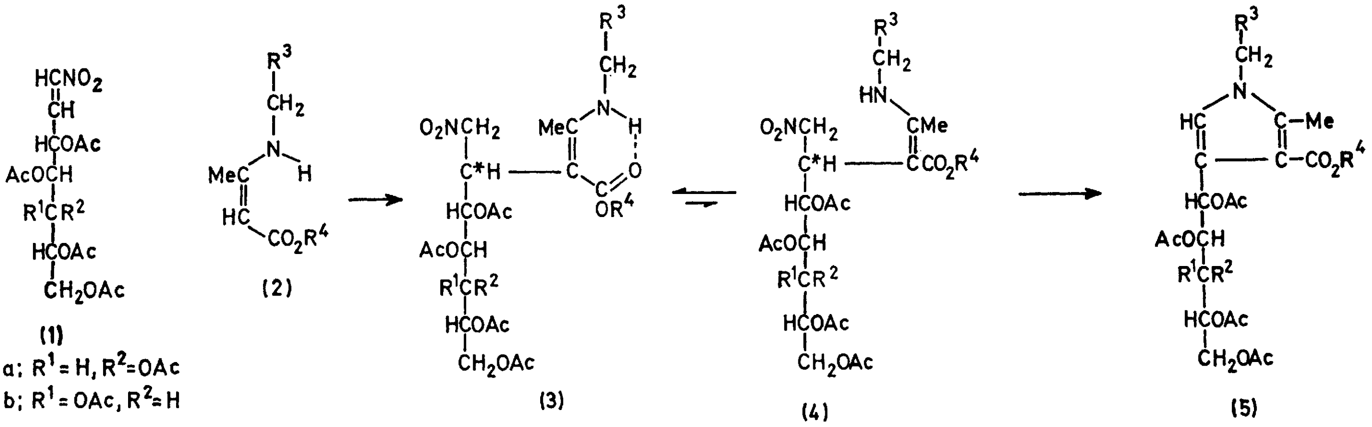
Synthesis of 3-(Polyacetoxyalkyl)pyrroles from 3-Aminocrotonic Esters and Open-chain Sugar Nitro-olefins

By **Antonio Gómez-Sánchez,*** **Manuel Mancera,** and **Francisco Rosado,** Departamento de Química Orgánica, Facultad de Química, Universidad de Sevilla, and Instituto de la Grasa, C.S.I.C., Seville, Spain
Juana Bellanato, Instituto de Optica, C.S.I.C., Madrid, Spain

D-*gluco*- and D-*galacto*-3,4,5,6,7-Penta-acetoxy-1-nitrohept-1-ene (1a and b) reacted with 3-(alkylamino)-crotonic esters (2) yielding the Michael-type adducts (3) which have a preference for the intramolecularly bonded (*Z*)-configuration. These compounds were cyclized into 4-(D-*gluco*- or D-*galacto*-penta-acetoxypentyl)-1-alkyl-2-methylpyrrole-3-carboxylic esters (5), the *O*-deacetylation of which afforded the corresponding polyols (8). Periodate or lead tetra-acetate oxidation of (8) gave the pyrrole-3-carbaldehydes (9).

OPEN-CHAIN sugar nitro-olefins (polyacetoxy-1-nitroalk-1-enes[1] and *O*-protected 2-*C*-glycosyl-1-nitroethylenes[2]) are attractive as potential starting materials for the synthesis of functionalized, branched-chain sugars and *C*-(polyhydroxyalkyl)- and *C*-glycosyl-heterocyclic compounds derived from them. We report here an easy way to obtain 3-(penta-acetoxypentyl)pyrrole derivatives (5), and therefrom the corresponding polyols (8) by a Michael-type addition of 3-(alkylamino)crotonic esters (2) to penta-acetoxy-1-nitrohept-1-enes (1) and the further cyclization of the adducts (3). (Pentahydroxypentyl)pyrroles similar to (8) have aroused some interest[3] as precursors of *C*-glycosylpyrroles and have been obtained by condensation of the rather inaccessible heptosamines with acetoacetic esters in very low overall yields. There are antecedents in the literature[4] on the synthesis of pyrroles by reaction of 1-nitroprop-1-ene with ethyl 3-(alkylamino)crotonates; addition compounds similar to (3) were supposed to be intermediates, and an adduct of this type was isolated in one instance.[4b]



a; $R^1 = H$, $R^2 = OAc$, $R^3 = Ph$, $R^4 = Me$
b; $R^1 = H$, $R^2 = OAc$, $R^3 = Ph$, $R^4 = Et$
c; $R^1 = H$, $R^2 = OAc$, $R^3 = 3,4-C_6H_3(OMe)_2$, $R^4 = Et$
d; $R^1 = H$, $R^2 = OAc$, $R^3 = n-C_3H_7$, $R = Et$
e; $R^1 = OAc$, $R^2 = H$, $R^3 = Ph$, $R^4 = Et$
f; $R^1 = OAc$, $R^2 = H$, $R^3 = 3,4-C_6H_3(OMe)_2$, $R^4 = Et$
g; $R^1 = OAc$, $R^2 = H$, $R^3 = n-C_3H_7$, $R^4 = Et$

