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THE PREPARATION AND CHEMISTRY OF α-NITROEPOXIDES[1]

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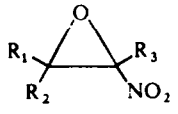
Abstract—The preparation of α-nitroepoxides from nitro olefins and hydrogen peroxide in the presence of base is reported and the behaviour of this new chemical species towards selected nucleophiles, acids and reducing agents is described. Mass spectral data is also presented.

ALTHOUGH the reaction of a variety of electronegatively substituted olefins such as α,β-unsaturated ketones,[2a] aldehydes,[2b] nitriles,[2c] dinitriles,[2d] diesters[2e] and cyanoesters[2f] with basic hydrogen peroxide to give the corresponding epoxides have been reported, a search of the literature failed to reveal the application of this reagent to nitro olefins. In fact, α-nitroepoxides (nitro oxiranes) **1**, the anticipated product of this reaction represents an heretofore unknown chemical species. We report here the preparation of this new chemical type and describe some of its chemistry.



We chose β-methyl-β-nitrostyrene **2** as our model nitro olefin for our initial studies.*

The reaction of **2** with basic peroxide did, in fact, lead to its rapid and smooth transformation to the α-nitroepoxide **3** in 67% yield. Similarly, *cis* α-nitro stilbene (**4**) and 1-cyclohekyl-2-nitro-ethylene (**5**) were transformed into the nitroepokides **6** and **7** respectively in 85 and 91% yields.

2: R = φ, R¹ = CH₃ — **3**: R = φ, R¹ = CH₃
4: R = R¹ = φ — **6**: R = R¹ = φ
5: R = cyclohexyl, R¹ = CH₃ — **7**: R = cyclohexyl, R¹ = CH₃

* We were concerned that the lower homolog, β-nitrostyrene, might lead to complications under the basic conditions of the reaction owing to the anticipated highly acidic nature of the proton α to the nitro substituent in the initially formed epoxide. In view of the recently reported results[3] concerning the conspicuously low acidity of the α-proton in nitrocyclopropanes one wonders how acidic this proton would in fact be in the related nitroepoxide. Our decision not to use β-nitrostyrene for our initial studies was however a fortunate one, since, as will be seen below, it did not give the desired nitroepoxide.

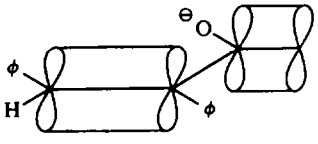
On the other hand, β-nitrostyrene did not appear to undergo this transformation under the above conditions. A mixture was obtained which appeared to contain starting β-nitrostyrene and benzaldehyde. More mildly basic conditions ($NaHCO_3$) left the β-nitrostyrene virtually unchanged.

The sharpness of the epoxide proton and Me signals in the various nitroepoxides, as well as the relatively sharp m.p. of the solid **6**, suggests that the epoxidation takes place stereospecifically.

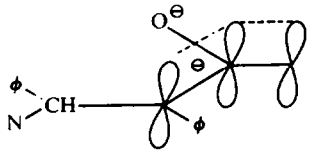
An attempt to establish the stereochemical course of the epoxidation was, however, thwarted by an unexpected complication.

Thus, we planned to prepare the epoxide of *trans* α-nitrostilbene (**8**), available from the *cis* isomer **4** by thermal isomerization[4], for comparison with **6**, however quite surprisingly **8** was recovered unchanged under the conditions which led to an 85% yield of **6** from the *cis* isomer **4**. Extending the reaction time was without effect.*

A likely explanation for this rather dramatic difference in reactivity is that in the case of the *trans* isomer **8** the severe eclipsing interaction between the α-phenyl and β-nitro substituents destabilizes that conformation of the NO_2 substituent in which it is planar to the olefinic moiety (see diagram A). As a result the driving force for nucleophilic (N) addition to nitro olefins, the stabilization of the resulting anion by the nitro group (see diagram B), is eliminated, rendering **8** relatively unreactive. In the *cis* isomer **4** the nitro substituent is *cis* to the much smaller hydrogen and the foregoing conformational restriction does not obtain.



A



B

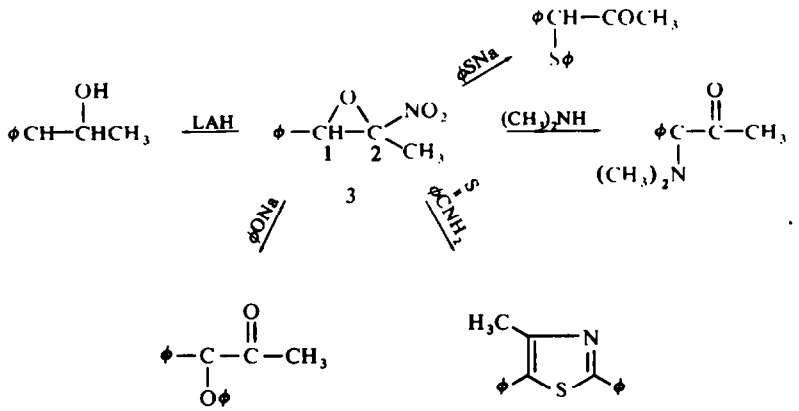
This enormous difference in reactivity between the *cis* and *trans* isomers was also observed towards methoxide ion and provided a convenient method for separating the two compounds hitherto accomplished either by a tedious fractional crystallization[4] or by thick-layer chromatography (Experimental). Thus, treating a mixture of the two with somewhat more than an equivalent of sodium methoxide in methanol results in the selective conversion, essentially instantaneously, of the *cis* isomer to the water soluble anion **9**, ($\phi CHOCH_3—{}^-C\phi NO_2$). Partitioning between water and organic solvent permits the separation of the *trans* isomer. (See Experimental for further details).

