A New Synthesis of Optically Active Alkyl Nitrites for Chiroptical and Photochemical Studies

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Summary Trans-esterification of chiral secondary carbinols with symmetric nitrite esters occurs readily in polar solvents at 25° without racemization or inversion, and provides a convenient source of chiral nitrite esters for stereochemical studies of optically active alcohols and for photochemical syntheses.

IN attempts to induce optical activity[1] in isopentyl nitrite it was treated at 25° with chiral carbinols in acetonitrile solution. A series of circularly dichroic bands ($\Delta\epsilon$ 0·01—0·58) appeared under the isotropic nitrite absorption bands in the spectral region 300—420 nm. The signs and relative intensities of the c.d. bands were characteristic of the corresponding chiral nitrite ester (Table) and, together with the large rotational strengths, indicated that trans-esterification[2] (redistribution of the nitrito-group) had occurred between the symmetric and chiral carbinols:

$$(+ \text{ or } -)\text{-ROH} + \text{iso-}C_5H_{11}ONO \rightleftharpoons (+ \text{ or } -)\text{-RONO} + \text{iso-}C_5H_{11}OH$$

These experiments illustrate a convenient synthesis of chiral nitrites and the value of c.d. for discrimination of closely related molecular species in solution.

The trans-esterification products from isopentyl nitrite and (−)-borneol (I) and (−)-menthol (II) in acetonitrile solution were identified by spectroscopic and chromatographic (t.l.c.) comparison with authentic samples of the corresponding alkyl nitrites prepared in the conventional manner[3-6] from the carbinols and nitrosyl chloride in pyridine. The identification was confirmed by isolation of (−)-bornyl nitrite in 40% yield from the trans-esterification solution on a silica gel column.

The relationship of absolute configuration to the sign of the c.d. of the chiral nitrites is under study. The tentative generalization, based on steroidal nitrites,[4] that *R*-configuration of the nitrito-carbinyl group gives rise to positive c.d. bands in a five-membered ring and to negative c.d. bands in a six-membered ring or acyclic structure could, in principle, be tested unequivocally only for compounds (II), (IV), (VI), (VII), and (VIII) with the data so far collected (Table). The signs for compounds (VI)—(VIII) fitted the generalization, whereas those for compounds (II) and (IV) were ambiguous. The role of the conformation of the nitrito-group in the c.d. spectra is not yet clear.

Circular dichroism spectra of nitrite esters synthesised by trans-esterification[a]

Chiral carbinol	M	Molarity of isopentyl nitrite	C.d. spectrum of nitrite ester λ_{max} in nm., ($\Delta\epsilon$)
(−)-(1*S*,2*R*)-Borneol (I)	0·33	0·019	386 (+0·395), 372 (+0·497), 357 (+0·393), 346 (+0·231), 335 (+0·112), 325sh (+0·049).
(−)-(1*R*,3*R*,4*S*)-Menthol (II)	1·30	0·022	393 (−0·567), 376 (−0·486), 368 (+0·315), 362 (−0·162), 356 (+0·360), 345 (+0·243), 334 (+0·126), 325sh (+0·072).
(+)-(1*R*,2*R*)-Fenchol (III)	1·30	0·026	392 (+0·218), 376 (+0·172), 367 (−0·093), 362 (+0·027), 355 (−0·113), 344 (−0·085), 334 (−0·067), 325sh (−0·046),
(−)-(*R*)-Octanol (IV)	0·38	0·020	394 (−0·094), 384 (+0·118), 369 (+0·261), 356 (+0·256), 345 (+0·174), 335sh (+0·105).
(2*S*,5*R* -1,4 : 3,6-Dianhydro-D-glucitol (V) ..	1·37	0·017[b]	398 (−0·029), 385 (+0·263), 369 (+0·246), 356 (+0·067), 348sh (+0·018), 342 (−0·012), 337 (+0·003), 331 (−0·026), 322 (−0·015).
(2*R*,5*R*)-1,4 : 3,6-Dianhydro-D-mannitol (VI) ..	1·37	0·020	385 (+0·580), 370 (+0·448), 357sh (+0·219), 349sh (+0·091), 342 (−0·020), 337 (+0·026), 330 (−0·041), 320 (−0·031), 310 (−0·011).
(2*S*,5*S*)-1,4 : 3,6-Dianhydro-L-iditol (VII) ..	1·37	0·018	391 (−0·253), 375 (−0·252), 360 (−0·202), 348 (−0·064), 337 (−0·016).
(3*S*)-5α-Cholestan-3β-ol (VIII)[c]	0·13	0·018	385 (+0·103), 371 (+0·117), 357 (+0·081), 347 (+0·047)
D-Glucose (IX)[d]	0·56	0·026	395 (+0·035), 377(+0·031), 369 (−0·030), 356 (−0·036), 344 (−0·030), 329 (−0·050).