SCHEME 1

The addition of 3-(alkylamino)crotonic esters (2) to the sugar nitro-olefins (1) to form compounds (3) took place readily at room temperature in a variety of solvents (ether, acetonitrile, alcohols), the reaction rate increasing with the polarity of the medium. T.l.c. control of the process showed that the addition was followed by a slower reaction that yielded the final pyrrole compounds (5) (Scheme 1). The two types of products could be distinguished by the colour reaction that they gave when treated with *p*-dimethylaminobenzaldehyde–hydrochloric acid (Ehrlich reagent) on the chromatoplates: the faster moving addition compounds (3) gave an ephemeral pink colour that turned brown on prolonged heating while pyrroles (5) gave persistent violet colours. The cyclization reaction was also favoured by an increase of the polarity of the solvent or the temperature. Adducts (3) could be obtained in very high yields merely by allowing the reactants to stand at room temperature in ether or acetonitrile till t.l.c. indicated their complete transformation, and evaporation of the solvent; under

TABLE 1

Physical constants and analytical data of adducts (3)

Compound (3)	M.p. (°)	$[\alpha]_{5461}$ (°)	R_F [a]	Yield (%)	Formula	Analysis Calculated C	H	N	Found C	H	N
(3a)	*b*	+29.6 *	0.56 [c]	92 [d]	$C_{29}H_{38}N_2O_{14}$	54.55	6.0	4.4	54.45	6.05	4.35
(3b)	*b*	+26.3 *	0.57 [c]	80 [d]	$C_{30}H_{40}N_2O_{14}$	55.2	6.15	4.3	55.0	6.35	4.2
(3c)	51—52 [d]	+37.3 *	0.66 [e]	92 [d]	$C_{32}H_{44}N_2O_{16}$	53.9	6.2	3.95	53.65	6.0	3.9
(3d)	*b*	*f*	0.61 [c]	87 [d]	$C_{27}H_{42}N_2O_{14}$	52.4	6.85	4.5	52.1	7.05	4.3
(3e)	107—108 [g]	−55.1 †	0.87 [c]	60 [g]	$C_{30}H_{40}N_2O_{14}$	55.2	6.15	4.3	55.15	6.2	4.55
(3f)	20—24 [g]	−64.2 †	0.46 [h]	20 [g]	$C_{32}H_{44}N_2O_{16}$	53.9	~6.2	3.95	53.6	6.45	3.85
(3g)	111—113 [g]	−99.8 †	0.80 [e]	50 [g]	$C_{27}H_{42}N_2O_{14}$	52.4	6.85	4.5	52.2	6.7	4.55

[a] T.l.c. on silica gel. [b] Amorphous solid. [c] Eluant: ether–hexane (7 : 1). [d] After column chromatography. [e] Eluant: ether. [f] Not measured. [g] After recrystallization from ethanol. [h] Eluant: ether–hexane (3 : 1).

* In pyridine. † In chloroform.

these conditions the cyclization was very slow. Pyrroles (5) were better obtained by heating the starting materials (1) and (2), or the intermediate adducts (3), in methanol under reflux; yields ranged from 30 to 60%. Both reactions were faster with ethyl 3-(n-butylamino)-crotonate than with the analogous *N*-benzyl and *N*-veratryl compounds; also nitro-olefin (1a) with the D-*gluco*-configuration reacted faster and gave less stable intermediates (3) than its D-*galacto*-isomer (1b).

Addition compounds (3a—d) arising from D-*gluco*-

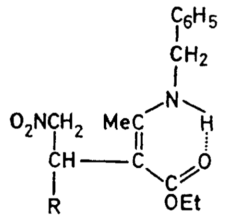
TABLE 2

Spectral data of adducts(3)

