707. *Some Alkyl* p-*Phenylazobenzoates and Ferrocenecarboxylates.*

By N. Baggett, A. B. Foster, A. H. Haines, and M. Stacey.

The preparation and light-sensitivity of various *p*-phenylazobenzoates are recorded. From the chromatographic properties of such esters of 1,3-dioxan derivatives, and of certain ferrocenecarboxylates, the rôle of ring-oxygen atoms and other groupings in adsorption on alumina is deduced.

The *p*-phenylazobenzoates in the Table were obtained during preparation of a series of alcohols for infrared spectroscopic examination.[1] Their crystallinity makes them useful *

Alkyl p-*phenylazobenzoates and ferrocenecarboxylates.*

	Data on Ester Derivatives									
				Found (%)			Required (%)			$\lambda_{max.}$ [a]
Alkyl	Yield (%)	M. p.	Formula	C	H	N	C	H	N	(10^{-3} ε)
			p-Phenylazobenzoates							
Ethyl [b]	75	85°	$C_{15}H_{14}N_2O_2$							324 (26·0)
Isopropyl [b]	59	85—86	$C_{16}H_{16}N_2O_2$							323 (24·2)
Cyclohexyl [b]	68	85—87	$C_{19}H_{20}N_2O_2$							325 (29·2)
Tetrahydropyran-3-yl	60	114—115	$C_{18}H_{18}N_2O_3$	69·85	5·8	8·8	69·7	5·8	9·0	325 (26·9)
Tetrahydropyran-4-yl	30	129—131	$C_{18}H_{18}N_2O_3$	69·85	5·7	8·9	69·7	5·8	9·0	324 (22·6)
1,3-*O*-Methyleneglycerol	64	175—176	$C_{17}H_{16}N_2O_4$	65·6	5·1	8·8	65·4	5·1	9·0	325 (23·8)
Tetrahydropyran-2-yl-methyl	66	80—82	$C_{19}H_{20}N_2O_3$	70·3	6·2	8·5	70·4	6·2	8·6	325 (27·4)
4-Formylbutyl	31	65—66	$C_{18}H_{18}N_2O_3$	69·6	6·1	8·9	69·7	5·8	9·0	325 (26·8)
Cyclopentylmethyl	30	72—73	$C_{19}H_{20}N_2O_2$	74·15	6·3	8·9	74·0	6·55	9·1	
Tetrahydrofurfuryl	70	84—85	$C_{18}H_{18}N_2O_3$	69·8	5·7	9·1	69·65	5·9	9·0	
1,2-*O*-Methyleneglycerol	70	108—110	$C_{17}H_{16}N_2O_4$	65·5	5·4	8·8	65·4	5·2	9·0	
cis-4-Phenylcyclohexyl	68	109—110	$C_{25}H_{24}N_2O_2$	78·2	6·5	6·7	78·1	6·3	7·3	
trans-4-Phenylcyclohexyl	80	156—157	$C_{25}H_{24}N_2O_2$	77·9	6·3		78·1	6·3		
5α-Cholestan-3α-yl	60	107—109	$C_{40}H_{56}N_2O_2$	80·2	9·4	4·4	80·45	9·5	4·7	
5α-Cholestan-3β-yl	50	187—194	$C_{40}H_{56}N_2O_2$	80·6	9·4	5·0	80·45	9·5	4·7	
Ethylene (bisester)	79	211—214	$C_{28}H_{22}N_4O_4$	69·95	4·3	11·9	70·3	4·6	11·7	325 (20·5) [c]
Glycerol (1-ester)	90	150—151	$C_{16}H_{16}N_2O_4$	63·6	5·2		64·0	5·4		
cis-1,3-*O*-Benzylidene-glycerol	65	209—210	$C_{23}H_{20}N_2O_4$	71·1	4·9	7·15	71·1	5·2	7·2	
1,2-*O*-Isopropylidene-glycerol	63	81—82	$C_{19}H_{20}N_2O_4$	67·0	5·9	8·1	67·0	5·9	8·2	
			Ferrocenecarboxylates							
				C	H	Fe	C	H	Fe	
1,3-*O*-Methyleneglycerol	35	110—112	$C_{15}H_{16}FeO_4$	57·0	5·0		57·0	5·1		
cis-4-Phenylcyclohexyl	34	88	$C_{23}H_{24}FeO_2$	70·8	6·5	14·2	71·1	6·2	14·4	
trans-4-Phenylcyclohexyl	35	175—176	$C_{23}H_{24}FeO_2$	71·7	6·3		71·1	6·2		

[a] In EtOH. [b] Cf. Woolfolk *et al.*[2] [c] In $CHCl_3$.

for characterisation,[2] *e.g.*, for tetrahydropyran-3-ol for which other methods failed.[1a] Tetrahydropyran-2-ol (5-hydroxypentanal) gave mainly 5-*p*-phenylazobenzoyloxypentanal,

* Other reagents have also been used for labelling alcohols [3, 4, 5] and acids [6] with azobenzene-containing residues.

