Azo Anions in Synthesis: α-Amino Carbanion Equivalents from t-Butyldiphenylmethylhydrazones

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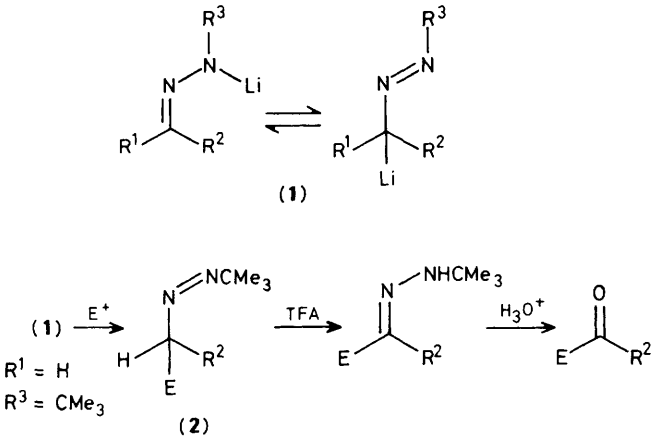
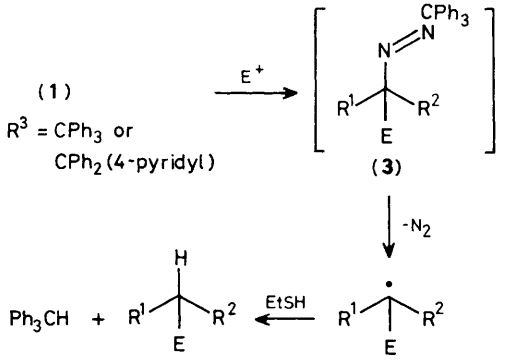
α-Amino carbanion equivalents ($>\bar{C}NH_2$) and α-hydrazino anion equivalents ($>\bar{C}NHNH_2$) are readily accessible from the C-alkylation products of t-butyldiphenylmethylhydrazones; these azoalkanes can be efficiently transformed into amines, hydrazines, and also alkanes under mild reaction conditions.

Recently we described the use of azo stabilized anions (**1**) for the synthesis of ketones,[1] acyloins,[1] alcohols,[2] alkanes,[2] alkenes,[2] and esters.[3] These products were derived by tautomerisation and hydrolysis (in the case of ketones or acyloins, Scheme 1) or *via* low temperature C-azo homolysis (in the case of alcohols, alkanes, or esters, Scheme 2) of the initial C-trapped azo products (**2**) and (**3**) respectively. However, these hindered azo products, (**2**) and (**3**), proved resistant to reductive cleavage to the amino compounds† thereby denying us access to a very general α-amino anion

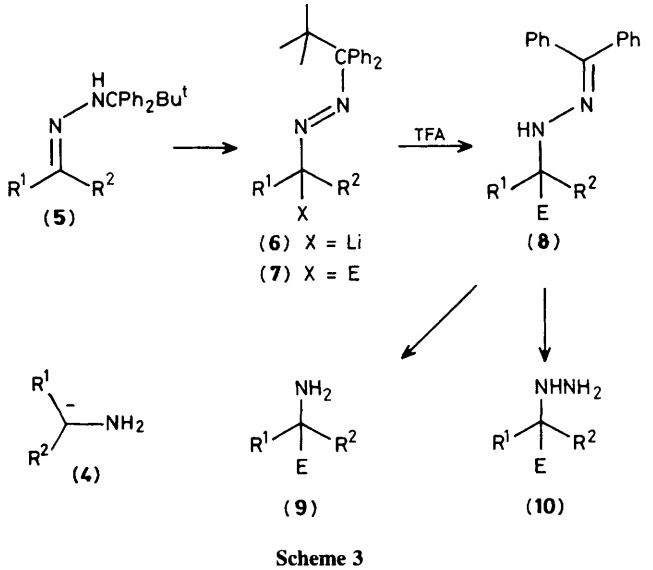
† Although reduction of the azo function to hydrazo species can be achieved,[6] the cleavage of *N,N'*-dialkylhydrazo species to amines has proved difficult. Such reductions are commonly achieved by high pressure catalytic hydrogenation methods[7] which are not compatible with sterically hindered azo products.