Compd.	U.v. absorption [a] $\lambda_{max.}$(nm) (log ε)	I.r. absorption (cm^{-1}) Phase	ν(N–H)	AcO	ν(C=O)	C=C–NH	$\nu_a(NO_2)$	$\nu(C–NO_2)$	^{1}H N.m.r. chemical shift (δ) [b] NH	=C–Me and OAc	N–CH$_2$	R^3	OR^4	CH$_2$NO$_2$
(3a)	294 (4.17)	KBr	3 260vw 3 230vw	1 752vs 1 371s	1 705sh [c] 1 650s	1 592s 1 585sh	1 551s	790w	10.42br	1.91, 1.98, 2.00, 2.05, 2.07, 2.12		7.26br	3.72, 3.74	
		CDCl$_3$	3 255vw 3 225vw	1 752vs 1 372s	1 705sh [c] 1 649M	1 598M 1 585sh	1 556s							
		CCl$_4$	3 255vw 3 220vw	1 759vs 1 372s	1 715vw [c] 1 657M	1 598M 1 585sh								
(3b)	295 (4.23)	KBr	3 260vw 3 230vw	1 752vs 1 371s	1 705sh [c] 1 648s	1 597s 1 585sh	1 552s	790w	10.31br	1.91, 1.99, 2.00, 2.03, 2.06, 2.13		7.24br	1.32 (t), 4.2 (q, *J* 7.0 Hz)	
		CDCl$_3$	3 250vw 3 230vw	1 750vs 1 371s	1 702sh [c] 1 642M	1 595M 1 585sh	1 555s							
		Me$_2$SO		1 749vs 1 370s	1 700sh [c] 1 642M	1 592M 1 582M	1 552s	791w						
(3c)	293 (4.14)	KBr	3 250vw	1 752vs 1 371s	1 702sh [c] 1 648M	1 596s	1 551s	790w	10.58br	1.90, 1.93, 1.96, 2.04, 2.05, 2.12		6.77br 3.83— 3.85	1.31 (t), 1.33 (t), 4.21br (q)	
		CDCl$_3$	3 250vw	1 750vs 1 371s	1 642s	1 597M 1 588sh	1 555s							
(3d)	295 (4.37)	KBr	3 250vw	1 752vs 1 372s	1 648s	1 596s	1 555s	791w	9.90br	1.90, 1.94, 2.01, 2.05, 2.08, 2.14		0.5— 1.7 (m)		
(3e)	296 (4.38)	KBr	3 250vw	1 764sh 1 755sh 1 748vs 1 730s	1 705sh [c] 1 640s	1 593s 1 584s	1 552s	795w	9.85	1.88, 2.06, 2.10, 2.12, 2.14, 2.16	4.34 (d)	7.20br	1.36 (t), 4.16 (q, *J* 7.0 Hz)	4.50 (m)
		CDCl$_3$	3 250vw	1 750vs 1 370s	1 642M	1 596M 1 584sh	1 553s							
(3f)	295 (4.46)	KBr	3 260vw 3 230vw	1 752vs 1 371s	1 649s	1 597s	1 553s	791w	9.50	1.90, 1.92, 1.94, 1.96, 2.00, 2.10	4.70 (d)	6.50br 3.74	1.35 (t), 4.2 (q, *J* 7.0 Hz)	4.50 (m)
		CHCl$_3$	3 240vw	1 748vs 1 370s	1 643M	1 596M	1 552s							
(3g)	294 (4.18)	KBr	3 245vw	1 755vs 1 744vs 1 371s	1 705vw [c] 1 638s	1 594s	1 551s	796w	8.50	1.90, 1.94, 1.96, 1.98, 2.00, 2.10	4.40 (d)	0.95— 1.00 (m)	1.35 (t), 4.2 (q, *J* 7.0 Hz)	4.40 (m)
		CDCl$_3$	3 245vw	1 748vs 1 370s	1 705sh [c] 1 640M	1 592M	1 553s							
		CCl$_4$	3 380vw [c] 3 230sh 3 220vw	1 756vs 1 370s	1 649M	1 595M								

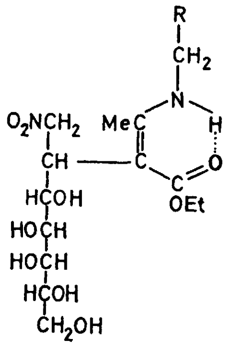
[a] In ethanol. [b] In CDCl$_3$. [c] Assigned to a small proportion of the (*E*)-isomer.

3,4,5,6,7-penta-acetoxy-1-nitrohept-1-ene (1a) were obtained as amorphous solids that became brown syrups on standing; those (3e—g) derived from the D-*galacto*-isomer (1b) were white, crystalline solids. A new chiral centre [marked * in formula (3)] is formed in the addition reaction and two diastereoisomers could result; in all cases we have only been able to isolate, or to detect chromatographically, a single product (however, see below for the discussion of the n.m.r. spectra). Yields, physical constants, and analytical data of adducts (3) are in Table 1. The structures of these substances followed from their elemental analyses and consideration of their spectroscopic and chemical properties.



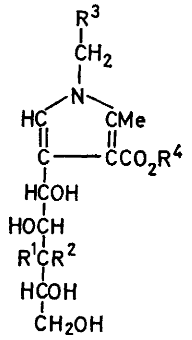
(6) a; R = Me

b; R = Ph



(7) a; R = Ph

b; R = $n-C_3H_7$



(8) a; $R^1 = H, R^2 = OH, R^3 = Ph, R^4 = Me$

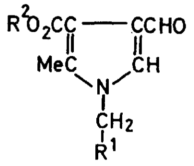
b; $R^1 = H, R^2 = OH, R^3 = Ph, R^4 = Et$

c; $R^1 = H, R^2 = OH, R^3 = 3,4-C_6H_3(OMe)_2, R^4 = Et$

d; $R^1 = H, R^2 = OH, R^3 = n-C_3H_7, R^4 = Et$

e; $R^1 = OH, R^2 = H, R^3 = 3,4-C_6H_3(OMe)_2, R^4 = Et$

f; $R^1 = OH, R^2 = H, R^3 = n-C_3H_7, R^4 = Et$

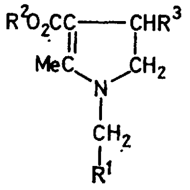


(9) a; $R^1 = Ph, R^2 = Me$

b; $R^1 = Ph, R^2 = Et$

c; $R^1 = 3,4-C_6H_3(OMe)_2, R^2 = Et$

d; $R^1 = n-C_3H_7, R^2 = Et$



(10)

