# Acylation of *O*-Alkylbenzohydroxamic Acids; Configurational Assignment, Interconversion, and Rearrangement of the *E*- and *Z*-Isomers of a New Group of *O*-Acyl Isoamides

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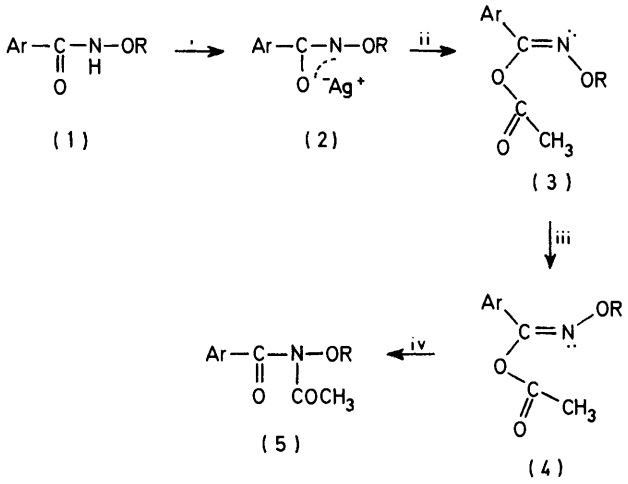
Acylation of the silver salts of *O*-alkylbenzohydroxamic acids (1) gives *Z*-acetic benzoalkoximic anhydrides (3) which do not rearrange to the isomeric *N*-acyl-*N*-benzoyl-*O*-alkylhydroxylamines (5) on heating. U.v. irradiation of the *Z*-isomers (3) in hexane or benzene induces a photostationary equilibrium of the *E*- and *Z*-isomers (4) and (3), which were separated by chromatographic methods. On heating at reflux for 30 min in carbon tetrachloride the *E*-isomers (4) rearrange to (5), by an O ⟶ N [1,3] acyl migration. The $^1$H n.m.r. chemical shifts and the u.v. extinction coefficients for isomers (3) and (4) were found to vary in the same relative way in the six pairs of compounds examined. Diazotization of *O*-(n-propyl)benzamidoxime in acetic acid yields only the *Z*-isomer (3), possibly *via* stereospecific reaction of acetate with an intermediate *N*-alkoxynitrilium ion (13). Consistent with this is the observation that only the *Z*-*O*-alkylbenzohydroximoyl chloride (9a) is formed on reaction of (13) with $Cl^-$ under similar conditions.

THE protonation, alkylation, and acylation sites of amides (nitrogen or oxygen) have been the subject of intense investigation and controversy.[1-3] In general, because O ⟶ N acyl group migrations are known to be rapid,[4] it is difficult to determine whether the *N*-acylated product isolated is formed under kinetic control or *via* preliminary *O*-acylation. An additional interesting aspect of this problem is the potential role of isomeric *O*-acyl materials which might be formed (due to the presence of the carbon–nitrogen double bond). The first isolation and rearrangement of pairs of these materials is the subject of this report.

We have initally investigated the acylation of the ambident anion derived from *O*-alkylbenzohydroxamic acids (1); acylation can give rise to three possible isomers, isoimides (3) and (4) and imides (5).[5] Although previous work has shown that varying proportions of *O*- and *N*-acylation products may be obtained depending on the structure of the hydroxamic acid, the counter ion, and the acylating agent,[6] no evidence was given either for the existence of isomeric *O*-acylated materials or indeed to account for the unusual observation that *O*-acylated materials can actually be isolated in this case. In connection with a mechanistic study of [1,3] acyl migrations in isoimides, *i.e.* (3) or (4) ⟶ (5),[7] and the establishment of the stereochemistry of reactions of nucleophiles with nitrilium ions, it was necessary to isolate and assign configurations to materials of this type; the hydroxamic acid system therefore provided a promising starting point.

*O*-Alkylbenzohydroxamic acids (1) were prepared by alkylation of potassium benzohydroxamate or by reaction of the appropriate aroyl chloride with methoxyamine hydrochloride in the presence of triethylamine as a catalyst. These in turn were converted to their silver salts (2) with silver nitrate in ethanol containing ammonia as a base. On stirring a suspension of the silver salt in ether with acetyl chloride the *Z*-isomer (3) of the *O*-acylated product was obtained as the only product. In




a; Ar = Ph, R = $CH_3$
b; Ar = Ph, R = $CH_2Ph$
c; Ar = Ph, R = $Pr^n$
d; Ar = *p*-$NO_2C_6H_4$, R = Me
e; Ar = *m*-$NO_2C_6H_4$, R = Me
f; Ar = *m*-$ClC_6H_4$, R = Me