Scheme 1



Scheme 2



Scheme 3

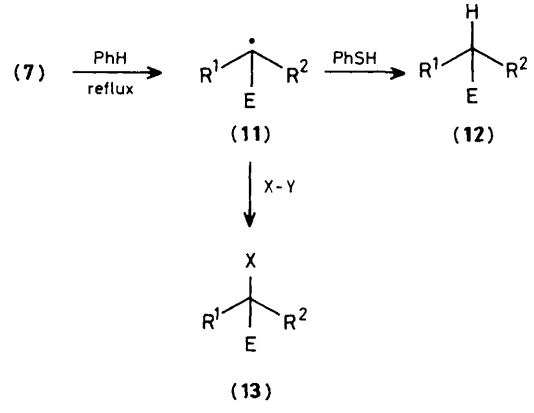
equivalent (**4**).[4] We have now found a simple solution to this problem by use of t-butyldiphenylmethylhydrazones (**5**) whose derived azo products (**7**) on treatment with acid [trifluoroacetic acid (TFA), 25 °C] gave the hydrazones (**8**) which we readily converted into primary amines (**9**) or hydrazines (**10**) (Scheme 3). Thus, azo anion (**6**) derived from

Table 1. Reaction of (**5**) with alkyl iodides and bromides (EX) to give azo compounds (**7**).

R^1	R^2	EX	Yield (**7**)/%
Me	H	n-$C_{10}H_{21}I$	95
Me	H	MeI	76
Me	H	$PhCH_2Br$	99
Me	H	n-C_4H_9I	89
Me	Me	MeI	84
Me	Me	$PhCH_2Br$	100
i-C_4H_9	H	n-$C_{10}H_{21}I$	79
i-C_4H_9	H	$BrC_5H_{10}Br$	89
i-C_4H_9	H	MeI	61
n-C_4H_9	H	$PhCH_2Br$	77
n-C_4H_9	H	n-$C_{10}H_{21}I$	70
$-[CH_2]_5-$		$PhCH_2Br$	100
$-[CH_2]_5-$		n-$C_7H_{15}I$	88
$-[CH_2]_{11}-$		$PhCH_2Br$	96
$-[CH_2]_{11}-$		n-C_4H_9I	97
$-[CH_2]_{11}-$		MeI	85

Table 2. Conversion of (**7**) into (**12**) using PhSH.

R^1	R^2	E	Yield of (**12**) [% from (**7**)]
Me	H	n-$C_{10}H_{21}$	94
i-C_4H_9	H	n-$C_{10}H_{21}$	84
n-C_4H_9	H	n-$C_{10}H_{21}$	93
$-[CH_2]_5-$		$PhCH_2$	71
$-[CH_2]_5-$		n-C_7H_{15}	64
$-[CH_2]_{11}-$		$PhCH_2$	78
$-[CH_2]_{11}-$		n-C_4H_9	72
$-[CH_2]_{11}-$		Me	87



Scheme 4

t-butyldiphenylmethylhydrazones (**5**)‡ reacted smoothly with alkyl iodides under standard conditions[1] to give the isolable C-trapped azo species (**7**) (Table 1). Noteworthy is the reaction with methyl iodide to give high yields (61—85%) of C-trapped azo products (**7**), whereas in the case of the less

‡ t-Butyldiphenylhydrazones (**5**) were prepared from t-butyldiphenylhydrazine by standard methods.[1] The hydrazine was prepared by treatment of ethyl pivalate with phenylmagnesium bromide (2.2 equiv.) to give t-butyldiphenylmethanol (70%) which was chlorinated ($SOCl_2$, $CHCl_3$, 1 h reflux) and treated with excess of hydrazine in refluxing dioxane (3.5 days). The hydrazine was isolated as its hydrochloride salt (69%), m.p. 144—148 °C.