Adducts (3) showed a maximum in the u.v. at the same wavelength and of similar intensity (Table 2) as those observed in the similarly constituted 3-aminocrotonic ester derivatives (6a), $\lambda_{max.}$ 297 nm (log ε 4.28),[4b] and (6b), $\lambda_{max.}$ 295 nm (log ε 4.27).[5] Their i.r. spectra (Table 2) were similar to those of the intramolecularly bonded (*Z*)-form of 3-(alkylamino)crotonic esters (2) [6] and to that of compound (6b) which also exists in the chelated (*Z*)-form.[5] The presence of a strong intramolecular hydrogen bond, and consequently the (*Z*)-geometric configuration, was indicated by the large displacements to low frequency of the ν(N–H) and ν(C=O) bands of the 3-aminocrotonic ester moiety of these molecules; the positions of these bands did not change significantly either by changing the medium or by dilution, thus confirming the chelated structure. A shoulder observed in all cases at the high frequency side of the ν(C=O) band may be attributed to a small proportion of the corresponding (*E*)-form (4). The strong band at *ca.* 1 595 cm^{-1} was considered to arise from a mixed vibration with a contribution from both the ν(C=C) and the ν(N–H) modes; this band is also present in the spectra of the parent compounds (2) and the model compounds (6) and has been assigned in this way on the basis of *N*-deuteriation experiments.[5,6] The strong bands due to the acetoxy and nitro groups appeared in the anticipated ranges. The whole pattern of strong bands between

TABLE 3

Physical constants and analytical data of pyrroles (5) and (8)

						Analysis					
						Calculated			Found		
Compound	M.p. (°)	$[\alpha]_{5461}$ (°)	R_F [a]	Yield (%)	Formula	C	H	N	C	H	N
(5a)	107—108 (EtOH)	+95.8 *	0.44 [b]	45	$C_{29}H_{35}NO_{12}$	59.05	6.0	2.35	58.8	5.85	2.3
(8a)	180—181 (MeOH)	+50.4 *	0.43 [c]	93	$C_{19}H_{25}NO_7$	60.15	6.65	3.7	60.25	6.65	3.65
(5b)	95—97 (EtOH)	+90.1 †	0.43 [b]	42	$C_{30}H_{37}NO_{12}$	59.7	6.15	2.3	59.65	5.95	2.5
(8b)	182—184 (MeOH)	+43.6 *	0.48 [c]	95	$C_{20}H_{27}NO_7$	61.05	6.9	3.55	60.85	7.1	3.45
(5c)	68—69 (ether–hexane)	+86.3 *	0.49 [b]	30	$C_{32}H_{41}NO_{14}$	57.9	6.2	2.1	57.8	6.15	2.35
(8c)	170—171 (MeOH)	+43.2 *	0.48 [c]	90	$C_{22}H_{31}NO_9$	58.25	6.9	3.1	57.95	7.0	3.15
(5d)	53—54 (MeOH)	+96.2 *	0.48 [b]	37	$C_{27}H_{39}NO_{12}$	56.95	6.9	2.45	56.65	6.65	2.3
(8d)	174—175 (MeOH)	+33.0 *	*d*	92	$C_{17}H_{29}NO_7$	56.8	8.05	3.9	56.6	7.85	3.65
(5e)	97—98 (EtOH)	+20.1 ‡	0.80 [b]	25	$C_{30}H_{37}NO_2$	59.9	5.85	2.35	59.45	6.15	2.4
(5f)	65—67 (ether–hexane)	+26.1 ‡	0.39 [c]	63	$C_{32}H_{41}NO_{14}$	57.9	6.2	2.1	57.7	6.4	2.05
(8e)	158—160 (MeOH)	+79.8 §	0.49 [c]	30	$C_{22}H_{31}NO_9$	58.25	6.9	3.1	58.0	6.85	2.95
(5g)	96—98 (EtOH)	+6.5 ‡	0.77 [b]	60	$C_{27}H_{39}NO_{12}$	56.95	6.9	2.45	56.9	6.7	2.5
(8f)	152—154 (MeOH)	+13.2 §	0.32 [c]	82	$C_{17}H_{29}NO_7$	56.8	8.15	3.9	56.85	7.9	3.85

[a] T.l.c. on silica gel. [b] Eluant: ether–hexane (7 : 1). [c] Eluant: chloroform–methanol (7 : 1). [d] Not measured.

* In pyridine. † In MeOH. ‡ In chloroform. § In EtOH.

