

231. Nitric Esters. Part II.¹ Characterisation of the Isomeric Glycerol Mononitrates.

By I. DUNSTAN, J. V. GRIFFITHS, and S. A. HARVEY.

Some derivatives of the isomeric glycerol mononitrates are described.

The ultraviolet spectra of glycerol trinitrate and the lower nitrates have been measured, and the effects of number and position of nitric ester groups are discussed.

Paper chromatography has been used to detect mono- and di-nitrates of glycerol in glycerol trinitrate.

ADAMS,² in 1920, suggested that Will's³ designations of the isomeric glycerol mononitrates, based on the results of nitration experiments, should be interchanged, after considering absorption spectra of glycerol nitrates measured by Hepworth.⁴ Although the compound designated glycerol 2-nitrate by Will has not been examined since 1920, the 1-nitrate has been mentioned,⁵ and the method of preparation and properties of the compound confirm the correctness of Will's designation. Availability of the lower nitric esters of glycerol has encouraged re-examination of their absorption spectra, and the results are discussed here. The opportunity has been taken to prepare several derivatives of the mononitrates.

In agreement with Will,³ glycerol mononitrates were obtained as crystalline solids by partial nitration of glycerol. The mononitrate isolated in greater yield was also prepared by treating glycidol (2,3-epoxypropan-1-ol) nitrate with hot water. Quantitative, periodic acid oxidation^{5b} of this product confirmed that it is glycerol 1-nitrate. Since glycerol 2-nitrate is more stable to oxidation, treatment with periodic acid is a convenient method for removing traces of 1-substituted isomer from the 2-nitrate.¹

Will³ prepared several derivatives of the glycerol mononitrates, and his results are substantiated here (Table 1). It is of interest that Verkade and his co-workers⁶ described a compound, m. p. 104–105°, formed by the action of silver nitrate in boiling benzene on the *p*-methoxybenzoates of glycerol 1- and 2-iodohydrin. By analogy with earlier work, these workers assumed that the product was glycerol 1-nitrate di-*p*-methoxybenzoate; melting points of *p*-methoxybenzoates given in Table 1 justify this assumption. The calcium nitrate complex of glycerol 1-nitrate described by Will³ was prepared and recrystallised without difficulty. Formation of an analogous complex occurred when an ethereal solution of the 1-nitrate was dried over granular calcium chloride. Neither complex is deliquescent when pure; each can be stored without deterioration.

Paper chromatography, used to confirm the purity of glycerol 1,2-dinitrate,¹ provides a very sensitive test for the presence of lower nitrates in glycerol trinitrate. Concentrations as low as 1 in 25,000 are detectable provided that preliminary separation is effected by shaking the trinitrate with octane-water-ethanol. The organic phase retains most of the trinitrate, and the aqueous phase, containing the lower nitrates, is used for chromatographic separation.

Ultraviolet (u.v.) spectra for a given nitric ester show that the change of molecular extinction coefficient with wavelength (Table 2) is similar in aqueous and hexane-ethanol solution, particularly over the range 215–230 m μ ; lower values of extinction coefficients in hexane-ethanol below 215 m μ may be due to poor transmission of solvent in this region. The absorptive power of each ester decreases markedly with increasing wavelength; at

¹ Part I, preceding Paper.

² Adams, *J. Amer. Chem. Soc.*, 1920, **42**, 1321.

³ Will, *Ber.*, 1908, **41**, 1107.

⁴ Hepworth, *J.*, 1919, **115**, 840.

⁵ (a) Nichols, Magnusson, and Ingham, *J. Amer. Chem. Soc.*, 1953, **75**, 4255; (b) Ingham and Nicholls, *ibid.*, 1954, **76**, 4477; (c) Urbanski and Witanowski, *Trans. Faraday Soc.*, 1963, **59**, 1047.