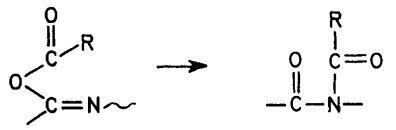
SCHEME Reagents: i, $NH_3$–$AgNO_3$; ii, $CH_3COCl$; iii, *hν*, hexane or benzene; iv, heat in toluene or chlorobenzene

some cases the products were liquids and were purified by dry column chromatography as attempted distillation of the esters resulted in decomposition (probably *via* thermally induced Lossen rearrangements). The spectral characteristics of these compounds were consistent with

[1] A. Williams, *J. Amer. Chem. Soc.*, 1975, **97**, 6278 and references therein.
[2] M. Liler, *Chem. Comm.*, 1971, 115.
[3] B. C. Challis in 'The Chemistry of the Amide Group,' Wiley–Interscience, 1968.
[4] C. G. McCarty in 'The Chemistry of the Carbon–Nitrogen Double Bond,' ed. S. Patai, Wiley–Interscience, New York, 1970, ch. 9.
[5] These compounds are named as mixed anhydrides of acetic and *O*-alkylbenzohydroximic acid as suggested by P. A. S. Smith, 'Open-chain Nitrogen Compounds,' Benjamin, New York, 1966, vol 2, p. 70.
[6] M. T. W. Hearn and A. D. Ward, *Austral. J. Chem.*, 1969, **22**, 161.
[7] A. F. Hegarty and D. G. McCarthy, following paper.

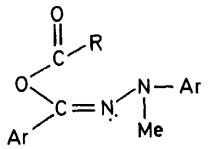
the *O*-acylated structure. The i.r. spectra showed carbonyl stretching frequencies in the region 1 770—1 790 $cm^{-1}$, which is in the region observed for vinylic acetates [8] and *O*-acylisoureas.[9] The $^1H$ n.m.r. (in the region δ 3.8—4.1 for the $NOCH_3$ or $NOCH_2$ protons and δ 2.1—2.35 for the acetyl group proton signal) agree with those reported for compounds possessing the azomethine linkage and *O*-acyl group linked to an unsaturated system. The u.v. spectra show absorptions in the region 250—300 nm (log ε 3.5—4.0), the latter being characteristic of compounds containing the oximate or oxime ether group (see below).

Rapid thermally induced rearrangement of the *O*-acyl isoimide group (6) to the *N*-acyl compound (7),



(6) (7)

through a [1,3] acyl migration, is well documented.[4,10,11] Thus in the work of Curtin and Miller [11] on the rearrangement of *N*-(2,4-dinitrophenyl)benzimidoyl benzoates and more recently in these laboratories [12] on the rearrangement in the hydrazone system (8), the only isomer of the isoimides isolated was either shown or presumed to be the *Z*-isomer *i.e.* where the acetate group and the lone pair of electrons on the imino-nitrogen are *trans* to each other. On heating, this isomer (8) was found to re-



(8)

arrange to the *N*-acyl compound. When the oxime derivative (3) obtained from acylation of the silver salt (2) was heated in toluene or chlorobenzene for 6—8 h, no change was found by i.r., n.m.r., or t.l.c. The rearrangement of (3) to (5) requires that the lone pair of electrons on the nitrogen be *cis* to the acetate group. Since there is considerable evidence to indicate that oxime ether derivatives do not undergo thermally induced *E*–*Z* isomerism in the absence of catalysts,[13] the absence of rearrangement with (3) indicates that the acetate group is trans to the lone pair on the nitrogen. Thus acylation of the silver salts (2) gives the *Z*-isomer of the isoimide (3).

U.v. irradiation of a 0.1M solution of the *Z*-isomer (3) in hexane or benzene for 6 h produced a photostationary state of the *Z*- and *E*-isomers (3) and (4). The *E* : *Z* ratio was generally in the range 2 : 3—1 : 1. For five of the isomer pairs the *E*-isomer could be separated from the photolysis mixture by preparative t.l.c. or dry column chromatography on silica. It was found that for the range of solvents used to separate (3) and (4), the $R_F$ value of the *E*-isomer was always less than that of the *Z*-isomer by 0.15—0.2. The i.r. spectrum of the *E*-isomer does not show any change in the carbonyl stretching frequency compared with that observed for the *Z*-isomer. However, the $^1H$ n.m.r. spectrum provides a convenient method for distinguishing between the two

