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Preparation and Reactions of 1-Lithio-oxy-1-lithio-amino-allene Derivatives

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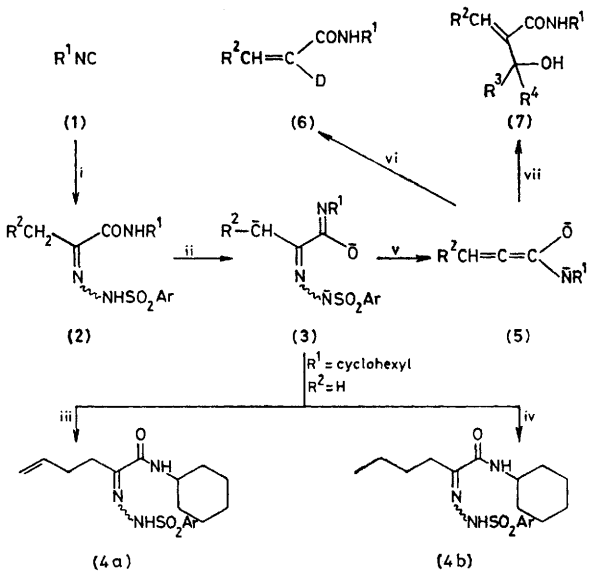
Summary The title compounds $Li^{+}_{2}[R^{2}CH{=}C{=}C(-\bar{O})\text{-}\bar{N}R^{1}]$, prepared from secondary α-keto-amides *via* the Shapiro reaction, reacted at C-2 with aldehydes, acetone, and deuterium oxide; the products $[R^{2}CH{=}C(CONHR^{1})\text{-}C(OH)R^{4}R^{5}]$ were intermediates for the synthesis of substituted 3-methylenetetrahydrofuran-2-ones.

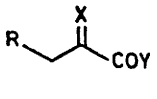
Recently we have demonstrated convenient applications of the Shapiro reaction to the synthesis of substituted 3-methylenetetrahydrofuran-2-one derivatives[1] and related systems.[2] Herein we report the preparation of the allenic dianions (**5**) and their application to the synthesis of diverse substituted acrylamide derivatives. Lithium [1-(ethoxycarbonyl)vinyl]hex-1-ynylcuprate, an ester equivalent of the dianion (**5**), has been described elsewhere.[3]

The secondary α-keto-amide 2,4,6-tri-isopropylphenylsulphonylhydrazones (**2**) were prepared in a 'one-pot' synthesis by the reaction of the isonitriles (**1**) with an acid chloride,[4] water, and 2,4,6-tri-isopropylphenylsulphonylhydrazine in sequence (Table and Scheme 1). Alternatively, for compounds (**2a**) and (**2c**), the α-keto-amides were purified before hydrazone formation. Ethyl pyruvate (**8b**) and 2-oxoheptanamide (**8d**)[5] were converted into their respective hydrazone derivatives (**8c**) and (**8e**).

The amide hydrazones (**2**) reacted with n-butyl-lithium, or lithium di-isopropylamide followed by n-butyl-lithium, in 1,2-dimethoxyethane to give the trianions (**3**) as orange solutions or suspensions. Efficient formation of the trianion (**3**, R^{1} = cyclohexyl, R^{2} = H) was consistent with *C*-allylation giving the hydrazone (**4a**) (70%). Generally, the trianions (**3**) were not efficiently alkylated. Formation of the hydroxy-hydrazone (**8a**), possibly *via* electron transfer and the azo-derivative (**9**), as a side reaction, was a complication.

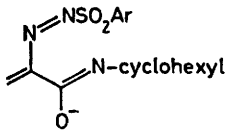


Scheme 1. Ar = 2,4,6-$Pr^{i}_{3}C_{6}H_{2}$. Reactions ii—vii were carried out in 1,2-dimethoxyethane. Products (**4**), (**6**), and (**7**) were isolated after quenching with $H_{2}O$ or neutralisation with acetic acid at −78 to −50 °C. i $R^{2}CH_{2}COCl$, $CH_{2}Cl_{2}$, heat; $H_{2}O$, tetrahydrofuran; $ArSO_{2}NHNH_{2}$; ii $Bu^{n}Li$ (3—5 equiv.), −78 °C; iii $CH_{2}{=}CHCH_{2}Br$, −78 to −65 °C; iv $Pr^{n}I$, −78 to −65 °C; v 25 °C; vi $D_{2}O$, −70 °C; vii $R^{3}COR^{4}$, −78 to −60 °C.

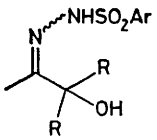


(8)

a; R = OH, X = $NNHSO_2Ar$, Y = NH-cyclohexyl
b; R = H, X = O, Y = OEt
c; R = H, X = $NNHSO_2Ar$, Y = OEt
d; R = Bu^n, X = O, Y = NH_2
e; R = Bu^n, X = $NNHSO_2Ar$, Y = NH_2
f; R = Bu^n, X = N_2, Y = NH_2



(9)