[1] (*a*) Brimacombe, Foster, Stacey, and Whiffen, *Tetrahedron*, 1958, **4**, 351; (*b*) Barker, Brimacombe, Foster, Whiffen, and Zweifel, *ibid.*, 1959, **7**, 10; (*c*) Brimacombe, Foster, and Haines, *J.*, 1960, 2582.

[2] Woolfolk, Beach, and McPherson, *J. Org. Chem.*, 1955, **20**, 391; Bergel and Cohen, *J.*, 1941, 795; Baxter, Robeson, Taylor, and Lehman, *J. Amer. Chem. Soc.*, 1943, **65**, 918; Bohlmann, Winterfeld, and Brackel, *Chem. Ber.*, 1958, **91**, 2194.

[3] Reich, *Compt. rend.*, 1939, **208**, T48; *Biochem. J.*, 1939, **33**, 1000.

[4] Craw and Sutherland, *Univ. Queensland Papers, Dept. Chem.*, 1948, **1**, No. 31; *Chem. Abs.*, 1950, **44**, 3945.

[5] Hurd and Zelinsky, *J. Amer. Chem. Soc.*, 1947, **69**, 243; Nasuyama, *J. Chem. Soc. Japan*, 1949, **70**, 232.

[6] Silberman and Silberman-Martyncewa, *J. Biol. Chem.*, 1946, **165**, 351.

a surprising result since the alcohol exists in solution predominantly as the cyclic hemiacetal.[1a,7] The authentic open-chain ester was obtained by acylation of 5-hydroxypentanal diethyl thioacetal followed by demercaptalation.

The *p*-phenylazobenzoate of *cis*-1,3-*O*-benzylideneglycerol was readily obtained but under similar conditions *trans*-1,3-*O*-benzylideneglycerol gave mainly the *cis*-ester, illustrating further the tendency of the *trans*-alcohol to isomerise on esterification.[8] A possible route to the *trans*-ester would be by condensation of benzaldehyde with glycerol 2-ester (cf. Bergmann and Carter [9]), but removing the benzylidene residue [10] from *cis*-1,3-*O*-benzylideneglycerol 2-*p*-phenylazobenzoate resulted in acyl migration [11] and yielded glycerol 1-*p*-phenylazobenzoate. The authentic 1-ester was obtained by treating 2,3-*O*-isopropylideneglycerol 1-*p*-phenylazobenzoate with 2,4-dinitrophenylhydrazine.[12]

The photosensitivity of the *trans*-*p*-phenylazobenzoates listed in the Table is not inconveniently high since chromatographically homogeneous products were usually obtained providing that the preparations were performed in subdued diffuse light. However, short exposure to sunlight or ultraviolet radiation caused the formation of *cis*-esters which had a much higher affinity for alumina than did the *trans*-isomers (cf. Cook and Jones [13]).

Brief irradiation of ethylene di-(*p*-phenylazobenzoate), which presumably has the *trans,trans*-configuration, gave a mixture of three components: *A*, the *trans,trans*-compound which had the lowest affinity for alumina; *B*, with $\lambda_{max.}$ 325 (ε 14,000) and 267 mμ (ε 6200); *C*, which had the greatest affinity for alumina and $\lambda_{max.}$ 325 and 268 mμ. Birnbaum *et al.*[14] found $\lambda_{max.}$ 263 mμ for the *cis*-forms of ethyl and isopropyl *p*-phenylazobenzoate. Products *B* and *C* were not obtained crystalline and only a trace of *C* was formed. It is probable that *A*, *B*, and *C* have respectively the *trans,trans*-, *cis,trans*-, and *cis,cis*-configuration at the azo-linkages.