TABLE 1

Chemical shifts (δ) for the *O*-methyl (or -methylene) and acetyl protons of isomers (3) and (4)

| Compound | δ($NOCH_2X$) [a] | δ($COCH_3$) |
|---|---|---|
| (3a) | 3.80 [b] | 2.15 |
| (4a) | 3.76 | 2.09 |
| (3b) | 4.98 [b] | 2.10 |
| (4b) | 4.95 | 2.01 |
| (3c) | 4.04 [b] | 2.20 |
| (4c) | 4.00 | 2.15 |
| (3d) | 3.85 [c] | 2.29 |
| (4d) | 3.90 | 2.22 |
| (3e) | 3.96 [c] | 2.35 |
| (4e) | 3.95 | 2.29 |
| (3f) | 3.81 [c,d] | 2.2 |
| (4f) | | 2.14 |

[a] X = H, Et, and Ph. [b] In $CCl_4$. [c] In $CDCl_3$. No chemical shift difference was observed for the $NOCH_3$ protons in compounds (3f) and (4f).

isomers (3) and (4). For the six sets of isomers prepared, the resonance of the acetyl group protons of the *Z*-isomer is shifted downfield from that of the *E*-isomer by 0.1 p.p.m., while for the methyl or methylene protons attached to the oxygen of the oximate group the order is the same except that the difference is much less, 0.05—0.01 p.p.m. (Table 1). The relative positions of these resonances for each isomer are independent of the solvent used, but the chemical shifts are solvent dependent to a small degree. In the case of the *meta*-substituted compounds, the difference in chemical shifts of the *N*-methoxy-group protons was small, <0.01 p.p.m. for (3e) and

(9) (10)

a; X = Cl
b; X = OR′
c; X = $NH_2$

(4e), and no difference is observable for (3f) and (4f). The chemical shifts of the $NOCH_3$ or $NOCH_2$ protons in the isomers (3) and (4) follow the same trend as those of the *E*- and *Z*-isomers of alkyl *O*-alkylbenzohydroxi-

[8] D. H. Williams and I. Fleming, 'Spectroscopic Methods in Organic Chemistry,' McGraw-Hill, London, 1966, p. 61.
[9] M. T. McCormack, Ph.D. Thesis, National University of Ireland, 1976.
[10] O. Mumm, H. Hesse, and H. Volquartz, *Ber.*, 1915, **48**, 379.
[11] D. Y. Curtin and L. L. Miller, *J. Amer. Chem. Soc.*, 1967, **89**. 637.
[12] M. T. McCormack and A. F. Hegarty, *J.C.S. Perkin II*, 1976, 1701.
[13] (*a*) D. Y. Curtin, E. J. Grubbs, and C. G. McCarty, *J. Amer. Chem. Soc.*, 1966, **88**, 2775; (*b*) A. Padwa and F. Albrecht, *ibid.*, 1974, **96**, 4849.

mates [14] (9b) and (10b) and *O*-alkylbenzohydroximoyl chlorides [15] (9a) and (10a).*

The u.v. spectra of five pairs of the *E*- and *Z*-isomers are also different. In some cases $\lambda_{max.}$ of the *E*-isomer was found to occur at slightly shorter wavelengths than that of the *Z*-isomer and in all cases the extinction coefficient at $\lambda_{max.}$ was greater for the *Z*-isomer by a factor of *ca.* 2 (Table 2). A number of examples of this behaviour can be found in the literature for the *E*- and *Z*-isomers of azobenzene,[16] *N*-benzylideneaniline,[17] and *O*-alkylbenzohydroximates.[18]

The isomer (4) was shown to have the *E*-configuration by heating it in carbon tetrachloride or toluene for 30 min, when it was found to have rearranged quantitatively to the *N*-acyl compound (5). The product formed was identical with that obtained from acylation of the potassium salt of (1), a process which gives considerable *N*-acylation. Conversion of (4) to (5) can be followed by observing the disappearance of the ester carbonyl band at 1 775 $cm^{-1}$, and the appearance of two new carbonyl bands near 1 720 and 1 695 $cm^{-1}$ due to the aliphatic and aromatic carbonyl groups in (5). On refluxing the reaction solution during photoisomerization of (3) it is possible to convert (3) into (5) completely *via* (4), and this provides a convenient method for the preparation of the pure imides (5). Thus, the observed rearrangement of (4) to (5), confirms that the acetate group and the lone pair of electrons on the imino nitrogen are *cis*, and confirms that (4) is indeed the *E*-isomer of the isoimide.