Chemistry of α-nitro epoxides

A. Behavior towards nucleophiles. The behavior of **3** towards the following representative nucleophiles was investigated: ϕONa, ϕSNa, $(CH_3)_2NH$, $\phi CSNH_2$, and LAH. The product obtained (Scheme 1) in each case resulted from attack at C-1.

* The relative instability of peroxide in base limits the variation in conditions that could be attempted.

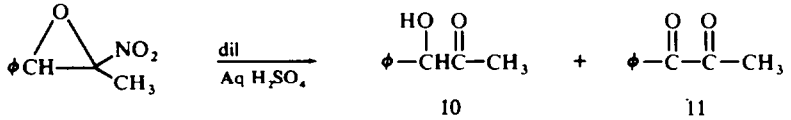
SCHEME I



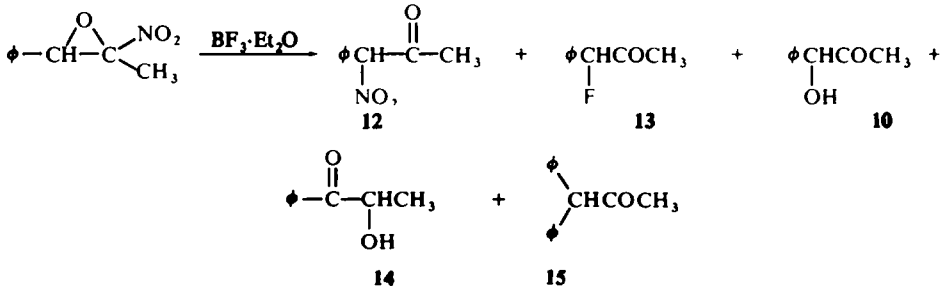
The behaviour of **5** towards nucleophiles thus parallels that previously observed for electronegatively substituted epoxides which are attacked at the carbon furthest from the substituent, a result which is rationalized in terms of an S_N2 transition state in which the reacting carbon center bears residual positive charge.[5]

In its behavior towards the nucleophiles investigated, **3** simulates that of an α-haloketone,* making it a useful alternative to this strongly lachrymatory species.

B. Behavior towards acids. The nitroepoxide **3** reacted in dilute aqueous sulfuric acid to give the anticipated l-phenyl-l-hydroxy acetone **10** along with smaller amounts of its oxidation product diketone **11** (ratio **10:11** ca. 3 : 1).

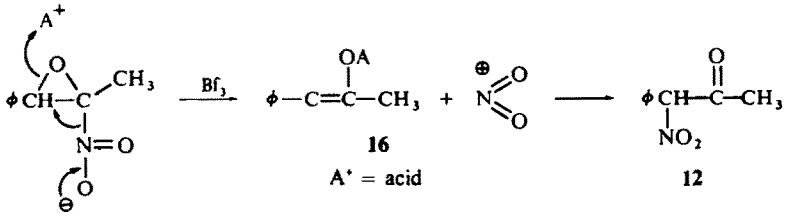


With boron trifluoride etherate in benzene, **3** gave a complex mixture consisting of the components indicated in the equation (evidence for structural assignments are detailed in the Experimental).



* The reaction of LAH and α-haloketones gives initially the halohydrin which in the presence of excess hydride can be further reduced to the alcohol[6].

The formation of the α-nitroketone **12** is a rather interesting result and can be accommodated by the following sequence:



16

A⁺ = acid

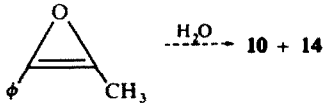
12

Acid catalysed attack of the epoxide oxygen leads to transformation into the enol **16** and nitronium ion which then recombine (intermolecularly or intramolecularly, presumably this question could be decided by appropriate labelling) to give the nitroketone **12**. Precedent for the nitration of enols appears in the work of Hass and Hudgin who prepared various α-nitroketones by vapor phase nitration of ketones with nitric acid[7a] and in the work of Bachman and Hokama who obtained α-nitroketones from the nitration of enol acetates.[7b]

The formation of **13** has precedence in the conversion of epoxides to fluorohydrins[8], while the formation of **15** by electrophilic attack on the benzene solvent is related to the alkylation of aromatic systems by epoxides in the presence of boron trifluoride etherate.[9]

The α-hydroxyketones **10** and **14** were obtained as an unresolved mixture (ratio **10**:**14** ca. 1:1·5) and while the formation of **10** is perhaps unexceptional especially in view of the behavior of **3** towards aqueous acid, the formation of **14** is rather surprising.

Two possible precursors of **14** were eliminated. Thus acid catalysed isomerization of **10** was precluded as a route to **14** by demonstrating (by NMR) that no **14** is formed when **10** is treated with boron trifluoride etherate in benzene under the conditions of the reaction. (This finding is in accord with previously reported equilibration studies on **10** and **14** in which it was found that mineral acids convert **14** completely to **10**.[10]) The possible intermediacy of the oxirene **17**, which could in turn be formed from **3** by elimination of nitrous acid, was also eliminated by conducting the reaction with **3** labelled with deuterium at C-1 (see numbering in Scheme 1).*

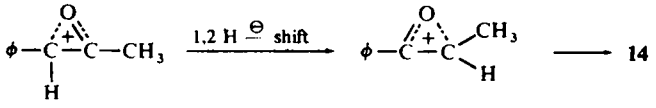


17

The involvement of an intermediate such as **17** would require that *no* deuterium be present in the hydroxy ketone **14** formed. In fact, the hydroxy ketone **14** that was obtained was indicated by NMR to be completely deuterated.