A complex mixture of stereoisomers could result on irradiation of sugar poly-*p*-phenylazobenzoates, with consequent complication of the chromatographic behaviour; hence precautions should be taken to minimise isomerisation if maximum resolution is to be obtained in their chromatography.

trans-1,3-*O*-Benzylideneglycerol (equatorial hydroxyl group) has a greater affinity for alumina in chromatography [4] than does the *cis*-isomer (axial hydroxyl group); similar behaviour is exhibited by the structural analogues *cis*- and *trans*-4-phenylcyclohexanol.[15] However, with the acetates,[8] benzoates,[16] and methyl [16] and benzyl ethers [8] of the 1,3-*O*-benzylideneglycerols the *cis*-isomer in each case, surprisingly, has the greater affinity for alumina. That the ring-oxygen atoms are involved to an important extent in the adsorption of the cyclic acetals on alumina is shown by the much firmer adsorption of the *p*-phenylazobenzoate of *cis*-1,3-*O*-benzylideneglycerol than of *cis*-4-phenylcyclohexanol. Further, the ring-oxygen atoms are apparently not simultaneously important since a mixture of tetrahydro-3-*p*-phenylazobenzoyloxypyran (one ring-oxygen atom) and 1,3-*O*-methyleneglycerol 2-*p*-phenylazobenzoate (two ring-oxygen atoms) could not be resolved. Similar results were obtained with the *p*-phenylazobenzoates of cyclopentylmethanol, tetrahydrofurfuryl alcohol, and 2,3-methyleneglycerol. Further analysis of the phenomenon is complicated by the fact that the six-membered cyclic acetals are flexible, so that the

[7] Hurd and Saunders, *J. Amer. Chem. Soc.*, 1952, **74**, 5324.
[8] Baggett, Brimacombe, Foster, Stacey, and Whiffen, *J.*, 1960, 2574.
[9] Bergmann and Carter, *Z. physiol. Chem.*, 1930, **191**, 211.
[10] Karrer, *Helv. Chim. Acta*, 1954, **37**, 379; Martin, *J. Amer. Chem. Soc.*, 1953, **75**, 5482.
[11] Cf. Daubert and King, *J. Amer. Chem. Soc.*, 1938, **60**, 3003.
[12] Cf. Fischer, *Ber.*, 1920, **53**, 1589.
[13] Cook, *J.*, 1938, 876; Cook and Jones, *J.*, 1939, 1309; Burawoy, *J.*, 1937, 1869; Cook, Jones, and Polya, *J.*, 1939; 1315.
[14] Birnbaum, Linford, and Style, *Trans. Faraday Soc.*, 1953, **49**, 735.
[15] Ungnade, *J. Org. Chem.*, 1948, **13**, 361.
[16] Dobinson and Foster, unpublished results.

conformation of the adsorbed molecules is unknown but might be different from that which predominates in solution.

Although the chromatographic properties of *p*-phenylazobenzoates may depend on various structural features [3,4,17,18] they are not often affected by stereochemical variations in the alkyl residue although mixtures of some of the isomeric carbohydrate polyesters can be resolved.[17] We have found that mixtures of 5α-cholestan-3α- and -3β-yl and of *cis*- and *trans*-4-phenylcyclohexyl *p*-phenylazobenzoate cannot be separated on alumina whereas the parent alcohols and other esters are readily separable.[15,19] This effect may be due to the bulk of the azo-ester group and/or its dominance in the array of polar centres involved in adsorption. To distinguish between these possibilities, chromatography of some ferrocenecarboxylates was examined since they have a molecular weight similar to that of the analogous azo-esters and, moreover, ferrocene itself is less strongly adsorbed than *trans*-azobenzene. A mixture of *cis*- and *trans*-4-phenylcyclohexyl ferrocenecarboxylate could not be resolved so that their use is not advantageous in this case. When mixtures of (*a*) cyclohexyl ferrocenecarboxylate and *p*-phenylazobenzoate and (*b*) *trans*-4-phenylcyclohexyl ferrocenecarboxylate and *p*-phenylazobenzoate were chromatographed on alumina the azo-ester was eluted first in both cases. This behaviour may be explained if largely the ester-carbonyl groups are assumed to be involved in adsorption. The K_a values of *p*-phenylazobenzoic and ferrocenecarboxylic acid ($1{\cdot}41 \times 10^{-5}$ and $1{\cdot}35 \times 10^{-6}$ respectively in 50% aqueous ethanol at 18°) indicate that the azobenzene group has a greater $-I$ effect. Thus, in the esters, the dipolar character of the carbonyl group, and hence the affinity for alumina, would be less for the azo-esters than for the ferrocenecarboxylates.