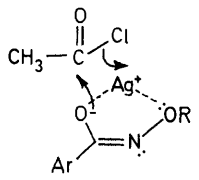
TABLE 2

U.v. absorption maxima for the isomeric isoimides (3) and (4) (solvent, MeOH)

| Compound | $\lambda_{max.}$/nm | $\epsilon_{max.}$ |
|---|---|---|
| (3a) | 250 | 16 727 |
| (4a) | 249 | 9 800 |
| (3b) | 257 | 24 600 |
| (4b) | 251 | 10 940 |
| (3c) | 257 | 16 527 |
| (4c) | 252 | 8 103 |
| (3d) | 298 | 22 440 |
| (4d) | 295 | 11 999 |
| (3e) | 254 | 24 505 |
| (4e) | 251 | 13 170 |

Having prepared both isomers (3) and (4), a search was made for the presence of the *E*-isomer in the acylation mixture from (2). Thus, t.l.c. analysis of the reaction during acylation of (2) failed to reveal any *E*-isomer either when the reaction was performed at room temperature or at −50°. Separate experiments showed that the *E*- and *Z*-isomers did not interconvert during the acylation reaction. Changing the metal cation present did not yield any *E*-isomer. Thus the thallium and potassium salts of (1c) were both acylated to give (3c) and (5c) in the ratios 4 : 3 and 5.5 : 1 respectively.

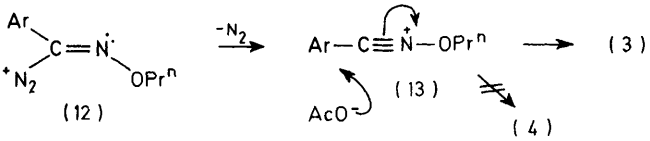
A possible explanation for the exclusive formation of the *Z*-isomer (3) rather than (4) in the initial acylation step is the existence of the ion-pair (11). In (11) the silver ion is associated with the more basic oxygen (rather than nitrogen) sites, and has the additional advantage of a five- (rather than four-) membered cyclic structure. This forces the hydroximate anion to adopt the configuration observed in the acylated product. When silver ion



(11)

is replaced by thallium or potassium the same type of ion pair can be formed but the acylation step can now also occur by attack through the unco-ordinated nitrogen since the driving force for silver chloride formation [which promotes oxygen attack in (11)] is absent.

*Reaction of Acetate with N-Alkoxynitrilium Ions.*— Having established the configurations of two acetates (3) and (4), we were interested in determining which products would be formed on the reaction of the *N*-alkoxycarbonium ion (13) with acetate ion. Because of the low reactivity of *N*-alkylhydroximidoyl chlorides (see below) towards $S_N1$ type hydrolysis (in contrast to simple halides [19]), the required ions (13) were generated by dediazoniation of the ions (12). On diazotization of amidoxime (9c) with sodium nitrite in glacial acetic acid the *Z*-isomer (3) was formed exclusively (as indicated by actual isolation and by t.l.c. analysis of the reaction mixture before work-up); preliminary experiments showed that the two isomers (3) and (4) did not interconvert under the conditions of diazotization. The observed formation of (3) is consistent with previous



(12) (13) (3) (4)

results from hydrazone systems which indicated [20] exclusive formation of the product in which the incoming nucleophile and the lone pair being formed on the adjacent nitrogen are *trans* in the reaction of nucleophiles with nitrilium ions.

There is however an alternative explanation which we cannot rule out for the observed stereospecificity in this

* The configurational assignments for the *E*- and *Z*-chlorides in ref. 15 have recently been reversed (J. E. Johnson, personal communication).

[14] J. E. Johnson, J. R. Springfield, J. S. Hwang, L. J. Hayes, W. C. Cunningham, and D. C. McClaugherty, *J. Org. Chem.*, 1971, **36**, 284.

[15] J. E. Johnson, E. A. Nalley, Y. K. Kunz, and J. R. Springfield, *J. Org. Chem.*, 1976, **41**, 252.

[16] C. Sandorfy, in ref. 4, p. 53.

[17] E. Fischer and Y. Frei, *J. Chem. Phys.*, 1957, **27**, 808.

[18] O. Exner, V. Jehlicka, and A. Reiser, *Coll. Czech. Chem. Comm.*, 1959, **24**, 3207.

[19] A. F. Hegarty, J. D. Cronin, and F. L. Scott, *J.C.S. Perkin II*, 1975, 429.

