

Azoacetates as Synthons for the Azetidinone and Diazetidinone Ring Systems

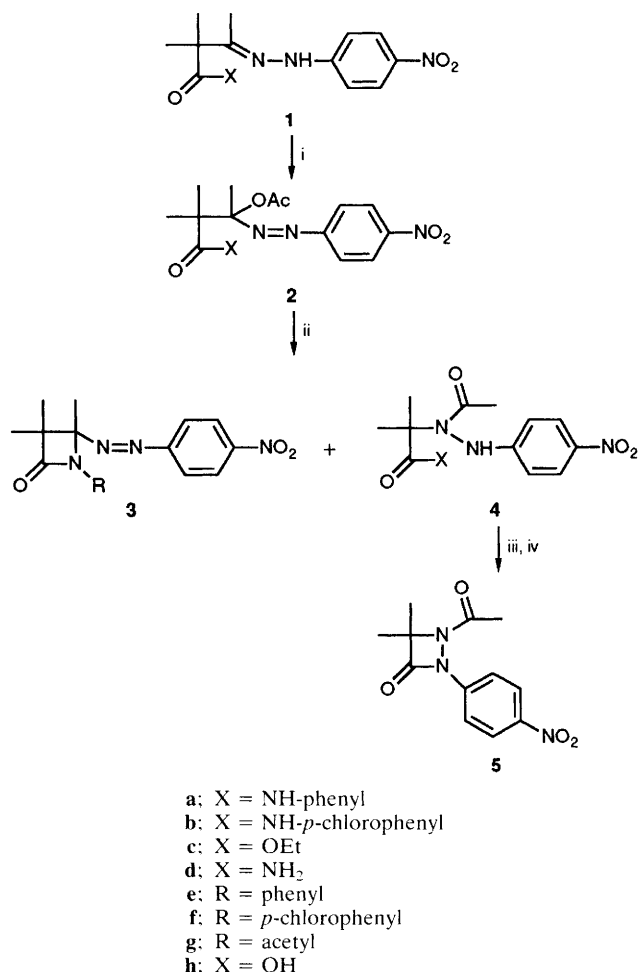
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The azoacetates derived from aryl hydrazones of α,α -disubstituted- β -ketoamides are readily transformed into azetidinones or diazetidinones.

Aryl hydrazones ($R^1R^2C=N-NH-Ar$) of ketones are in general readily transformed to azoacetates [$R^1R^2C(OAc)-N=N-Ar$] on treatment with lead tetraacetate (LTA), iodobenzene diacetate or thallium triacetate in solvents such as acetic acid and methylene chloride.^{1,2} Azoacetates **2** are

easily obtained by oxidation of aryl hydrazones **1** derived from β -keto compounds. Acyclic azoacetates have received relatively little attention as substrates for cyclisation to heterocycles with the exception of their transformation to five-membered heterocycles *e.g.* imidazoles and pyrazoles.³



Scheme 1 Reagents: i, lead tetraacetate, methylene chloride; ii, base, acetone or alcohol; iii, NaOH, H₂O; iv, DCC, MeCN

We now report an important contribution to the chemistry of azoacetates **2** which results in their cyclisation to four-membered rings **3** or **5** (see Table 1). Azoacetates **2a–d** are formed in high yield from the corresponding hydrazones **1a–d** and LTA in methylene chloride (>80%). Azoacetates of α,α -dimethylated- β -ketoamides **2a,b** cyclise to the azetidin-

Table 1

	Reagent	Product [yield (%)]
2a	K ₂ CO ₃ , acetone	3e (28)
2b	K ₂ CO ₃ , acetone	3f (50)
2a	KCN, propanol	3e (44), 4a (13)
2b	KCN, propanol	3f (34), 4b (44)
2b	KCN, ethanol	3f (48), 4b (25)
2c	KCN, ethanol	4c (30)
4a	H ⁺ , H ₂ O	4h (55)
4c	NaOH, H ₂ O	4h (80)
4h	DCC, MeCN ^a	5 (45)

^a DCC = 1,3-dicyclohexylcarbodiimide.

2-one ring **3e,f**, a β -lactam with unusual substitution. Acetylation of the primary amide **2d** allows cyclisation after base treatment to the lactam **3g**. When the reaction of **2a,b** with base is carried out in alcohol the β -lactam is accompanied by an unusual rearrangement product **4a,b**. The azoacetate **2c** derived from β -ketoester hydrazone **1c** gives an improved yield of the rearrangement product **4c**. The rearrangement is thought to follow deacetylation of the azoacetate. On hydrolysis, **4a–c** give the carboxylic acid **4h** which is readily cyclised to the 1,2-diazetidin-3-one **5**, and represents a new route to this ring system (see Scheme 1).⁴ In previous reports on base treatment of azoacetates the products are five-membered rings together with parent ketone and hydrazone.⁵

The generality of the reactions described and their extension to more appropriately substituted structural types is under investigation.

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