* Definitive evidence for the transient existence of this interesting, but heretofore, elusive species has only recently been presented.[11] The compound is a cyclic 4 π electron system and would be predicted to exhibit antiaromatic character.[12]

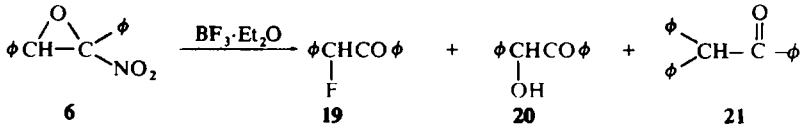
The formation of hydroky Setone **14** would be compatible with hydride shift in carbonium ion **18** generated from **3** by acid catalysed loss of nitronium ion or concertedly with the loss of NO_2^+.



18 **18a**

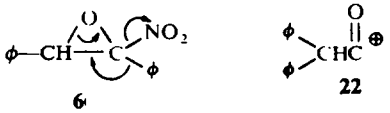
Consistent with the postulated hydride shift is the finding that the amount of **14** produced relative to **10** was considerably reduced using the deuterium labelled **3** as substrate, (from 1·5:1 to 1:4) presumably the result of an H/D isotope effect.

Treatment of 1,2-diphenyl-nitrooxirane (**6**) with boron trifluoride etherate in benzene gave products **19, 20** and **21** corresponding to **13, 10** (**14**) and **15** obtained from **3**. None of the corresponding α-nitroketone could be detected.



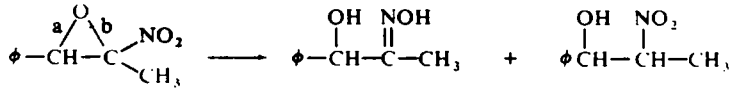
6 **19** **20** **21**

The acylium ion **22** arising *via* acid catalysed rearrangement of **6** (either concertedly or stepwise; the arrows simply indicate direction of electron flow) was ruled out as a precursor of **21** by conducting the reaction in benzene-d_6 and showing, by NMR and mass spectrometry that the deuterium labelled aromatic ring in the **21** obtained was attached to the methine carbon. (Experimental).



6 **22**

C. Behavior towards reducing agents. The behavior of **3** towards catalytic and chemical reducing agents was briefly investigated. With platinum oxide in ethyl acetate, **3** was rapidly reduced to a mixture of 1-phenyl-1-hydroxy acetone oxime **23** and 1-phenyl-1-hydroxy-2-nitro propane **24**. The latter product was obtained as a mixture of *erythro* and *threo* isomers which could be separated by partition chromatography on Celite 545. With zinc and aqueous acetic acid the oxime **23** was obtained.



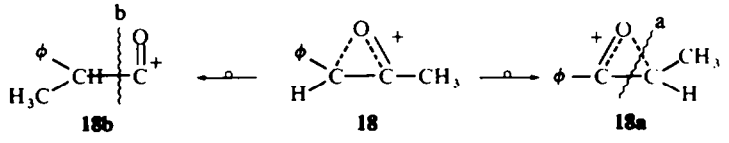
3 **23** **24**

An interesting contrast is thus observed in the behavior of **3** towards nucleophiles, where preferential cleavage of the carbon-oxygen bond in the epoxide take place at (a) (see labelling in equation above) and reducing agents, where bond (b) is preferentially broken.

This difference would be consistent with the operation of two different mechanistic pathways: a heterolytic one in the case of nucleophilic substitution and a homolytic one in the case of reduction. (The formation of **24** would indicate that, at least to some extent, bond (b) is being attacked directly rather than through initial attack at the nitro substituent).

Mass spectra. The mass spectrum of **3** shows a parent peak at *m/e* 179 along with prominent fragments at 133 and 105 (base peak). The 105 fragment is indicated to arise from the further fragmentation of the 133 ion by the presence of a metastable peak at 83. The mass spectrum of deuterated **3** shows, along with the parent peak now at 180, fragments corresponding to the above at 134, 105 and 106, the last peak being very much more intense than that at 105. The expected metastable at 84 was also present.

The foregoing data is explicable on the basis that the 133 fragment resulting from loss of NO_2 from the parent ion is comprised of two species, the carbonium ion **18** and the hydride shifted ion **18a**. (Compare with the species postulated above as being precursors of hydroxy ketone 14.) Further fragmentation of **18a** along (a) leads to the



18b **18** **18a**

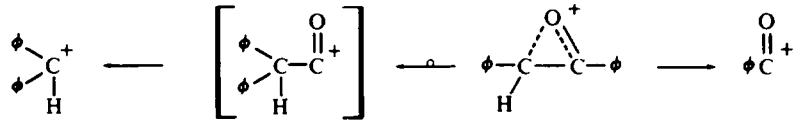
105 fragment ϕCO^+, while rearrangement of **18** to **18b** followed by fragmentation along (b) leads to the 105 fragment $\phi\dot{C}HCH_3$. The latter fragment corresponds to the 106 ion in the mass spectrum of deuterated **3**.

Since the rearrangement **18**→**18a** would be expected to be disfavored in deuterated **3** because of the deuterium isotope effect, a greater amount of fragmentation along the path **18**→ **18b** $\xrightarrow{b}$ would be anticipated for deuterated **3**. (If the magnitude of this effect were known for our system we could assess the relative amounts of ϕCO^+ and $\phi\dot{C}HCH_3$ in the 105 peak in **3**.)*

The mass spectrum of **6** shows a weak molecular ion at 241 (much weaker than the molecular ion in **3**) along with the prominent fragments at 195, 167 and 105. Metastable peaks at 143 and 56 indicate that the 167 and 105 ions result from the further fragmentation of the 195 ion.

