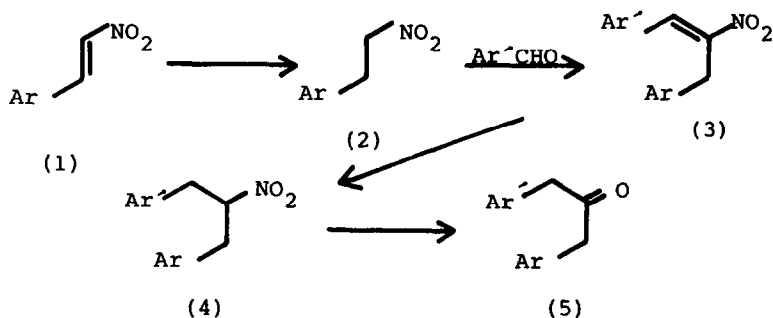


SYNTHESIS OF UNSYMMETRICAL DIBENZYLKETONES: NEW PROCEDURES
FOR THE PREPARATION AND REDUCTION OF NITROSTYRENES

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In connection with our studies of the design of substrates for oxidative phenol coupling ¹ we required a series of unsymmetrical oxygenated dibenzyl ketones. Finding existing procedures unsuitable ² we have developed the new route outlined below.



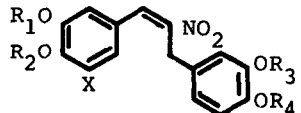
The β -phenylnitroethanes (2) were prepared in high yield by $\text{NaBH}_4/\text{MeOH}$ reduction of the corresponding nitrostyrenes (1). (Table 1).

Table 1. Preparation of β -nitroethanes (2, Ar =)

R ₁	R ₂	MPT	YIELD
Me	Bz	63-64°	92%
Bz	Me	87-88°	90%
-	CH ₂	57-58°	82%

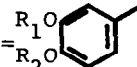
Condensations of (2) with aromatic aldehydes could not be achieved under the conditions normally used ³⁻⁵ for the preparation of simple nitrostyrenes (1), but when the reaction was carried out at reflux using $\text{MeNH}_3\text{Cl}/\text{KOAc}/\text{MeOH}$ with $\text{HC}(\text{OMe})_3$ present as a water scavenger the required nitrostyrenes (3) were obtained in good yield (Table 2). These condensation conditions also proved

Table 2. Preparation of substituted nitrostyrenes (3)



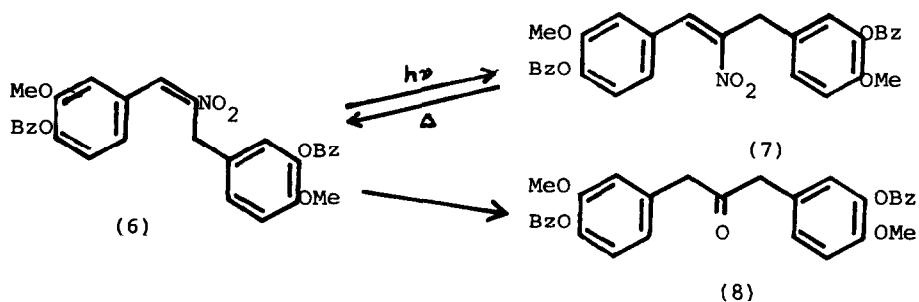
R ₁	R ₂	R ₃	R ₄	X	MPT	YIELD
Me	Bz	Bz	Me	H	107-108 ^o	77%
Bz	Me	Me	Bz	H	130-131 ^o	75%
Me	Bz	- CH ₂ -		H	110-111 ^o	65%
- CH ₂ -		Me	Bz	H	114-115 ^o	75%
Me	Me	Me	Bz	OMe	94-95 ^o	77%

excellent for the preparation of simple nitrostyrenes (1) and in most cases the products crystallised out from the clean reaction mixtures on cooling. (Table 3).

Table 3. Preparation of simple nitrostyrenes (1) (Ar = )

R ₁	R ₂	MPT	YIELD
Bz	Me	125-126 ^o (lit ³ 125-7 ^o)	79%
Me	Me	141-142 ^o (lit ⁵ 140-1 ^o)	64%
- CH ₂ -		161-162 ^o (lit ⁴ 161 ^o)	94%

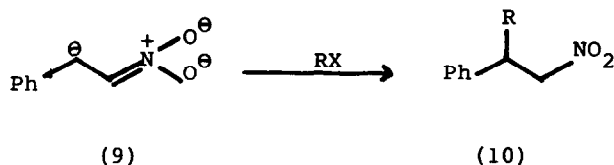
The appearance of a low field proton at $\delta 8.2$ in the ¹H nmr spectra of each of the nitrostyrenes (3) indicated the Z-configuration (cf. $\delta 7.9$ ⁶ for the corresponding proton in the simple trans-nitrostyrenes (1)). Photolysis of a methanolic solution of (6) brought about a clean isomerisation to the isolable E-isomer (7) ($\delta 6.2$) which slowly reverted to the more stable (6) on storage.



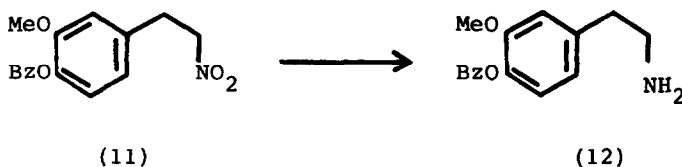
Borohydride reduction of (6) gave the corresponding nitroalkane (as (4)) and further reduction using TiCl₃/MeOH/aq.NaOH afforded the dibenzyl ketone (8)

in 67% overall yield.

The two step conversion of (2) to (4) represents a highly efficient α -alkylation of β -phenylnitroethanes. Direct α -alkylation is not feasible⁷, since (a) the monoanions of nitroalkanes alkylate preferentially on oxygen⁷, and (b) the dianion (9) of β -phenylnitroethane alkylates in the β -position to give (10)⁸.



Finally reduction of (11) by Al/Hg/aq.MeOH gave the phenethylamine (12) in 94% yield. A new 2-step procedure is therefore available for the reduction of nitrostyrenes (1) to β -phenethylamines and for large-scale work this may prove cheaper and safer than the traditional method³ using LiAlH₄/THF at reflux.



Clearly β -phenylnitroethanes are versatile intermediates which may be regarded as synthons for the species $\text{ArCH}_2\text{CHNH}_2$ and $\text{ArCH}_2\text{CH}_2\text{NH}_2$.

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