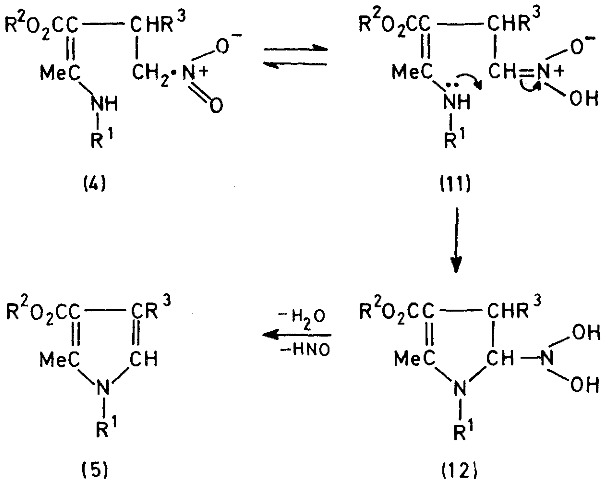
1 800 and 1 300 cm^{-1} is highly characteristic of these compounds.

The n.m.r. spectra of adducts (3) were rather complex but showed features (Table 2) consistent with the chelated structure assigned. The low field N–H signal indicated again the presence of the hydrogen bond and the (*Z*)-configuration.[5-7] The :C·Me singlet appeared at δ 1.90—2.01, overlapping the acetoxy signals, in accord with the observations made [5-7] for compounds (2) and (6); 2-substituted 3-aminocrotonic esters similar to (3) but with the (*E*)-configuration would be expected [7] to show the :C·Me signal at lower field (δ 2.2—2.3). Some adducts (3) showed broadening, and even splitting, of signals which can be accounted for by the presence of two epimers at the carbon atom marked * in formula (3); for instance, adduct (3a) had two CO_2Me singlets of almost the same intensity, with a total integral of three protons, at δ 3.72 and 3.74.

Treatment of adducts (3e and g) with sodium methoxide in methanol afforded, after deionization with Amberlite IR-120 (H$^+$), good yields of the corresponding *O*-deacetylated derivatives (7a and b). These substances were obtained as crystalline, chromatographically homogeneous solids that showed u.v. absorptions, $\lambda_{max.}$ 297 nm (log ε 4.1—4.2), very similar to those of adducts (3) and reference compounds (6). Likewise, their i.r. spectra showed the pattern of absorption in the range 1 700—1 500 cm^{-1} [1 670—1 665 (C=O), 1 610—1 600 (C=C–N–H), and 1 540 cm^{-1} (NO_2)] found to be typical of adducts (3) and compounds (6). The n.m.r. spectra showed the singlet at δ 1.9—2.0 (:C·Me) and the broad signal at 8.5—9.0 (N–H) typical of 3-(alkylamino)crotonic esters with the (*Z*)-configuration.[7] Other features of the i.r. and n.m.r. spectra (see Experimental section) of these compounds were also consistent with structures (7).

Physical constants, yields, and analytical data of pyrroles (5) are in Table 3. Catalytic (sodium methoxide–methanol) *O*-deacetylation of these acetates afforded high yields of the corresponding polyols (8). The physical constants of these substances have also been included in Table 3.

Pyrroles (5) and (8) had u.v. absorptions (Table 4) similar to those of previously known [3,8] 4- (and 5)-(D-*arabino*-tetrahydroxybutyl)-2-methylpyrrole-3-carboxylic esters. Their i.r. spectra (Table 4) showed the pyrrolecarboxylic ester and the pyrrole ring bands at the



SCHEME 2

expected[3,8,9] frequencies; other bands in these spectra could be easily assigned to functional groups present in these structures. The n.m.r. spectra (Table 4) of the acetylated derivatives (5) showed the pyrrole proton (5-H) as a singlet at δ *ca.* 6.5; this signal usually appeared overlapping a doublet ($J_{1',2'}$ *ca.* 5 Hz) assigned to 1'-H of the sugar side-chain on the basis of the observed splitting and the consideration that this proton would resonate at lower field than the remaining protons of the sugar chain. Other features of these spectra were consistent with structures (5).

Oxidations of polyols (8) with sodium periodate required four moles of oxidant per mole. These reactions, or similar oxidations with lead tetra-acetate, gave high yields of pyrrole-3-carbaldehydes (9); two (9b and d) of these aldehydes were already known.[9]

TABLE 4

Spectral data of pyrroles (5) and (8)