A scheme corresponding to the one above would account for these observations. Thus loss of NO_2 from the M^+ ion of **6** would lead to **25** (*m/e* 195) which then either fragments directly or undergoes hydride shift and then fragments (or both, one could not tell in this case owing to the symmetry of the system) to give ion **26** (*m/e* 105). Prior phenyl migration in **25** followed by fragmentation would lead to **28** (*m/e* 167).

* The unlikely possibility that the $\phi\dot{C}HCH_3$ ion arises by the path **18a** $\xrightarrow{a}$ 18b $\xrightarrow{b}$ is also eliminated by the much greater intensity of the 106 peak relative to 105 in deuterated **3**.



28 27 25 26

A measure of the relative rates of the competing fragmentation processes is indicated by the 2:1 ration in which the two fragments (**26** and **28** respectively) are produced.

EXPERIMENTAL

Mps and bps are uncorrected. The NMR spectra were determined on a Varian A-60 spectrometer, the mass spectra on an AEI MS-9 spectrometer. $MgSO_2$ was used for drying. TLC were run on phosphor-containing silica gel plates (Anal Tech Inc. Wilmington, Delaware). Thick-layer chromatograms were run on 2 mm silica gel plates containing phosphor. (E. M. Reagents Division, Brinkmann Instrument Co., Westbury, N.Y.).

1-*Phenyl*-2-*methyl*-2-*nitrooxirane* (**3**). To a stirred, cooled (ice-water) suspension of 32 g (0·2 mole) β-methyl-β-nitro styrene[13] in 400 ml MeOH containing 90 ml 15% $_2O_2$aq (ca. 0·3 mole) was added rapidly (ca. 3 min) with stirring, 50 ml 2N NaOH (0·1 mole). The temp of the reaction mixture rose rapidly to ca. 25°, the system becoming largely homogeneous and pale yellow in color. After stirring in the cooling bath for an additional 10 min (a turbidity developed during this time), the reaction mixture was poured into ice-water, acidified and the organic product extracted into ether. The ethereal extracts were washed with water, bicarbonate, dried and evaporated to yield 27·4 g of a yellow liquid which was distilled *in vacuo* to give 23·9 g [67%] of **3** as a yellow liquid, b.p. 88–91° (0·1 mm). The spectral properties of this product were identical with those of the analytical sample obtained from a smaller scale experiment; λ_{max}^{film} 6·47 μ (strong, NO_2); λ_{max}^{MeOH} 290 (plateau) (ε 450) and 230 mμ (plateau) (ε 4500) and end absorption; δ_{TMS}^{CDCl} 7·40 (finely split singlet, 5 aromatic protons), 4·58 (songlet, C-1 H) and 1·83 (singlet, C-2 CH_3). (Found C, 60·70; H,[5]·12; N,[7]·96. Calcd. for $C_9H_9NO_3$ (179·17): C, 60·33; H, 5·06; N, 7·82%).

(The various spectra were essentially unchanged when determined again after two months at room temp).

Acidification of the bicarbonate extracts gave 1·5 g of a colorless solid, identified as benzoic acid by m.p. (119–121°) and IR spectral comparison with an authentic specimen.

The corresponding 1-*deutero analog* was similarly obtained using C_6H_5CDO. The latter was prepared by LAD (alpha Inorganics, Beverly, Mass.) reduction of N-benzoylaziridine according to the procedure of Brown *et al.*[14]

1,2,-*Diphenyl*-2-*nitrooxirane* (**6**). Essentially the procedure described for the preparation of **3** was followed. To a stirred cooled (ice–water) suspension of 9 g (0·04 mole) *cis* α-nitrostilbene[15] in 100 ml MeOH containing 18 ml 15% H_2O_2aq (ca. 0·6 mole) was added 10 ml 2N NaOH (0·02 mole). The temp of the reaction mixture rose rapidly to ca. 25° and a new colorless solid quickly formed. After 10 min ice–water was added and the colorless solid collected, washed well with water and air dried to yield 8·2 g (85%) of **6**, m.p. 104–109°. The analytical sample obtained by recrystallization from MeOH melted at 108–110°; λ_{max}^{Nujol} 6·45 μ (strong, No_2); λ_{max}^{MeOH} 290 (plateau) (ε 800), 232 nm (plateau) (ε 6000) + end absorption; $\delta_{TMS}^{CDCl_3}$ 7·35–7·00 (multiplet, 10 aromatic protons), 4·75 (singlet 1H). (Found: C, 69·88; H, 4·69; N, 5·94. Calcd. for $C_{14}H_{11}NO_3$ (241·24): C, 69·70; H, 4·59; N, 5·80%).

1-*Cyclohexyl*-2-*nitro*-2-*methylethylene* (**5**). Prepared according to the procedure of Shechter *et al.*[16] B.p. 58–60° (0·1 mm) (yellow liquid); λ_{max}^{Nujol} 6·6 μ (strong, C=C—NO_2); $\lambda_{TMS}^{CDCl_3}$ 6·95 (d, J = 10 Hz, vinyl H split by methine H of cyclohexyl ring), 2·16 (d, J = ⩽ 1 Hz, vinyl CH_3) 1·8–1·2 (m, cyclohexyl protons). (Found: C, 64·29; H, 9·01; N, 7·50. Calcd. for $C_9H_{15}NO_2$ (169·22): C, 63·88; H, 8·94; N, 8·28%).