[20] A. F. Hegarty and M. T. McCormack, *J.C.S. Chem. Comm.*, 1975, 168.

case. Thus the configuration of the starting diazonium ion (12) is unknown, but from the dipole moment studies of Exner *et al.*,[21] the thermodynamically most stable isomer of the amidoxime is (9c) [rather than (10c)]. Further work in these laboratories [22] indicates that *E* : *Z* isomerisation in amidoximes (both unsubstituted and *O*-alkylated) is extremely fast under acid conditions. Therefore the predominant (or exclusive) amidoxime species present under diazotization conditions would be protonated (9c). Diazotization with retention of configuration would thus give the ion pair (with acetate ion) in which the diazonium ion would have configuration (12). Collapse of the ion pair formed on loss of nitrogen (13) without the intervention of solvent [23] could theoretically lead to the formation of (3) and/or (4) [we have observed only the formation of (3)]. However the origin of the unusual ' memory effects ' observed in the decomposition of alkanediazonium ions is controversial and Bereson [24] has put forward the alternative view that reaction of the nucleophile with the carbonium ion (or, more commonly, rearrangement) occurs *before* the carbonium ion reaches its normal equilibrium structure [which would be (13) in this case]. In these terms, the azacarbonium ion formed from (12) would be non-linear and retention of this non-linear structure leads (on reaction with the nucleophile) to (3) rather than (4).

When diazotization of the hydrochloride of (9a; Ar = Ph, R = Pr$^n$) was carried out in the presence of hydrochloric acid, just two products were formed, (*Z*)-*O*-n-propylbenzohydroximoyl chloride (9a; Ar = Ph, R = Pr$^n$) (see footnote on p. 1082), (71%), and a trace of *O*-n-propylbenzohydroxamic acid (1; Ar = Ph, R = Pr$^n$). Significantly none of the *E*-isomer (10a; Ar = Ph, R = Pr$^n$) could be detected. The formation of just the *Z*-chloride parallels the formation of (3) [rather than (4)] on reaction of (13) with acetate ion.

In conclusion therefore, acylation of the silver salts (2) leads to exclusive formation of the *O*-acyl isoamides (3) which do not thermally rearrange to the *N*-acyl isomers (5). Formation of (5) from (3) therefore involves a prior $Z \longrightarrow E$ isomerisation (which may only be achieved photochemically in this system). The *Z*-acetate (3) is also formed by stereospecific reaction of the nitrilium ion (13) with acetate, while chloride ion also reacts stereospecifically to give only the product (9a) in which the lone pair and the entering nucleophile are *trans*.

## EXPERIMENTAL

*General.*—M.p.s were determined on a Thomas Hoover m.p. apparatus and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 257 spectrophotometer and u.v. spectra were run on a Perkin-Elmer 124 instrument. $^1$H N.m.r. spectra were obtained on a Perkin-Elmer R20-A spectrometer operating at 60 MHz with tetramethylsilane as an internal standard. T.l.c. was run on silica gel (Merck $HF_{254}$) while preparative t.l.c. was carried out on silica gel (Merck $PF_{254}$). For dry-column chromatography silica gel (Woelm; activity III, 30 mm) containing 0.5% inorganic fluorescent indicator (obtained from I.C.N. Pharmaceuticals Ltd.) was used.

Photoisomerisation reactions were carried out using a Hanovia 100 W mercury arc lamp contained in a quartz housing. The lamp was water cooled throughout, and was immersed in an 8 × 18 cm cylindrical flask containing the solution to be photolysed.

*Substrates.*—*O*-Benzylbenzohydroxamic acid, m.p. 101° (lit.,[25] 103—105°), and *O*-n-propylbenzohydroxamic acid, m.p. 58° (lit.,[25] 58—59°), were prepared by alkylation of potassium benzohydroxamate.

*O*-Methyl-*p*-nitrobenzohydroxamic acid was prepared as follows. *p*-Nitrobenzoyl chloride (18.56 g, 0.1 mol) in dry ether (100 ml) was added dropwise to a stirred suspension of methoxyamine hydrochloride (8.35 g, 0.1 mol) and dry triethylamine (20.2 g, 0.2 mol) in dry tetrahydrofuran (250 ml). The mixture was then stirred for 12 h at room temperature, the precipitated amine hydrochloride was removed by filtration, and washed with ether (100 ml). Evaporation of the filtrate to dryness under reduced pressure gave a yellow solid which was recrystallised from chloroform–ethyl acetate (1 : 1), m.p. 180—181° (lit.,[26] 180°). Similarly prepared were O-*methyl*-m-*nitrobenzohydroxamic acid*, m.p. 157.5—159.5° (ethanol–water 1 : 1). $\nu_{max.}$ (KBr) 3 170 (NH) and 1 655 (C=O) cm$^{-1}$, δ ([$^2H_6$]acetone) 3.81 (3 H, s), 7.7 (1 H, t), and 8.3 (3 H, m) (Found: C, 48.6; H, 4.3; N, 14.5. $C_8H_8N_2O_4$ requires C, 49.0; H, 4.1; N, 14.3%); O-*methyl*-m-*chlorobenzohydroxamic acid*, m.p. 115—116° [chloroform–light petroleum (b.p. 40—60°) 1 : 1], $\nu_{max.}$ (KBr) 3 170 (NH) and 1 645 (C=O) cm$^{-1}$; δ ($CDCl_3$) 3.8 (3 H, s) and 7.5 (4 H, q) (Found: C, 52.1; H, 4.7; N, 7.5; Cl, 18.3. $C_8H_8ClNO_2$ requires C, 51.8; H, 4.3; N, 7.6; Cl, 19.1%); and *O*-methylbenzohydroxamic acid, m.p. 62° (lit.,[25] 63.5—64.5°).