Compd.	U.v. absorption [a] $\lambda_{max.}$(nm) (log ε)	I.r. absorption (cm^{-1}) [b]				^{1}H N.m.r. chemical shift (δ) [c]					
		ν(OH)	AcO	Pyrrole CO_2R^4	Pyrrole ring	OAc	R^3	OR^4	⁚C·Me	⁚CH	N·CH_2
(5a)	240 (3.86), 254sh		1 748vs, 1 371s	1 702s	1 575vw, 1 530w	1.86, 1.98, 2.00, 2.02	7.24 (m), 6.90 (m)	3.79	2.36	6.48	4.96br
(8a)	239 (3.82), 262sh	3 445M, 3 405M, 3 300sh, 3 250vs		1 696vs	1 568vw, 1 520M						
(5b)	239 (3.82), 254sh		1 748vs, 1 370s	1 697s	1 570vw, 1 529w	1.85, 1.96, 1.98, 2.00	7.24 (m), 6.92 (m)	1.34 (t), 4.28 (q)	2.35	6.48	4.96br
(8b)	243 (3.79), 261sh	3 450M, 3 300s, 3 260s		1 691vs	1 568vw, 1 520M						
(5c)	236 (4.14), 260sh		1 751vs, 1 371s	1 697s	1 555vw, 1 520s	1.86, 1.98, 2.00, 2.02	6.74 (d), 6.44 (d), 6.49, 3.81, 3.79	1.34 (t), 4.29 (q)	2.37	6.46	4.87br
(8c)	236 (4.21), 262	3 515s, 3 400s,br		1 693vs	1 568vw, 1 520vs						
(5d)	243 (3.94) 254sh		1 750vs, 1 371s	1 700s	1 568vw, 1 528w	1.86, 1.98, 2.00, 2.04	0.80— 1.75 (m)	1.37 (t), 4.31 (q)	2.43	6.48	3.77 (t)
(8d)	244 (3.85), 258sh	3 430s 3 285vs, 3 240sh		1 697vs	1 562vw, 1 520s						
(5e)	238 (4.20), 260sh		1 745vs, 1.365s	1 695s	1 560vw, 1.530M	1.80, 1.96, 1.98, 2.00	7.00 (m), 6.70 (m)	1.30 (t), 4.20 (q)	2.30	6.40	4.95br
(5f)	238 (4.04), 265sh		1 750vs	1 703s	1 567vw, 1519s	1.95, 1.98, 2.04, 2.12	6.50 (m), 3.74	1.40 (t), 4.30 (q)	2.34	6.48	4.94br
(8e)	239 (4.14), 265	3 370vs		1 680vs	1 565vw, 1 520M						
(5g)	239 (4.20), 258sh		1 750vs 1.370s	1 695s	1 560vw, 1.527w	1.90, 1.96, 2.00, 2.10	0.96 (m)— 2.75 (m)	1.45 (t), 4.30 (q)	2.10	6.46	3.70 (m)
(8f)	240 (4.11), 260	3 340vs		1 690vs	1 510M						

[a] In ethanol. [b] In KBr pellets. [c] In $CDCl_3$.

The mechanism of formation of pyrroles (5) from adducts (3) is uncertain. Grob *et al.*[4a] proposed the intermediacy of pyrrolines (10), formed by the intramolecular nucleophilic displacement of the nitro group by the alkylamino group in the (*E*)-form [similar to (4)] of the adducts, and their further oxidation by the nitrous acid produced in this reaction. As an alternative hypothesis, Grob and Schad[4b] considered the intramolecular addition of the amino group to the C=N bond of the nitronic acids which are tautomers of the nitro-compounds (3). We suggest a mechanism (Scheme 2) in line with the second hypothesis: the isomerization of the (*E*)-form (4) of the adducts into the nitronic acids (11) will probably be assisted by the tautomeric aminocrotonate system contained in the molecule. Cyclization of (11) could occur by nucleophilic attack of the amino nitrogen on the electron-deficient carbon next to the nitronic acid group to yield the nitroso-compound (12) from which the final pyrroles (5) can be derived. This mechanism is analogous to that suggested[10c] for the formation of furans by a similar reaction of 1,3-dicarbonyl compounds with nitro-olefins;[10] fairly stable (probably intramolecularly bonded) nitronic acid forms of the intermediate Michael adducts were isolated[10a] in these reactions and converted into the furans.

EXPERIMENTAL

Specific rotations were recorded at 5 461 Å with a 143C Bendix-NPL polarimeter. U.v. spectra were taken in ethanol with a Unicam SP 800 spectrophotometer and i.r. spectra with a Perkin-Elmer 457 or 621 spectrophotometer. N.m.r. spectra (in deuteriochloroform unless otherwise stated) were measured with a Varian XL-100 spectrometer or with a Perkin-Elmer R-12B instrument. T.l.c. was performed on silica gel (Merck HF_{254}) with the solvent indicated for each compound and detection by sulphuric acid–water (1 : 1) or with Ehrlich reagent.[11] Column chromatography was performed on silica gel 60 (Merck, 70—230 mesh) using the same solvents as in t.l.c. Solutions were dried with magnesium sulphate and evaporated under diminished pressure below 50°. Identification of compounds was based on mixed m.p., i.r. spectral, and chromatographic comparisons.

Formation of Adducts (3).—Nitro-olefin (1) (0.43 g, 1 mmol) was added to a solution of 3-(alkylamino)crotonic ester (2) (1 mmol) in acetonitrile (5 ml) and the suspension was stirred at room temperature until dissolution was complete. After 3—8 h, t.l.c. showed the presence of adduct (3) and, in some cases, trace amounts of starting materials and pyrrole (5). Evaporation of the solvent left a syrup that was washed thoroughly with benzene. The semi-solid obtained was treated with ether, and the slightly turbid solution filtered. Evaporation of the filtrate yielded the adduct (3) as a chromatographically homogeneous solid which was dried *in vacuo*. These preparations are pure enough for further transformations. Adducts (3a—d) were purified before analysis by column chromatography; adducts (3e—g) were recrystallized from ethanol.