1-Cyclohexyl-2-nitro-2-methyloxirane (7). A cooled (ice–water) soln of 4·25 g (0·025 mole) of 5 in 60 ml MeOH containing 11·3 ml 15% H_2O_2 aq (0·038 mole) was treated with 6·25 ml 2N NaOH (0·013 mole). (The addition of base was accompanied by an exotherm.) The reaction mixture was stirred in the cooling bath for 5 min (a colorless solid separated during this time) then allowed to come to room temp with stirring during 15 min (in which time the solid disolved). The reaction mixture was poured into ice–water, the mixture acidified with dil HCl and extracted with ether. The ethereal extracts were washed with water, bicarbonate, dried and evaporated to yield 4·2 g (91%) of 7 as a pale yellow liquid, b.p. 68–71° (0·1 mm); λ_{max}^{film} 6·40 μ (strong, NO_2); λ_{max}^{MeOH} only end absorption; $\delta_{TMS}^{CDCl_3}$ 3·17 (m, C-1H), 1·93 (sharp s, C-2 CH_3) 1·9–1·1 (broad m, cyclohexyl protons). (Found: C, 58·43; H, 8·23; N, 7·93. Calcd. for $C_9H_{15}NO_3$ (185·33): C, 58·36; H, 8·16; N, 7·56%).

A small amount of the colorless crystalline solid which separated after 5 min in the cooling bath was removed and an abortive attempt was made to characterize it. It left a residue on burning, gave a negative peroxide test with starch–iodide paper and melted indefinitely and incompletely over ca. a 25° range (64–90°). Its IR spectrum showed only weak absorption in the CO region at 6·0 μ and in the NO_2 region at 6·35 μ. After subjecting to high vacuum pumping at room temp overnight, the solid, now pale yellow, did *not* melt up to 280° and showed a simple non-characterizable IR spectrum.

Isomerization of cis *α-nitrostilbene* (4). Two grams of *cis* α-nitrostilbene[15] was heated at 185° in the presence of a crystal of iodine for 14·5 hr. The brown liquid product which solidified on standing at room temp for 4 hr showed two spots on TLC (φH-*n*-hexane 1:1), R_f ca. 0·5 and 0·6 (*cis* and *trans* α-nitrostilbene respectively).

Separation

Method A. By thick-layer chromatography of a 200 mg sample using φH-*n*-hexane 1:1 for development. (The zones were cut out and eluted with acetone containing some MeOH). The faster running spot (29 mg) (*trans*-α-nitrostilbene) melted at 121–127° (Lit.[4] 128°); the slower moving spot (143 mg) (*cis*-α-nitrostilbene) melted at 68–71° (Lit.[14] 75°).

Method B. A soln of the isomeric mixture (785 mg) was disolved in MeOH (8 ml) and treated with somewhat more than an equivalent of 1M methanolic NaOMe (4 ml). After 3·5 min at room temp, the dark orange soln was poured into ice–water and the mixture extracted with ether. Drying and evaporating the ether left *trans* α-nitrostilbene (93 mg) [completely free of *cis* (by TLC)] as a somewhat oily solid which was recrystallized from MeOH.

Reaction of 3 *with LAH*

1-phenyl-2-propanol. An ethereal soln containing 1·8 g (0·01 mole) of 3 was added dropwise during 15 min to a stirred suspension of 0·65 g (0·017 mole) of 35 ml ether. After stirring for an additional hr at room temp, the excess hydride was destroyed by the slow addition of water and the mixture was poured into ice–water. Concentrated NaOH aq was added to form soluble aluminium hydroxides and the organic product extracted with ether. Drying and evaporating the ether gave 1·3 g (100%) of a colorless liquid which distilled at 62–63° (0·1 mm). The product was identical (refractive index, IR spectrum, b.p.) to an authentic sample of 1-phenyl-2-propanol[17a] prepared by LAH reduction of commercially available phenylacetone.

Reaction of 3 *with sodium thiophenolate*

1-phenyl-1-thiophenylacetone. A methanolic soln containing 0·01 mole sodium thiophenolate was prepared by adding 1·1 g (0·01 mole) thiophenol to 10 ml 1M NaOMe in MeOH (0·01 mole). The soln was cooled (ice–water) and 1·8 g (0·01 mole) of 3 in 10 ml MeOH was added rapidly. After 3 hr at room temp the reaction mixture was poured into ice–water and the organic product extracted into ether. The ethereal extracts were washed with dil NaOH aq dried and evaporated to yield a pale yellow solid which was triturated with light petroleum (b.p. 30–60°) and collected; yield 2 g (83%), m.p. 61–65°. Recrystallization from n-hexane furnished the analytical sample, m.p. 64–66°, λ_{max} 5·85 μ. (Found; C, 74·64; H, 5·68; S, 13·07. Calcd. for $C_{15}H_{14}OS$ (242·26): C, 74·36; H, 5·83; S, 13·20%).

Reaction of 3 *with thiobenzamide*

2,5-Diphenyl-4-methyl thiazole. A soln of 1·4 g (0·01 mole) thiobenzamide (Eastern Chemical Corp., Pequannock, N.J.) and 1·8 g (0·01 mole) of 3 in 25 ml MeOH was heated under reflux for 16 hr, then

poured into water and the oily product extracted with ether. Drying and evaporating the ethereal extracts left 2·3 g of a yellow liquid [shows primarily one spot on TLC (benzene)] which was distilled *in vacuo*. After a 125 mg forerun b.p. 65–155° (0·1 mm), 1·5 g of a yellow liquid was collected, b.p. 169–171° (0·1 mm) which solidified on refrigerating overnight. The somewhat oily solid was triturated with light petroleum (b.p. 30–60°), collected and pressed on filter paper to yield a pale yellow solid m.p. 42–50°. The product was freed from small amounts of impurities by thick-layer chromatography using benzene as the developing solvent.The colorless thiazole thus obtained was recrystallized from n-hexane to give the analytical sample, m.p. 52–55°. (Found: C, 76·51; H, 5·06; N, 5·72; S, 12·94. Calcd. for $C_{16}H_{13}NS$ (251·77): C, 76·47; H, 5·22; N, 5·57; S, 12·74%).