Table 3. Formation of (**13**) from (**7**) using various trapping reagents X–Y.

R^1	R^2	E	X	XY	Yield of (**13**) [% from (**7**)]
Me	H	n-$C_{10}H_{21}$	PhSe	$(PhSe)_2$	77
$-[CH_2]_{11}-$		n-C_4H_9	PhSe	$(PhSe)_2$	54
Me	H	n-$C_{10}H_{21}$	Br	*N*-Bromosuccinimide	50
Me	H	n-$C_{10}H_{21}$	Cl	*N*-Chlorosuccinimide	50
Me	H	Me	*trans*-CH=CHPh	β-Nitrostyrene	48

Table 4. Formation of hydrazines (**10**) from (**7**).

R^1	R^2	E	Yield [% from (**7**)]	m.p./°C[a]
Me	H	Me	(**10**) 60	111—113
Me	H	$PhCH_2$	(**10**) 74	119—120.5
Me	Me	Me	(**8**) 80[b]	189—191
Me	Me	$PhCH_2$	(**10**) 25	137—139

[a] M.p.s are in agreement with literature values. [b] Hydrolysis of this hydrazone to t-butylhydrazine hydrochloride (60%) has been reported (ref. 5).

Table 5. Reduction of (**7**) to the amines (**9**).

R^1	R^2	E	Yield of (**9**) [% from (**7**)]	m.p./°C[a]
Me	Me	$PhCH_2$	67[b]	194—195
$-[CH_2]_5-$		$PhCH_2$	71[b]	288—289
$-[CH_2]_{11}-$		Me	38[b]	215—219
Me	H	$PhCH_2$	68[c]	167—171
Me	H	n-$C_{10}H_{21}$	68[b]	89—91

[a] M.p.s are in agreement with literature values. [b] Isolated as hydrochloride salt. [c] Isolated as oxalate salt.

hindered t-butylhydrazones, the N-methylation pathway was predominant.[1] The product (**7**) could be diverted to alkanes (**12**) and t-butyldiphenylmethane (Table 2, Scheme 4) *via* radical (**11**) by simple thermolysis in the presence of thiol [benzene, 2 h reflux, PhSH (>5 equiv.)] or alternatively (**11**) could be intercepted by alternative radical trapping reagents (X–Y) to products (**13**) (Table 3, Scheme 4).

The primary amines or hydrazines were accessible in a simple fashion. Thus, upon treatment with TFA at room temperature, the azo products (**7**) derived from both ketone and aldehyde t-butyldiphenylmethylhydrazones (**5**) underwent clean dealkylation to form benzophenone hydrazones (**8**). These hydrazones have been reported elsewhere[5] as readily converted into hydrazine products. Thus acidic hydrolysis (EtOH, conc. HCl, 25 °C, 15 h) of (**8**) gave good yields of secondary hydrazines and moderate yields of tertiary hydrazines (**10**)§ (Scheme 3, Table 4). Alternatively, in acid media, the hydrazones (**8**) could be catalytically reduced [EtOH, conc. HCl, 10% Pd–C, H_2 (1 atm), 50 °C] to the amines (**9**) (Table 5).¶

In summary, the t-butyl group serves to bias the electrophilic attack on (**6**) along the desired C-alkylation pathway at the same time as providing a labile functionality in the C-trapped azo product (**7**) which operationally provides efficient α-amino and α-hydrazino carbanion equivalents. The two step alkane synthesis *via* the isolated azo product (**7**) also represents a more convenient method than the low temperature route from tritylhydrazones previously described.[2]

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§ Tertiary hydrazines are reported to be labile to acidic conditions.[5]

¶ Diphenylmethane has been isolated as a by-product in this reaction. We have also shown that hydrazines (**10**) give amines (**9**) under these hydrogenation conditions. Thus it is probable that the reduction of (**8**) to the amine (**9**) proceeds *via* formation *in situ* of the hydrazine (**10**).

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