[a] In acetonitrile solution unless otherwise stated.
[b] Essentially the same spectrum was obtained with 0·02M-n-butyl nitrite.
[c] In dioxan solution plus 2 drops acetic acid.
[d] In dimethyl sulphoxide solution.

Equilibration of the chiral carbinol and symmetric nitrite occurred rapidly in acetonitrile at room temperature. With (−)-octan-2-ol (IV) and isopentyl nitrite in hexane, however, the initial c.d. spectrum was extremely weak. After addition of 2 drops of acetic acid the spectrum increased in intensity over a period of several hours (Figure 1). The nitrito-bands finally reached constant values which agreed as to frequency and relative intensity with those reported by Kuhn and Lehmann[7] for (+)-2-octyl nitrite, but had opposite signs and *ca.* 15% greater rotational strengths.

With 3β-cholestanol (VIII) (0·13M) and isopentyl nitrite (0·018M) in dioxan with added acetic acid the final spectrum (12 hr.) corresponded in frequency, sign, and relative intensities of the nitrito-bands with that reported for 3β-cholestanyl nitrite in dioxan–pyridine (500 : 1).[3,4] The rotational strengths of the bands indicated *ca.* 75% conversion.

A similar equilibration of (−)-menthol (II) and isopentyl nitrite in dioxan solution is illustrated in Figure 2. D-Glucose (IX) and isopentyl nitrite in dimethyl sulphoxide equilibrated more rapidly. During these experiments the isotropic nitrito-absorption bands showed a small blue shift (1—2 nm.) indicating the conversion of primary to secondary nitrite ester.[8]

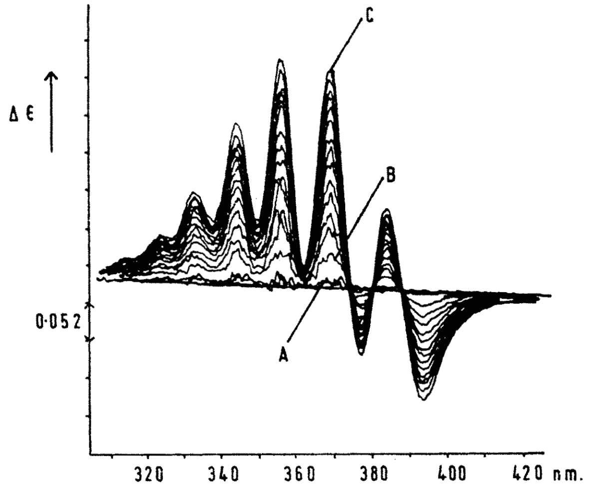

FIGURE 1. *C.d. spectrum (instrument trace) of isopentyl nitrite* (0·024M) *and* (−)-(R)-*octan-2-ol* (0·76M) *in hexane*: (A) *initial spectrum*, (B) *after addition of two drops of glacial acetic acid*, (C) *final spectrum* (3·5 hr.).

It appears at this stage that the rate of trans-esterification is dependent on (a) the stereochemistry of the secondary carbinol (b) the polarity of the solvent, and (c) the presence of protic acid catalysts.[2]

The trans-esterification synthesis, in addition to permitting determination, by circular dichroism spectrometry, of configuration (and possibly conformation) of chiral alcohols such as carbohydrates, steroid and terpene alcohols, *etc.*, provides a ready source of alkyl nitrite substrates for photochemical synthesis.[9,10] In the latter case both the synthesis of the substrate and the photochemical reaction could be monitored in the dichrometer.

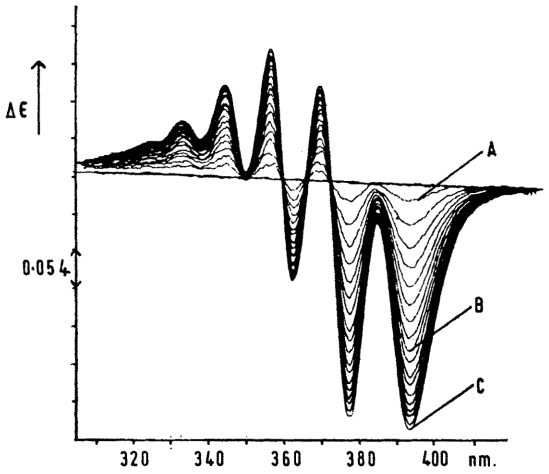

FIGURE 2. *C.d. spectrum (instrument trace) of isopentyl nitrite* (0·18M) *and* (−)-(1R,3R,4S)-*menthol* (1·30M) *in dioxan*: (A) 5 *min. after mixing*, (B) *after* 90 *min.*, (C) *final spectrum.*

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