Reaction of **3** *with dimethylamine*

1-*Phenyl*-1-*dimethylamino acetone*. A soln of 1 g (0·006 mole) **3** in 10 ml MeOH at room temp was treated with 1 ml 40% aqueous Me_2NH (ca. 0·4 g of amine or 0·009 mole). After 3 hr at room temp, the reaction mixture was poured into ice–water and the mixture extracted with ether. Drying and evaporating the ether left 0·7 g of a lime-colored liquid which was treated directly with ethereal HCl to yield a hydrochloride salt, initially as an oil but which solidified on rubbing during 10 min. The solid was collected and washed with ether; yield 0·45 g; m.p. 184–194°. Recrystallization from acetonitrile furnished the analytical sample, m.p. 194–201° (Lit.[17b] 193–195°). (Found; C, 61·67; H, 7·36; N, 6·63; Cl, 16·33. Calcd. for $C_{11}H_{16}NOCl$ (213·70): C, 62·02; H, 7·57; N, 6·58; Cl, 16·65%).

Reaction of **3** *with sodium phenoxide*

1-*Phenyl*-1-*phenoxyacetone*. To a cooled (ice–water) soln of 0·33 g (0·0035 mole) of phenol in 3·5 ml 1M NaOMe in MeOH (0·0035 mole) was added 0·63 g (0·0035 mole) of **3**. The resulting soln was kept at room temp for 17 hr, then poured into ice–water and the organic product extracted into ether. The ethereal soln was washed with cold dilute NaOH aq water, dried and evaporated to yield 0·45 g of a light orange liquid which showed a major spot on TLC (benzene) at R_f ca. 0·6. The compound corresponding to this spot was isolated by thick-layer chromatography (benzene). In agreement with its formulation as 1-phenyl-1-phenoxyacetone, its IR spectrum showed CO absorption at 5·85 μ and its NMR ($CDCl_3$) spectrum showed signals at 7·6–6·8 δ (10-proton in aromatic protons), 5·53 δ (1-protons, methine proton) and 2·19 δ (3-protons, $—CH_3$).

Reaction of **3** *with* 3N H_2SO_4

1-*Phenyl*-1-*hydroxyketone* [**10**) *and* 1-*phenyl-propane*-2,3-*dione* (**11**). A suspension of 10 g (0·056 mole) of **3** in 150 ml 3N H_2SO_4 was heated at 75–80° for 2·5 hr with vigorous stirring. A brown gas was evolved. Ice was added to the mixture which was then extracted with ether. The ethereal extracts were washed with $NaHCO_3$ aq, water dried and evaporated to yield 5·3 g (63%) of a dark orange liquid indicated by TLC (φH-EtOAc 20:1) to be a two component mixture (R_f ca. 0·3 and 0·7). The faster running component was separated by thick-layer chromatography (200 mg sample) using benzene as the developing solvent (the slower component remained at the origin in this solvent) and identified as the dione **11** by IR, UV and NMR spectral and TLC comparisons with an authentic specimen.[17c]

The slower moving component was separated in another chromatographic run using φH-EtoAc 20:1 for development and identified as **10** by IR and NMR spectral comparisons with an authentic specimen[10] and conversion in high yield to 1-phenyl-1-hydroxyacetone oxime, m.p. 108–112° (Lit.[18] 112°) identical (IR, NMR) with this compound obtained by the Zn/HOAc reduction of **3** (see below).

The ratio of **10** to **11** in the mixture was ca. 3:1.

Reaction of **3** *with* $BF_3 \cdot Et_2O$

A soln of 12 g (0·07 mole) of **3** in 200 ml anhyd benzene was treated with 24 ml $BF_3 \cdot Et_2O$ at room temp. The resulting mild exotherm was counteracted by brief cooling in ice–water. After 10 min, the reaction mixture was poured into ice–water and the acid neutralized with solid $NaHCO_3$. The mixture was extracted with ether and the ethereal extracts dried and evaporated to yield 11·2 g of a fairly dark brown liquid whose IR spectrum showed strong bands at 5·75 and 6·40 μ and a weak band at 5·75 μ. The product was disolved in ether and the ethereal soln was extracted with cold dilute (≤ 2N) NaOH. Acidification of the basic extracts with cold dil HCl, extraction with ether and drying and evaporating the latter left 3·3 g of a fairly dark brown liquid which was distilled *in vacuo* to give after a 0·35 g forerun boiling at 64–97° (0·1 mm), 1·6 g of **12** as a yellow liquid b.p. 104–107° (0·1 mm); λ_{max}^{film} 5·75 (S)

(C=O) and 6·41 μ (S) (NO_2); $\delta_{TMS}^{CDCl_3}$ 7·46 (5-protons, aromatic protons), 6·30 (1-protons, on α-carbon) and 2·17 (3-proton s, acetyl CH_3).

The ethereal soln remaining after base extraction was washed with water dried and evaporated to yield 4·9 g of a brown liquid which was fractionally distilled *in vacuo*, four fractions being collected.