Experimental

Preparation of p-*Phenylazobenzoates.*—Commercial *p*-phenylazobenzoyl chloride, after recrystallisation from light petroleum (b. p. 60—80°), had m. p. 93° and (in Nujol mull) $\nu_{max.}$ 1740 and 1770 cm.$^{-1}$ (C=O); benzoyl chloride [20] has $\nu_{max.}$ 1736 and 1773 cm.$^{-1}$.

The azo-esters in the Table were prepared essentially by the method of Woolfolk *et al.*[2] The tetrahydropyran, tetrahydrofuran, 1,3-dioxan, and 1,3-dioxolan derivatives were prepared as previously described,[1b] and the remaining alcohols as follows: 4-phenylcyclohexanols, ref. 15; 5α-cholestan-3α-ol, ref. 21, and -3β-ol, ref. 22; cyclopentylmethanol, ref. 23.

Recrystallisation of the crude product from tetrahydropyran-2-ol gave 5-*p*-phenylazobenzoyloxypentanal (31%), m. p. 65—66°, $\nu_{max.}$ (KCl disc) 1725 (C=O) and 2740 cm.$^{-1}$ (aldehyde-CH). Chromatography of the mother-liquors on alumina gave *A* (*ca.* 2 mg., 0·3%), m. p. 83—84°, $\nu_{max.}$ (KCl disc) 1702 cm.$^{-1}$ (C=O) (no absorption for aldehyde CH), followed by a further amount 5-*p*-phenylazobenzoyloxypentanal; traces of several other components were also present.

trans-1,3-*O*-Benzylideneglycerol reacted with *p*-phenylazobenzoyl chloride much less readily than did the *cis*-isomer. A solution of *trans*-1,3-*O*-benzylideneglycerol (80 mg., m. p. 64—65°) in dry pyridine (4 ml.) was treated with a slurry of the acyl chloride (170 mg., 3 mol.) in dry pyridine (4 ml.) at 40° for 3 days, yielding a crude product (58·3 mg., 34%) from which was separated *cis*-azo-ester (34·3 mg.), m. p. and mixed m. p. 210°. Chromatography of the mother-liquor on alumina gave material (16 mg.; eluted with ether), m. p. 185°, raised to 191—192° by recrystallisation from benzene–light petroleum (b. p. 60—80°), and then the *cis*-azo-ester (14 mg.), m. p. 205°, raised by recrystallisation to 209—210°. On slight change of the conditions the *cis*-ester predominated but the m. p. of the second component varied widely.

[17] Coleman *et al.*, *J. Amer. Chem. Soc.*, 1942, **64**, 1501; 1943, **65**, 1589; 1945, **67**, 381; Mertzweiller Carney, and Farley, *ibid.*, 1943, **65**, 2367; Boissonnas, *Helv. Chim. Acta*, 1947, **30**, 1689, 1703.

[18] Umberger and Curtis, *J. Biol. Chem.*, 1949, **178**, 265; Coffman, *J. Biol. Chem.*, 1941, **140**, xxviii; Ladenberg, Fernholz, and Wallis, *J. Org. Chem.*, 1939, **3**, 294; Schroeder, *Ann. New York Acad. Sci.*, 1948, **49**, 204.

[19] Brooks, Klyne, and Miller, *Biochem. J.*, 1953, **54**, 212.

[20] Rasmussen and Brattain, *J. Amer. Chem. Soc.*, 1949, **71**, 1073.

[21] Vavon and Jakubowicz, *Bull. Soc. chim. France*, 1933, **53**, 584.

[22] Nace, *J. Amer. Chem. Soc.*, 1951, **73**, 2379.

[23] Noller and Adams, *J. Amer. Chem. Soc.*, 1926, **48**, 1080.

Careful chromatography on alumina of the crude product obtained on acylation of *cis*-1,3-*O*-benzylideneglycerol revealed a single component.