Similar experiments using ether (5 ml) as solvent required longer reaction times (3—5 days) and gave somewhat higher yields.

A typical example of the reaction in methanol using nitro-olefin (1b) is as follows. A suspension of (1b) (0.87 g, 2 mmol) in methanol (20 ml) containing ethyl 3-(benzylamino)-crotonate (0.41 g, 2 mmol) was stirred at room temperature until dissolution (*ca.* 24 h). T.l.c. (ether–hexane 7 : 1) indicated the formation of adduct (3e) (R_F 0.87; major product) and pyrrole (5e) (R_F 0.08). Concentration of the solution to half its volume gave crystalline (3e) (0.78 g, 60%), m.p. 104—105°. Recrystallization from ethanol gave the analytical sample.

Yields of products are in Table 1; elemental analyses, physical constants, and spectral data are in Tables 1 and 2.

O-*Deacetylation of Adducts* (3e *and* g).—A suspension of (3e) (1.0 g) in methanol (10 ml) was stirred with a 0.25M solution (3 ml) of sodium methoxide in methanol at room temperature for 48 h. T.l.c. (chloroform–methanol 7 : 1) of the resulting solution indicated the formation of (7a) (R_F 0.50) as the only product. The solution was treated with an excess of Amberlite IR 120 (H^+) resin, filtered, and evaporated to yield *ethyl* β-*benzylamino*-α-(2,3,4;5,6-*pentahydroxy*-1-*nitromethylhexyl*)*crotonate* (7a) (0.40 g, 70%), m.p. 150—152° (from methanol), $[\alpha]_{5461}^{24}$ −15° (*c* 0.5 in EtOH), $\lambda_{max.}$ 297 nm (log ε 4.22), $\nu_{max.}$ (KBr) 3 505, 3 415, 3 295 and 3 255 (OH), 1 667 and 1 248 (CO_2Et), 1 610 and 1 602 (C=C–N–H), and 1 540 cm^{-1} (NO_2), δ ([$^2H_6$]Me_2SO) 1.35 (3 H, t, *J* 6.7 Hz, CO_2Et), 1.92 (3 H, s, ⁚C·Me), 3.30 (5 H, s), 3.60 (1 H, m, =C–CH), 3.80 (2 H, m, C*H*$_2$OH), 4.35 (2 H, q, CO_2Et), 4.6—4.8 (4 H, m, NCH_2 and CH_2NO_2), 5.10—5.90 (4 H, m), 7.25 (5 H, s, C_6H_5), and 8.80br (1 H, s NH) (Found: C 54.4; H 6.95; N, 6.0. $C_{20}H_{30}N_2O_9$ requires C, 54.3; H, 6.85; N, 6.35%).

In a similar way adduct (3g) gave *compound* (7b) (60%), m.p. 153—155° (from methanol), $[\alpha]_{5461}^{24}$ −25° (*c* 0.5 in EtOH), $\lambda_{max.}$ 297 nm (log ε 4.10), $\nu_{max.}$ (KBr) 3 450 and 3 300 (OH), 1 665 and 1 240 (CO_2Et), 1 605 (C=C–N–H), and 1 540 cm^{-1} (NO_2), δ ([$^2H_6$]Me_2SO) 0.95 [3 H, m, C*H*$_3$(CH_2)$_3$N], 1.30 (3 H, t, *J* 6.8 Hz, CO_2Et), 1.5—1.7 [4 H, m, CH_3(C*H*$_2$)$_2$-CH_2N], 1.98 (3 H, s, ⁚CMe), 2.80 (5 H, s), 3.13 (3 H, m, CH_2N and ⁚CCH), 4.00 (2 H, m, C*H*$_2$OH), 4.30 (2 H, q, CO_2Et), 4.80 (2 H, m, CH_2NO_2), 5.0—5.5 (4 H, m), and 8.50br (1 H, s, NH) (Found: C, 49.8; H, 7.6; N, 7.15. $C_{17}H_{32}N_2O_9$ requires C, 50.0; H, 7.9; N, 6.85%).

Formation of Pyrroles (5).—Nitroheptene (1) (2.20 g, 5 mmol) was added to a solution of 3-(alkylamino)-crotonic ester (2) (5 mmol) in 96% ethanol (8 ml) and the mixture was stirred and warmed until dissolution and then heated under reflux. T.l.c. indicated the rapid formation of the adduct (3) and then its conversion into the pyrrole (5). Heating was continued till the concentration of (5) appeared to reach a maximum (t.l.c.) without much darkening of the reaction mixture. Pyrroles (5a and b) crystallized by refrigeration of the reaction mixtures; evaporation of the mother liquors and column chromatography of ether solutions of the syrupy residues afforded additional amounts of these compounds. For the isolation of the remaining pyrroles (5c—g), the mixtures were evaporated, the syrupy residues chromatographed as indicated before, and the pure compounds recrystallized. Yields and elemental analyses of the products (5) are in Table 3; physical constants and spectral data are in Tables 3 and 4.

The same pyrroles were obtained by heating adducts (3) (1 mmol) in 96% ethanol (5 ml) and following as indicated above.