Fraction 1. B.p. 40–45° (0·1 mm); 1·38 g (yellow liquid); λ_{max}^{film} 5·80 (S) (C=O) and 9·55 μ (S) (C—F); $\delta_{TMS}^{CDCl_3}$ 7·40 (5-proton, aromatic protons), 5·67 (1-proton, $J_{HF} = 49$ Hz, proton on α-carbon) and 2·20 (3-proton, $J_{CH_3F} = 4$ Hz, acetyl CH_3). (Found; C, 70·71; H, 6·03; F, 12·11. Calcd. for C_9H_9FO (152·16) ($\phi CHFCOCH_3$): C, 71·04; H, 5·96; F, 12·49%).

Fraction 2. B.p. 55–77° (0·1 mm); 0·64 g (yellow liquid). Indicated by its NMR spectrum to be a mixture of Fractions 1 and 3.

Fraction 3. B.p. 77–111° (0·1 mm); 0·60 g (yellow liquid). The distillate, after freeing from additional minor impurities by thick-layer chromatography using benzene–EtOAc 20:1 for development, was indicated to be roughly a 1:1·5 mixture of **10** and **14** by its IR [λ_{max}^{film} 3·0 (M) (OH) 5·85 (S) (C=O in **10**) and 5·98 μ (S) (C=O in **14**)] and NMR [$\delta_{TMS}^{CDCl_3}$ 1·42 (d $J = 6$ Hz, CH_3 in **14**), 2·07 (s CH_3 in **10**) ca. 5·1 (α-H in **10** and **14**) and aromatic proton resonance] spectra. Spectra of authentic specimens[10] of **10** and **14** were used for comparisons.

Fraction 4. B.p. 111–126° (0·1 mm); 0·78 g (yellow, fairly viscous liquid). Minor impurities present were separated by thick-layer chromatography (ϕH). Its IR [λ_{max}^{film} 5·74 μ (S) (C=O)] and NMR [$\delta_{TMS}^{CDCl_3}$ 7·33 (10-proton singlet, aromatic protons), 5·13 (1-proton s, proton on α-carbon) and 2·33 (3-proton s, acetyl CH_3)] indicated it to be **15**.

Solid derivatives of **12**, **13** (Fraction 1) and **15** (Fraction 4) were prepared.

2,4-*DNP of* 1-*phenyl*-1-*nitro acetone* (**12**). Prepared according to the general procedure of Hurd et al.,[19] m.p. 156–159° dec; $\delta_{TMS}^{CDCl_3}$ 6·39 (1-proton s, proton on α-carbon) 2·10 (3-proton s, —C—CH_3) and, in addition, the expected aromatic proton absorptions. (Found: C, 50·42; H, 3·47; N, 19·22. Calcd. for $C_{15}H_{13}N_5O_6$ (359·29): C, 50·14; H, 3·65; N, 19·49%).

2,4-*DNP of* 1-*phenyl*-1-*fluoroacetone* (**13**). Prepared according to the general procedure of Hurd *et al.*;[19] m.p. 125–132 dec.(Found: C, 54·54; H, 4·08; F, 5·59; N, 16·84. Calcd. for $C_{15}H_{13}FN_4O_4$ (332·28): C, 54·22; H, 3·94; F, 5·72; N, 16·86%).

Oxime of 1,1-*diphenylacetone* (**15**). Prepared according to method B of Shriner and Fuson;[20] m.p. 162–165°. (Lit.[17d] 164·5°). (Found: C, 79·97; H, 6·82; N, 6·19. Calcd. for $C_{15}H_{13}NO$ (225·28): C, 79·97; H, 6·71; N, 6·22%).

Reaction of deuterated **3** *with* $BF_3 \cdot Et_2O$

The foregoing procedure was used with deuterated **3** (2 g) and $BF_3 \cdot Et_2O$ (4 ml) in dry benzene (30 ml) except that the base insoluble residue (950 mg) was thick-layer chromatographed directly (without prior fractional distillation). The deuterated hydroxyketone mixture **10** and **14** isolated (the R_f of this mixture on TLC was ca. 0·25 and was well separated from the other faster moving components) was shown by NMR (relative intensities of the Me group protons in **10** and **14**; these protons appeared, as expected, as a broadened singlet in the deuterated **14**) to contain the two in a 4:1 ratio (**10**:**14**) in contrast to the 1:1·5 ratio observed for the reaction with nondeuterated **3**.

Reaction of 1,2-*diphenyl-nitrooxirane* (**6**) *with* $BF_3 \cdot Et_2O$

To a soln of 1·5 g (0·0062 mole) of **6** in 25 ml anhyd benzene at room temp was added 3 ml of $BF_3 \cdot Et_2O$. Brown fumes were evolved almost instantaneously and the reaction mixture bubbled although no significant exotherm could be detected. After 10 min at room temp, the reaction mixture was poured into ice–water and the mixture extracted with ether. The combined ethereal extracts were washed with water, $NaHCO_3$aq, dried and evaporated to yield 1·36 g of a light brown, somewhat oily solid which showed strong absorption in the CO region at 5·98 μ and was transparent in the NO_2 region (6·4–6·6 μ). Trituration of the oily solid with ether gave 0·72 g of 1,1-diphenylacetophenone[20] as a pale brown solid (single spot on TLC (ϕH), R_f ca. 0·65) which after recrystallization from MeOH melted at 133–137°; λ_{max}^{Nujol} 5·99 μ (S); $\delta_{TMS}^{CDCl_3}$ 6·03 (1-proton singlet, ϕ_2CH—) and multiple absorption in the aromatic proton region (15 protons). (Found: C, 88·14; H, 5·81. Calcd. for $C_{20}H_{16}O$ (272·33): 88·20; H, 5·92%).