A solution of *cis*-1,3-*O*-benzylideneglycerol 2-*p*-phenylazobenzoate (19 mg.) in dry chloroform (2 ml.) was treated with a trace of sodium methoxide in dry methanol (1 ml.) at room temperature overnight. Water (0·5 ml.) was then added and the mixture neutralised with carbon dioxide. After evaporation the residue was chromatographed on alumina. Methyl *p*-phenylazobenzoate (12 mg.), m. p. 125° [from light petroleum (b. p. 60—80°)], was eluted with benzene, followed by *cis*-1,3-*O*-benzylideneglycerol (9 mg.; m. p. 80°) on elution with ether.

Synthesis of 5-p-*Phenylazobenzoyloxypentanal.*—A solution of 5-hydroxypentanal diethyl thioacetal[7] (1 g.; b. p. 134—136°/~8 mm.) in dry pyridine (20 ml.) was treated with *p*-phenylazobenzoyl chloride (1·4 g., 1·1 mol.) at room temperature for 15 hr. On dilution with ice-water an oil, presumably 5-phenylazobenzoyloxypentanal diethyl thioacetal, was formed. Extraction with chloroform and concentration of the extract gave a residue (1·8 g.) which was dissolved in water (2 ml.) and acetone (10 ml.). After addition of cadmium carbonate (2 g.) the mixture was vigorously stirred and treated with mercuric chloride (2·7 g.) in acetone (3 ml.) during 15 min. After a further 24 hours' stirring the mixture was diluted with acetone, filtered, and evaporated. Recrystallisation of the residue from light petroleum (b. p. 60—80°) gave 5-*p*-phenylazobenzoxypentanal (0·44 g., 30%), m. p. 67—68° alone or in admixture with the product obtained on acylation of tetrahydropyran-2-ol; the two esters gave indistinguishable infrared spectra (KCl discs and ~10% solutions in $CHCl_3$). A second product (0·13 g., 9%), m. p. 78—80°, was obtained from the mother-liquors, apparently a dimorph since the infrared spectra (KCl discs) were indistinguishable.

Glycerol 1-p-*Phenylazobenzoate.*—A solution of 2,3-*O*-isopropylideneglycerol *p*-phenylazobenzoate (60 mg.) in dioxan (10 ml.) was heated with 2,4-dinitrophenylhydrazine (65 mg.) in methanol (15 ml.) containing concentrated hydrochloric acid (0·25 ml.) at 80° for 2 hr., then evaporated *in vacuo*. The residue was passed in chloroform through a short column of alumina. After dilution with chloroform elution with methanol–chloroform (1 : 4 v/v) isolated glycerol 1-*p*-phenylazobenzoate (48 mg.), m. p. 150—151° [from ether–light petroleum (b. p. 60—80°)].

Preparation of Ferrocenecarboxylates.—A solution of ferrocenecarboxylic acid[24] [0·1 g.; m. p. 160—170° (decomp.)] in dry benzene (1·1 ml.) was stirred at room temperature for 2 hr. with phosphorus pentachloride (100 mg.), then filtered; benzene was removed from the filtrate by freeze-drying, yielding syrupy acid chloride. (The acid chloride has recently been obtained crystalline.[25]) A solution of 1,3-*O*-methyleneglycerol (84 mg.) in dry pyridine (1·1 ml.) was added and the mixture was stored overnight at room temperature, then poured into water and extracted with chloroform, and the chloroform extract washed with ice-cold N-hydrochloric acid, 10% aqueous cadmium chloride, and water. Ferrocenecarboxylic acid was removed by passage of the chloroform solution through a short column of alumina and elution with the same solvent. Evaporation of the eluate gave 1,3-*O*-methyleneglycerol 2-ferrocenecarboxylate (100 mg.).

The ferrocenecarboxylates included in the Table were prepared essentially by the above method.

Chromatography.—Alumina of activity Brockmann III was used.[8] The ratio of adsorbent to adsorbed material was usually ~6 : 1. It was necessary to protect the columns from the direct sunlight or fluorescent light for both the azo-esters and the ferrocenecarboxylates. The identity of components eluted from the columns was established wherever possible by their m. p.s and infrared spectra.

The authors thank Drs. D. H. Whiffen and K. J. Morgan for assistance with infrared spectroscopy. One of them (N. B.) thanks D.S.I.R. for a grant.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15. [*Received, February 2nd,* 1960.]

[24] Rinehart, Motz, and Sung Moon, *J. Amer. Chem. Soc.*, 1957, **79**, 2753.
[25] Lan and Hart, *J. Org. Chem.*, 1959, **24**, 280.