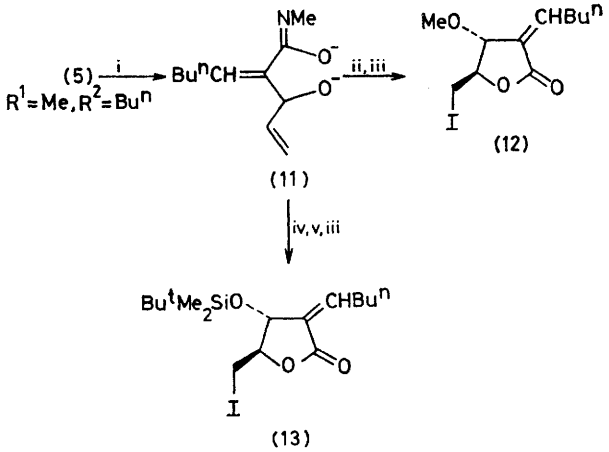


(10)

a; R = Bu^n
b; R = Bu^t

On warming to 25 °C, the orange colour due to the trianion (**3**) faded; sequential arenesulphinate and nitrogen elimination gave the allenic† dianions (**5**) as pale yellow suspensions. Addition of deuterium oxide, acetone, or aldehydes to these gave the expected acrylamide derivatives (**6**) and (**7**) (see Table and Scheme 1). Attention is drawn to the highly selective 1,2-addition of the dianion (**5**) to propenal. The geometric purity of the products was assigned on the basis of their n.m.r. spectra. By analogy[6–8] the reaction between the dianion (**5**) and (4*R*)-2,2-dimethyl-4-formyl-1,3-dioxolan[8] was assumed to be *erythro*-selective.

In contrast to the secondary amide-hydrazones (**2**), the hydrazone (**8c**) reacted with lithium di-isopropylamide and



(11) (12) (13)

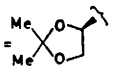
SCHEME 2. Reactions i and ii were carried out in 1,2-dimethoxyethane, and iii, iv, and v in tetrahydrofuran. i CH_2=CHCHO, −78 °C; ii MeI, 25 °C; iii I_2, H_2O, 25 °C; iv Bu^tMe_2SiCl, heat; v NaH, MeI, 25 °C.

TABLE. Yields of products in the reactions involving the dianion (**5**) (Schemes 1 and 2).[a]

Compound	R^1	R^2	% Yield	Compound	% Yield
(**2a**)	c-C_6H_{11}	H	93[b]	(**4a**)	70[b]
(**2b**)	"	Bu^n	85[b]	(**4b**)	38[b,c]
(**2c**)	"	n-$C_{13}H_{27}$	92[b]	(**8c**)	86[b]
(**2d**)	Me	H	55[b]	(**8e**)	95[b]
(**2e**)	"	Bu^n	91[b]	(*E*)-(**12**)	22[e,k]
(**2f**)	"	n-$C_{13}H_{27}$	65[b]	(*Z*)-(**12**)	10[e,k]
(**6a**)	c-C_6H_{11}	H	82[d]	(**13**)	54[h,l]
(*E*)-(**6b**)	"	Bu^n	62[d,e]		

Compound	R^1	R^2	R^3	R^4	% Yield
(**7a**)	c-C_6H_{11}	H	Me	Me	59
(**7b**)	"	H	H	H	59
(**7c**)	"	H	Et	"	80
(**7d**)	"	"	CH_2=CH	"	81
erythro-(**7e**) / *threo*-(**7e**)	"	"	Diox	"	46[f] / 14[f]
(*Z*)-(**7f**)	"	Bu^n	Me	Me	21[e,g]
(*Z*)-(**7g**)	"	"	CD_3	CD_3	38[e,g]
(**7h**)	"	"	CH_2=CH	H	51[h]
(**7i**)	Me	"	Et	"	64[h,i]
(**7j**)	Me	"	CH_2=CH	"	50[h,i]
(*Z*)-*erythro*-(**7k**) / (**7k**)	Me	"	Diox	"	21[e,f] / 13[j]

[a] All new compounds were fully characterised by microanalysis and spectral data except for (*E*)-(**12**) which, although not obtained microanalytically pure, exhibited the correct molecular ion in the high-resolution mass spectrum. [b] Hydrazone geometry undetermined. [c] Product accompanied by hydroxy-hydrazone (**8a**) (14%) and unchanged starting material. [d] *ca.* 100% deuterium incorporation by n.m.r. and mass spectroscopy. [e] Olefin geometry assigned using n.m.r. spectroscopy. [f] Relative configurations tentative. [g] Products accompanied by the acrylamide (**6b**) (24%) or the protio-analogue of (**6b**) (38%). [h] Mixture of geometric isomers not separated (*E* > *Z*). [i] Microanalysed as the *O*,*N*-dimethyl derivatives. [j] Contains the remaining three isomers, which were inseparable. [k] Yields based on the hydrazone (**2e**). [l] Yield based on the amide (**7j**).

c-C_6H_{11} = cyclohexyl Diox = 

† The anions (**5**) were assigned allenic structures since related ester systems have been shown to be allenic by their i.r. spectra providing the counter cation was lithium. These ester analogues were prepared by the conjugate addition to propynoate esters (J. Klein and R. Levene, *J. Chem. Soc., Perkin Trans.* 2, 1973, 1971).

n- or t-butyl-lithium in sequence to give the hydroxy-hydrazones (**10a**) and (**10b**) (32 and 31% respectively). Since the hydrazone (**8e**) reacted with excess of n-butyl-lithium to give only the α-diazo-amide (**8f**) (54%), C-H deprotonation could not have taken place.

Clearly, the Shapiro reaction provides the most convenient synthesis of the lithio-acrylate equivalents (**5**); α-bromo-αβ-unsaturated esters are thereby unnecessary. The acrylamides (**7**) are versatile intermediates. For example, the lactones (**12**) and (**13**) were readily prepared (Scheme 2 and Table). Application to the synthesis of 3-methyleneazetidin-2-one derivatives will be reported elsewhere.[7]

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