⁶ Hoefnagel, deJongh, van den Brink, Schuil, and Verkade, *Rec. Trav. chim.*, 1962, **80**, 63.

longer wavelengths the extinction coefficients are relatively small and differences are not significant.

It is apparent that a secondary nitric ester group substituted in glycerol is a more effective chromophore than is a primary group (cf. 1- and 2-mononitrates). However, comparison of 1,3- with 1,2-dinitrate show that the presence of an adjacent nitric ester group reduces absorptive power; the relatively low coefficients observed for trinitrate at longer wavelengths confirm this conclusion.

Clearly, no simple arithmetic relationship exists between the molecular extinction coefficients of the glycerol nitrates, even at lower wavelengths where the absorptive powers are in the order anticipated from the molecular formulæ. For this reason, the suggestion² that the designations of the mononitrates should be reversed is unacceptable. This suggestion was based on a comparison of molecular extinction coefficients of glycerol trinitrate and the lower nitrates in aqueous solution, measured at 233 and 238 μ . At these wavelengths the observed molecular extinction coefficients are very low and bear no direct relationship to the number and orientation of nitric ester groups.

EXPERIMENTAL

Melting points and infrared (i.r.) spectra were measured as described previously.¹

Glycerol 1- and 2-Nitrate.—Partial nitration of glycerol¹ yielded the mononitrates as liquids, n_D^{20} 1.4690 (lit.^{5b} 1.4682) and 1.4686, which crystallised slowly, giving solids, m. p. 55° (58–59°³) and 54° (54°³). Crystal densities of the isomeric mononitrates, measured by flotation in carbon tetrachloride–1,1,2,2-tetrabromoethane–benzene, were 1.583 and 1.590 g./c.c. The viscous liquid, b. p. 123°/0.5 mm. (lit.,³ 155–160°/15 mm.), d_4^{20} 1.4185 g./c.c., obtained by heating glycidol nitrate with water,⁴ gave a crystalline solid identical with glycerol 1-nitrate prepared from glycerol.

Derivatives of Glycerol Mononitrates.—The compounds in Table I were prepared conventionally.¹

TABLE I.
Derivatives of glycerol mononitrates.

No.	Derivative	Form	Solvent	M. p.
1	Glycerol 1-nitrate dibenzoate	Needles	MeOH–H ₂ O	68° (lit., ³ 68–69)
2	Glycerol 2-nitrate dibenzoate*	Prisms	MeOH–H ₂ O	56
3	Di- <i>p</i> -nitrobenzoates	Prisms	EtOH	137–138 (lit., ³ 139)
4		Leaflets	EtOH	152 (lit., ³ 152)
5	Bis-3,5-dinitrobenzoates	Pale yellow plates	EtOAc–MeOH	127
6		Cream needles	EtOAc–Pet (b. p. 60–80°)	139–140
7	Di- <i>p</i> -methoxybenzoates	Plates	MeOH	105 (lit., ⁶ 104–105)
8		Needles	MeOH	109

No.	Found (%)			Formula	Required (%)		
	C	H	N		C	H	N
1	59.3	4.5	4.2	C ₁₇ H ₁₅ NO ₇	59.1	4.4	4.1
2	59.4	4.6	4.2	"	"	"	"
3	47.1	3.3	9.9	C ₁₇ H ₁₃ N ₃ O ₁₁	46.9	3.0	9.65
4	46.9	3.2	9.4	"	"	"	"
5	38.7	2.1	13.4	C ₁₇ H ₁₁ N ₅ O ₁₅	38.85	2.1	13.3
6	39.0	2.3	13.3	"	"	"	"
7	56.0	4.7	3.8	C ₁₉ H ₁₉ NO ₉	56.3	4.7	3.5
8	56.4	5.0	3.3	"	"	"	"

* Purified by chromatography on alumina, using benzene as eluant.