The silver salts of the *O*-alkylbenzohydroxamic acids were prepared by Johnson's [14] method and satisfactory analytical data was obtained for each salt prepared.

The potassium salt of (1c) was prepared and acylated by the method of Ward.[6]

*Thallium*(I) *Salt of* (1c).—Thallium(I) ethoxide (1.3 g) in dry ether (60 ml) was added to a solution of *O*-n-propylbenzohydroxamic acid (0.89 g) in dry ether (50 ml) and the mixture was stirred at room temperature under nitrogen for 5 h. The salt was acylated *in situ* by the same method used for the potassium salt.

*Acetylation of Silver Salts* (2).—(*Z*)-*Acetic* O-*n-propylbenzohydroximic anhydride* (3c). Acetyl chloride (0.8 g, 0.01 mol) in dry ether (20 ml) was added dropwise to a stirred suspension of the silver salt (2.87 g, 0.01 mol) in dry ether (50 ml). The mixture was stirred at room temperature for 4 h and protected from moisture throughout ($CaCl_2$ tube). Silver chloride was then removed by filtration and washed with ether (50 ml). Evaporation of the combined filtrates gave a liquid. This was purified by dry column chromatography on silica (300 g) with $CCl_4$–ether (1 : 1) as the mobile phase, giving the *isoimide* (3) as a liquid; $\nu_{max.}$ ($CCl_4$) 1 775 (C=O) and 1 610 (C=N) cm$^{-1}$ (Found: C, 65.5; H, 7.2; N, 6.0. $C_{12}H_{15}NO_3$ requires C,

[21] O. Exner, V. Jehlicka, A. Dondoni, and A. C. Boicelli, *J.C.S. Perkin II*, 1974, 567.
[22] A. F. Hegarty and K. J. Dignam, unpublished results.
[23] C. J. Collins, *Chem. Rev.*, 1975, **4**, 251.
[24] J. A. Bereson, *Angew. Chem.*, 1968, **80**, 765.
[25] J. H. Cooley, W. D. Bills, and J. R. Throckmorton, *J. Org. Chem.*, 1960, **25**, 1734.
[26] O. Exner and J. Holubek, *Coll. Czech. Chem. Comm.*, 1965, **30**, 940.

65.2; H, 6.8; N, 6.3%). The following compounds were obtained by this method: (Z)-*acetic* O-*methylbenzohydroximic anhydride* as a yellow liquid, $\nu_{max.}$ ($CCl_4$) 1 772 (C=O) $cm^{-1}$ (Found: C, 62.35; H, 5.9; N, 7.4. $C_{10}H_{11}NO_3$ requires C, 62.2; H, 5.7; N, 7.25%); (Z)-*acetic* O-*benzylbenzohydroximic anhydride*, m.p. 42—44° (lit.,[6] 44—45°), $\nu_{max.}$ ($CCl_4$) 1 785 (C=O) $cm^{-1}$; (Z)-*acetic* m-*chloro*-O-*methylbenzohydroximic anhydride*, liquid, $\nu_{max.}$ ($CCl_4$) 1 780 (C=O) $cm^{-1}$ (Found: C, 53.0; H, 4.3; N, 6.50; Cl, 16.0. $C_{10}H_{10}ClNO_3$ requires C, 52.8; H, 4.4; N, 6.15; Cl, 15.6%); (Z)-*acetic* O-*methyl*-p-*nitrobenzohydroximic anhydride*, m.p. 85—86° [chloroform–light petroleum (b.p. 40—60°) 2 : 1], $\nu_{max.}$ ($CHCl_3$) 1 775 (C=O), 1 595 (C=N), and 1 520 and 1 350 ($NO_2$) $cm^{-1}$ (Found: C, 50.2; H, 4.3; N, 11.8. $C_{10}H_{10}N_2O_5$ requires C, 50.4; H, 4.2; N, 11.8%); (Z)-*acetic* O-*methyl*-m-*nitrobenzohydroximic anhydride*, m.p. 91—92° [chloroform–light petroleum (b.p. 40—60°) 1 : 1], $\nu_{max.}$ ($CHCl_3$) 1 773 (C=O), 1 610 (C=N), and 1 530 and 1 355 ($NO_2$) $cm^{-1}$ (Found: C, 49.9; H, 4.4; N, 11.7. $C_{10}H_{10}N_2O_5$ requires C, 50.4; H, 4.2; N, 11.8%).