The residue obtained on evaporating the ethereal mother liquor, an oily solid, was further resolved by thick-layer chromatography (150 mg sample) using benzene for development. The major component of the mixture (50 mg) showed an R_f of ca. 0·5 and melted at 53–58°; λ_{max}^{Nujol} 5·90 μ (S); $\delta_{TMS}^{CDCl_3}$ 6·47 (1-proton d, $J_{HF} = 49$ Hz) and multiple absorption in the aromatic proton region (15 protons) in

agreement with its formulation as **19**. (Found: C, 78·16; H, 5·19; F, 9·21. Calcd. for $C_{14}H_{11}FO$ (214·23): C, 78·49; H, 5·18; F, 8·88%).

The next most abundant component (25 mg) was additional amounts of **21**, R_f ca. 0·6 (the zones due to **19** and **21** partially overlapped. A zone containing a mixture of the two (30 mg) was therefore cut out in the overlap region).

Present in smallest quantity (10 mg) was benzoin (**20**) (m.p. 130–132°) which showed an R_f of ca. 0·2 and was identified by m.p. IR spectral and TLC comparisons with an authentic specimen.[17e]

Repetition of the above experiment in ϕH-d_6 gave **21** completely labelled in the methine phenyl group as indicated by no change in the resonance of the *ortho* protons of the benzoyl moiety in its NMR spectrum which appeared as a multiplet centered about 8·00 δ and the presence of the *m/e* 105 fragment (base peak, ϕCO^+·) in its mass spectrum.

Reaction of **3** *with zinc in aqueous acetic acid*

1-*phenyl*-1-hydroxyacetone Oxime (**23**). A soln of 1·8 g (0·01 mole) of **3** in 25 ml anhyd ether containing 4 g Zn dust was stirred at room temp while adding, during 2–3 min, 5 ml of 75% aqueous AcOH. The resulting exothermic reaction caused the ether to boil. An additional 5–10 ml of ether was added and stirring continued for a total of 25 min. The reaction mixture was filtered, the filter cake washed with ether and the combined filtrates were washed with dilute (<IN) HCl, water, $NaHCO_3$ aq dried and evaporated to yield 0·8 g of a colorless oil [essentially one spot, R_f ca. 0·6, on TLC (ϕH–EtOAc 1:1)] which crystallized relatively slowly on seeding with authentic **23** (see above). The somewhat oily crystals were pressed on filter paper to give 0·66 g (40%) of **23**, melting at 108–111·5°; λ_{max}^{Nujol} 3·05 μ; $\delta_{TMS}^{(CD_3)_2CO}$ 7·34 (5-proton m, aromatic protons) 5·27 (1- proton broadened s, ϕC<u>H</u>OH—) and 1·63 (3-proton s, CH_3). Analytically pure material could be obtained by thick-layer chromatographic purification using ϕH–EtOAc 1:1 for development.

Hydrogenation of **3** *over platinum oxide in ethyl acetate.* A soln of 1·8 g (0·01 mole) of **3** in 25 ml EtOAc was hydrogenated in a Parr shaker over 0·18 g PtO_2 for 15 min. Two pounds (ca. 0·024 mole) of H_2 was consumed during this time. the catalyst was separated by filtration and the filtrate diluted with ether and washed with dilute HCl, water, dried and evaporated to yield 1·35 g of a pale yellow liquid. Partition chromatography on Celite 545 using heptane–EtOAc–MeOH–water 90:10:17:4 for development permitted the separation of the stereoisomers of nitro alcohaol **24**, obtained as light orange liquids: faster moving isomer—141 mg; slower moving isomer—290 mg. The column MeOH wash yielded 335 mg of **23** identified by m.p., IR, NMR and TLC comparisons with **23** isolated above.

Spectral properties of the stereoisomeric nitro alcohols

Faster moving isomer. λ_{max}^{film} ca. 2·8 (M) (OH) and 6·48 μ (S) (NO_2). $\delta_{TMS}^{CDCl_3}$ 7·37 (5-proton s, aromatic protons), 5·38 (1-proton d, J = 3 Hz, ϕC<u>H</u>OH—) 6·33 (1-proton octet, —O_2C<u>H</u>CH_3) and J = 6 Hz, —O_2NCHC<u>H</u>$_3$). d, J = 6 Hz, —$_2$NCHC<u>H</u>$_3$).

Slower moving isomer. λ_{max}^{film} ca. 2·8 (M) (OH) and 6·48 μ (S) (NO_2); $\delta_{TMS}^{CDCl_3}$ 7·37 (5-proton s, aromatic proton m, ϕC<u>H</u>OHC<u>H</u>NO_2CH_3, unlike the other isomer, this one exhibited overlapping chemical shifts for these protons) and 1·26 (3-proton d, J = 6 Hz, —O_2NCHC<u>H</u>$_3$).

These same two isomers, as indicated by IR and NMR spectral comparisons, were obtained from the reaction of benzaldhyde and nitroethane according to the general procedure of Hollman.[21]

A solution of 4·2 g (0·04 mole) of benzaldehyde and 5 g (0·067 mole) of nitroethane in 30 ml MeOH was cooled in ice–water and treated with a soln of 6·4 g (0·17 mole) of NaOH in 10 ml water. The resulting colorless soln was kept in the ice-bath for 15 min, then poured into a mixture of glacial AcOH and ice. The mixture was extracted with ether and the ethereal extract washed with $NaHCO_3$ aq, water, dried and evaporated to yield a liquid residue which contained considerable amounts of benzaldehyde. Practically all of the latter was removed by high vacuum pumping at room temp for 35 hr. The remaining 1·8 g of liquid residue consisted very largely of the isomers of **24**, and were separated by partition chromatography as described above.

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