Calcium nitrate complex of glycerol 1-nitrate. The mononitrate (5.5 g., 0.04015 mole) was warmed with calcium nitrate (1.6 g., 0.00975 mole) in ethanol (5 ml.). The complex, which separated on cooling, was obtained as equant crystals (from ethanol), m. p. 117° (117°³) [Found: C, 21.0; H, 4.6; N, 11.7; vicinal OH, 18.9. Calc. for (C₃H₇NO₅)₄Ca(NO₃)₂: C, 20.2; H, 4.0; N, 11.8; vicinal OH, 19.1%].

Calcium chloride complex of glycerol 1-nitrate. The complex, which crystallised as needles from a warmed mixture of calcium chloride (1.11 g., 0.01 mole), glycerol 1-nitrate (5.48 g., 0.04 mole), and ethanol (5 ml.), had m. p. 98–100° (from ethanol–ether) [Found: C, 21.9; H, 4.3; N, 8.9; vicinal OH, 20.4. $(C_3H_7NO_5)_4CaCl_2$ requires C, 21.85; H, 4.3; N, 8.5; vicinal OH, 20.6%]. Attempts to recrystallise the complex from acetone–ether caused partial removal of glycerol 1-nitrate, the product becoming deliquescent owing to contamination with calcium chloride.

Paper Chromatography of Glycerol Nitrates.—Using Whatman No. 1 paper and a mobile phase consisting of the upper layer from a 20 : 1 : 9 (v/v) mixture of octane–water–ethanol, the following rates of movement were observed: solvent, 4.56; trinitrate, 0.89; dinitrates,

TABLE 2.

Molecular extinction coefficients for glycerol nitrates.

λ (m μ)	1-Nitrate		2-Nitrate		1,2-Dinitrate		1,3-Dinitrate		Trinitrate	
210	2535 *	2327 †	2466	2165	4397	3972	4829	3895	5875	5281
215	1693	1605	1765	1736	2799	2583	3072	2628	3298	2849
220	1032	1009	1187	1238	1608	1530	1794	1597	1685	1487
225	607	606	782	834	884	870	985	916	832	754
230	348	352	491	529	478	485	531	511	414	392

* In water. † In 90 : 10 (v/v) hexane–ethanol.

0.32; mononitrates, 0.04 in./hr. R_F values were not measured because it was necessary to allow the solvent to flow off the end of the paper to achieve adequate separation. Nitric esters were detected with ethanolic diphenylamine and u.v. irradiation.¹ Glycerol 1-nitrate was identified by spraying a duplicate paper with 1% (w/v) lead tetra-acetate in benzene; when solvent was allowed to evaporate the paper became brown except where the mononitrate reduced the reagent to lead acetate.

Distinct separations were achieved when a 25,000 : 1 : 1 (w/w) mixture of glycerol trinitrate, 1,3-dinitrate, and 1-nitrate was analysed by chromatography, after separating most of the trinitrate by shaking the sample with the two phase mixture of octane–water–ethanol; the lower nitric esters were readily detected by chromatography of the aqueous phase. The limit of detection was about 1 part of mononitrate or dinitrate in 800 parts of trinitrate if the preliminary separation, by extraction, was omitted.

Ultraviolet Spectra of Glycerol Nitrates.—U.v. spectra of solutions of glycerol trinitrate and the lower nitric esters in water and in 90 : 10 (v/v) hexane–ethanol were measured with a Unicam S.P. 500 spectrophotometer using 1-cm. quartz cells. Carefully purified esters were used, and each ester was subjected to appropriate purity tests (i.r., chromatography, nitrate content, m. p.). Validity of Beer's law was confirmed for each nitrate at 210 and 230 m μ , using up to 80-fold changes in concentration and 40-fold changes in pathlength. Cell corrections were applied to all measurements. The molecular extinction coefficients in Table 2 are mean values at several concentrations; variations from the mean were <1%.

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EXPLOSIVES RESEARCH AND DEVELOPMENT ESTABLISHMENT,
MINISTRY OF AVIATION, WALTHAM ABBEY, ESSEX.

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