(E)-*Acetic* O-n-*Propylbenzohydroximic Anhydride* (4c).—*Photoisomerisation of* (3c). A solution of (3c) (0.1M, 200 ml) in dry degassed hexane was irradiated for 6 h under nitrogen. Removal of the solvent under reduced pressure without heating gave a yellow oil. Analysis by n.m.r. showed the presence of (3c) and (4c) in the ratio 58 : 42. T.l.c. (chloroform–cyclohexane 1 : 1) showed (3c), $R_F$ 0.7, and (4c), $R_F$ 0.42. Dry column chromatography gave a pure sample of (4c) as a liquid. Similarly the following compounds were obtained: (E)-*acetic* O-*methylbenzohydroximic anhydride* (4a), ratio (3a) : (4a) 57 : 43. $R_F$ 0.35 and 0.2 (chloroform–cyclohexane 1 : 1); (E)-*acetic* O-*benzylbenzohydroximic anhydride* (4b), ratio (3b) : (4b) 52 : 48. $R_F$ 0.7 and 0.61 (chloroform) [pure (4a) was obtained as a liquid by preparative t.l.c. (chloroform–cyclohexane 3 : 1)]; (E)-*acetic* m-*chloro*-O-*methylbenzohydroximic anhydride* (4f), ratio (3f) : (4f) 48 : 52, $R_F$ 0.58 and 0.4 (chloroform–cyclohexane 3 : 1) in this case the isomers were not separated; (E)-*acetic* O-*methyl*-p-*nitrobenzohydroximic anhydride* (4d), ratio (3d) : (4d) 45 : 55 (irradiated in benzene), $R_F$ 0.81 and 0.74 (chloroform) [(4d) was obtained by preparative t.l.c. on the mixture above using ether–light petroleum (b.p. <40°) (1 : 1) as eluant, m.p. 87—88°, $\nu_{max.}$ 1 775 (C=O) $cm^{-1}$].

(E)-*Acetic* O-*methyl*-m-*nitrobenzohydroximic anhydride* (4e), ratio (3e) : (4e) 49 : 51 (in benzene), $R_F$ 0.62 and 0.46 (cyclohexane–chloroform 1 : 3) {preparative t.l.c. [(ether–light petroleum <40°) 1 : 1] gave a pure sample of (4e), m.p. 76—78°}.

N-*Acetyl*-N-*benzoyl*-O-*n-propylhydroxylamine* (5c).—*Rearrangement of* (4c). A mixture of (3c) and (4c) (2.0 g) was refluxed in dry toluene (20 ml) for 10 h. Removal of the solvent *in vacuo* gave a yellow oil. T.l.c. (cyclohexane–chloroform 1 : 1) showed two spots due to (3c) and (5c), $R_F$ 0.25. Dry column chromatography on silica gave pure (5c) (0.53 g), b.p. 96—98° at 0.025 mmHg, $\nu_{max.}$ ($CCl_4$) 1 720 and 1 690 (C=O) $cm^{-1}$, $\lambda_{max.}$ (MeOH) 234 nm (log ε 4.1), δ ($CCl_4$) 7.4 (5 H, m), 3.6 (2 H, t), 2.32 (3 H, s), 1.3 (2 H, sextet), and 0.63 (3 H, t) (Found: C, 64.7; H, 7.1; N, 5.9. $C_{12}H_{15}N_2O_3$ requires C, 65.2; H, 6.8; N, 6.3%). Also obtained in this manner and purified by preparative t.l.c. were: N-*acetyl*-N-*benzoyl*-O-*methylhydroxylamine* (5a), obtained as a pale yellow liquid with chloroform–cyclohexane (3 : 1) as eluant, $R_F$ 0.55, $\nu_{max.}$ ($CCl_4$) 1 725 and 1 698 (C=O) $cm^{-1}$, $\lambda_{max.}$ (MeOH) 235 nm (log ε 4.19), δ ($CCl_4$) 7.45 (2 H, m), 7.2 (3 H, m), 3.46 (3 H, s), and 2.31 (3 H, s); N-*acetyl*-N-*benzoyl*-O-*benzylhydroxylamine* (5b), eluted with chloroform, m.p. 69° (lit.,[6] 69°) [chloroform–light petroleum (b.p. 40—60°) 1 : 5]; N-*acetyl*-N-p-*nitrobenzoyl*-O-*methylhydroxylamine* (5d), eluted with chloroform–ethyl acetate (1 : 1), $R_F$ 0.62, m.p. 105—107° (cyclohexane–chloroform 10 : 1), $\nu_{max.}$ ($CHCl_3$) 1 705 and 1 730 (C=O) $cm^{-1}$, $\lambda_{max.}$ (MeOH) 262 nm (log ε 4.3), δ ($CDCl_3$) 8.1 (2 H, d), 7.53 (2 H, d), 3.46 (3 H, s), 2.45 (3 H, s); N-*acetyl*-N-m-*nitrobenzoyl*-O-*methylhydroxylamine* (5e), eluted with chloroform–ethyl acetate (1 : 1), $R_F$ 0.7, m.p. 116—117.5° (chloroform–hexane 1 : 5), $\nu_{max.}$ ($CHCl_3$) 1 704 and 1 728 (C=O) $cm^{-1}$, $\lambda_{max.}$ (MeOH) 255 nm (log ε 3.74), δ ($CDCl_3$) 8.1 (3 H, m), 7.4 (2 H, q), 3.7 (3 H, s), and 2.48 (3 H, s); N-*acetyl*-N-m-*chlorobenzoyl*-O-*methylhydroxylamine* (5f), $\nu_{max.}$ ($CHCl_3$) 1 700 and 1 725 (C=O) $cm^{-1}$, δ ($CDCl_3$) 7.3 (4 H, m), 3.54 (3 H, s), and 2.36 (3 H, s).