O-*Deacetylation of Pyrroles* (5).—A solution of (5) in dry methanol was treated with a few drops of a 0.2M solution of sodium methoxide in methanol at room temperature and then refrigerated. The crystalline product (8) that separated was filtered and recrystallized. Yields, analytical data, and physical constants are in Tables 3 and 4.

Pyrrole-3-carbaldehydes (9).—(*a*) A solution of polyol (8a) (0.25 g) in acetic acid (6 ml) and benzene (6 ml) was treated portionwise with a slight excess (positive recation to KI–starch paper) of lead tetra-acetate for 0.5 h at 0°. The solid was filtered off and the filtrate evaporated. Recrystallization of the crystalline residue from ethanol–water (1 : 1) gave 1-*benzyl*-4-*methoxycarbonyl*-5-*methylpyrrole*-3-*carbaldehyde* (9a) (0.14 g, 80%), m.p. 80—81°, $\lambda_{max.}$ 266 and 287 nm (log ε 3.92 and 3.85), $\nu_{max.}$ (KBr) 3 140 (pyrrole ⁚CH), 1 705 (CO_2Me), 1 657 (CHO), 1 522 and 1 523 (pyrrole ring), and 804 cm^{-1} (pyrrole ⁚CH), δ 2.42 (3 H, s, ⁚CMe), 3.83 (3 H, s, CO_2Me), 5.04 (2 H, s, CH_2N), 6.97 and 7.32 (5 H, m, C_6H_5), 7.26 (1 H, s, pyrrole ⁚CH), and 10.33 (1 H, s, CHO) (Found: C, 69.8; H, 5.8; N, 5.2. $C_{15}H_{15}NO_3$ requires C, 70.2; H, 5.85; N, 5.45%).

(*b*) A solution of polyol (8b) (50 mg) in ethanol (25 ml) was treated with 0.25M-sodium metaperiodate (20 ml) for 24 h at 0°. The solid that separated was recrystallized from ethanol–water (2 : 1), yielding 1-benzyl-4-ethoxycarbonyl-5-methylpyrrole-3-carbaldehyde (9b) (24 mg, 70%), m.p. 134—135°, $\lambda_{max.}$ 267 and 288 nm (log ε 3.88 and 3.84), $\nu_{max.}$ (KBr) 3 140 (pyrrole :CH), 1 698 (CO_2Et), 1 648 (CHO), 1 557 and 1 522 (pyrrole ring), and 807 cm^{-1} (pyrrole :CH), δ 1.36 (3 H, t, *J* 6.8 Hz, CO_2Et), 2.44 (3 H, s, :CMe), 4.30 (2 H, q, CO_2Et), 5.02 (2 H, s, CH_2N), 6.98 and 7.26 (5 H, m, C_6H_5), 7.26 (1 H, s, pyrrole :CH), and 10.33 (1 H, s, CHO), identical with the substance previously described.[9]

Similarly prepared were: 4-*ethoxycarbonyl*-5-*methyl*-1-*veratrylpyrrole*-3-*carbaldehyde* (9c) [72% from (8c) by procedure (*a*); 70% from (8e) by procedure (*b*)], m.p. 134—135° (from ethanol–water), $\lambda_{max.}$ 270sh and 285 nm (log ε 3.91 and 3.97), $\nu_{max.}$ (KBr) 3 120 (pyrrole :CH), 1 698 (CO_2Et), 1 670 (CHO), 1 547 and 1 528 (pyrrole ring), and 798 cm^{-1} (pyrrole :CH), δ 1.34 (3 H, t, *J* 7.0 Hz CO_2Et), 2.44 (3 H, s, :CMe), 3.80 and 3.83 (3 H each, s, 2 OMe), 4.32 (2 H, q, CO_2Et), 4.96br (2 H, s, CH_2N), 6.66 (2 H, m, benzene :CH), 7.27 (1 H, s, pyrrole :CH), and 10.33 (1 H, s, CHO) (Found: C, 65.0; H, H, 6.3; N, 4.0. $C_{18}H_{21}NO_5$ requires C, 65.25; H, 6.4; N, 4.2%); 1-n-butyl-4-ethoxycarbony-5-methylpyrrole-3-carbaldehyde (9d) [71% from (8d) by procedure (*b*)], m.p. 39—40° (from hexane), $\lambda_{max.}$ 267 and 288 nm (log ε 3.96 and 3.92), $\nu_{max.}$ (KBr) 3 125 (pyrrole: CH), 1 701 (CO_2Et), 1 668 (CHO), 1 542 and 1 528 (pyrrole ring) and 800 cm^{-1} (pyrrole :CH), δ 0.93 and 1.98 [7 H, m, $CH_3(CH_2)_2CH_2N$], 1.38 (3 H, t, *J* 7.0 Hz, CO_2Et), 2.52 (3 H, s, :CHe), 3.87 (2 H, t, *J* 6.6 Hz, CH_2N), 4.33 (2 H, q, CO_2Et), 7.26 (1 H, s, pyrrole :CH), and 10.34 (1 H, s, CHO), identical with the substance previously described.[9]

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