

***NN*-Dimethylhydrazones as Protecting Groups in Synthesis**

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DURING another study,¹ we observed that *NNN*-trimethylhydrazonium iodides (I) are unstable towards mild alkali, or even water, being converted into carbonyl compounds (IIa) (and, presumably, *NNN*-trimethylhydrazinium iodide) ‡. As compounds (I) are formed under very mild conditions from *NN*-dimethylhydrazones (IIb) the sequence (IIb) → (I) → (IIa) compound affords a mild

method for the conversion of (IIb) into a carbonyl compound (Table 1).

As compounds (IIb) are easily accessible,^{2,3} rather unreactive, and well characterized,²⁻⁴ they are convenient protecting groups for carbonyl compounds (Table 2) in enolate alkylation, alcohol oxidation, alkaline hydrolysis, complex hydride reduction, hydroboration, and double-bond

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‡ The easy hydrolysis of compounds (I) under acidic and alkaline conditions, has been noted (ref. 4) but the synthetic potentialities of the reaction have not previously been developed.

epoxidation. In some cases, (IIb) decomposed during the work-up, either because it had been alkylated in the reaction to give (I), or transformed to an oxidized species [presumably (III) or (IV)]; both (I) and (III) (or IV) can be readily hydrolysed.

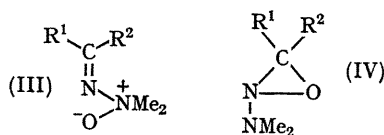
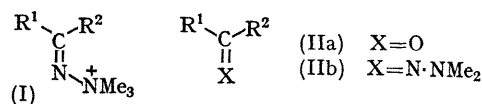
extent, salts of type (I) resemble eniminium salts, which have been suggested as protecting groups for enones.⁵ Compounds (IIb) should, however, be superior to eniminium

TABLE 1

Compound (IIb)	Procedure*	Carbonyl compound yield
Ph ₂ C=N-NMe ₂	A*	80—85%
PhCMe=N-NMe ₂	A	85—90
[CH ₂] ₅ C=N-Me ₂	A	85—90
PhCH=N-NMe ₂	A	80—85
5 α -Cholestan-3-one deriv.	B	85—90
Cholest-5-en-3-one deriv.	B	80—85
Oestr-4-ene-3,17-dione 3-deriv.	B	80—85
9-Hydroxycarvomenthone deriv.	B	

* Procedure A: isolation of (I), followed by hydrolysis.

Procedure B: one-step reaction; a mixture of (IIb), methyl iodide, and 95% ethanol (or water) is heated under reflux.



salts in all cases when an electrophilic reaction is performed under alkaline conditions (*e.g.* enolate alkylation), because eniminium salts are destroyed by base, whereas compounds (IIb) are not.

TABLE 2

Starting material (NN-dimethylhydrazone of)	Reaction	Product
17 β -Hydroxyandrost-4-en-3-one	(i) MeI-Bu ^t OK; (ii) H ₂ O	17 β -Hydroxyandrost-4-en-3-one
17 β -Hydroxyandrost-4-en-3-one	(i) CrO ₃ -pyridine; (ii) H ₂ O	Androst-4-ene-3,17-dione
17 β -Hydroxyandrost-4-en-3-one	CrO ₃ -H ₂ SO ₄ (0°, 3 min.)	Androst-4-ene-3,17-dione 3-NN-dimethylhydrazone
3 β -Hydroxypregn-5-en-20-one	CrO ₃ -H ₂ SO ₄ (0°, 3 min.)	Pregn-5-ene-3,20-dione 20-NN-dimethylhydrazone
3 β -Acetoxypregn-5-en-20-one	5% -KOH-EtOH	3 β -Hydroxypregn-5-en-20-one NN-dimethylhydrazone
Androst-4-ene-3,17-dione (3-deriv.)	{ NaBH ₄ -EtOH (room temp.) or LiAlH ₄ -tetrahydrofuran. Room temp. }	17 β -Hydroxyandrost-4-en-3-one NN-dimethylhydrazone
(-)-Dihydrocarvone	(i) B ₂ H ₆ (ex situ) (ii) H ₂ O ₂ , NaOH	9-Hydroxycarvomenthone NN-dimethylhydrazone
Cholest-4-en-3-one	(i) B ₂ H ₆ (ex situ) (ii) H ₂ O ₂ -NaOH	Cholest-4-en-3-one NN-dimethylhydrazone
Cholest-4-en-3-one	(i) <i>p</i> -nitroperbenzoic acid in chloroform, room temp. (1 equiv.) (ii) H ₂ O	Cholest-4-en-3-one
3 β -Acetoxypregn-5-en-20-one	(i) <i>p</i> -nitroperbenzoic acid (1 equiv.) (ii) H ₂ O	3 β -Acetoxypregn-5-en-20-one
3 β -Acetoxypregn-5-en-20-one	<i>p</i> -nitroperbenzoic acid (2 equiv.)	5,6 α -Epoxy-3 β -acetoxypregnan-20-one

Since compounds (IIb) are formed under slightly alkaline conditions, and can be converted into carbonyl compounds under neutral conditions, they may prove valuable alternatives to dioxolans, which require acidic conditions both for their formation and for their hydrolysis. To some

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