O-*n-Propylbenzamidoxime* was prepared by the procedure of Fuller and King [27] as a liquid (71%), b.p. 61—63° at 0.05 mmHg, $\nu_{max.}$ ($CCl_4$) 3 480 and 3 400 (NH) and 1 630 (C=N) $cm^{-1}$, δ ($CCl_4$) 7.2 (5 H, m), 4.7br (2 H, s), 3.9 (2 H, t), 1.65 (2 H, m), and 0.9 (3 H, t) (Found: C, 67.6; H, 8.05; N, 16.4. $C_{10}H_{14}N_2O$ requires C, 67.4; H, 7.8; N, 16.0%). Diazotization of *O*-n-propylbenzamidoxime in acetic acid was carried out using the procedure of Tiemann.[28] (*Z*)-*O*-n-Propylbenzohydroximoyl chloride (9a; R = $Pr^n$) was obtained by the action of $PCl_5$ on *O*-n-propylbenzohydroxamic acid, b.p. 72—73° at 0.03 mmHg (lit.,[14] 82—83° at 0.3 mmHg). (*E*)-*O*-n-Propylbenzohydroximoyl chloride (10a; R = $Pr^n$) was obtained by irradiating the *Z*-isomer (2 g) in dry hexane (200 ml) for 6 h. N.m.r. analysis showed (9a) and (10a) in the ratio 63 : 37. A pure sample of (10a) was obtained by dry column chromatography using $CCl_4$–ether (1 : 1) as eluant, δ ($CCl_4$) 7.7 (2 H, m), 7.3 (3 H, m), 4.03 (2 H, t), 1.7 (2 H, sextet), and 0.91 (3 H, t).

*Diazotization of* O-*n-Propylbenzamidoxime in Hydrochloric Acid.*[29]—The amidoxime hydrochloride (formed by bubbling HCl gas through a solution of the amidoxime in dry ether) (0.65 g, 3 mmol) was dissolved in 5N-HCl (20 ml) and the solution was cooled in an ice-bath. Sodium nitrite (0.216 g, 3 mmol) in water (10 ml) was added dropwise. The solution gradually became turbid and was stirred for 30 min after the addition of sodium nitrite. The mixture was diluted with water (200 ml) and extracted with ether (3 × 30 ml). The ether was washed with 10% $NaHCO_3$ solution (50 ml) and dried ($MgSO_4$). Evaporation of the ether gave a yellow liquid (0.42 g, 71%). This was shown by t.l.c. ($CCl_4$) to consist of (*Z*)-*O*-n-propylbenzohydroximoyl chloride (9a; R = $Pr^n$) and a trace of *O*-n-propylbenzohydroxamic acid. A control experiment showed that the *E*-isomer (10a; R = $Pr^n$) did not isomerise to the *Z*-isomer under the reaction conditions.

Use of the free base of the amidoxime gave a poor yield of the chloride (<20%) together with a large amount of starting material (t.l.c. and i.r.). This is due to the previously noted low solubility of the amidoxime in aqueous media.[30]

[6/1225 *Received*, 24*th June*, 1976]

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