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COMPLEX BASES. XIV. USE OF SODAMIDE CONTAINING COMPLEX BASES AS VERSATILE, INEXPENSIVE REAGENTS TO GENERATE CARBANIONS

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Summary : It is shown that Complex Bases $NaNH_2$-RONa are very efficient in carbanion preparations and allow alkylation of imines, aldehydes, 1,3-dithianes, dithioketals as well as methylsulfenylation of ketones.

Generation of carbanions by proton abstraction with strong basic reagents in aprotic solvents continues to be of interest[1]. In this area, the most widespread bases used are lithium reagents and only a few sodium counterparts exist. Taking into account that organosodium derivatives may be preferred to those of lithium[2] it is clear that there is a lack of sodium basic reagents.

Some years ago, we discovered and developed the concept of bases synergy. The basic properties of sodamide may be strongly modified by sodium alkoxides, sodium ketone enolates as well as by inorganic salts[3]. The new bases thus obtained were called Complex Bases (abbreviated C.B.) and the results were extended to the activation of sodium hydride[4] and to lithium or potassium amides[3b,5].

C.B. have been used to perform elimination-additions, syn-eliminations as well as anionic polymerisations[5,6,7]. Concerning the generation of carbanions, we first showed that C.B. were able to abstract the proton from tri- and diphenylmethane[8] and from a few other substrates[5a,8b].

In the present paper we wish to describe some representative examples of the possibilities offered by C.B. The main results obtained have been summarized in the Table and they merit the following comments.

From experiments not reported, it appeared that from among the numerous alkoxides (activating agents) capable of activating sodamide[5a], the best are found among tertiary alkoxides and diethylene glycol monoalkyl ethers.

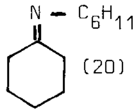
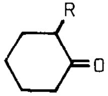
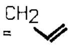
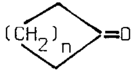
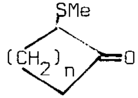
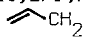
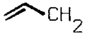
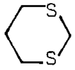
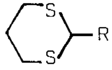
To obtain good results, excess of C.B. must be used. However it should be emphasized that, as observed with tri- or diphenylmethane[8], unreacted C.B. does not interfere with the carbanionic condensation even with base-sensitive electrophiles and the condensation selectively takes place with the generated carbanion.

Generally speaking the results obtained with C.B. compare favorably with those described with more sophisticated bases. Alkylation of thioketals or acetals and methylsulfenylation of ketones are particularly demonstrative if compared with literature data[2,9]. Indeed C.B. give comparable or better yields and allow simpler experimental conditions.

Finally, these reactions are very easy to perform as exemplified by the preparation of 2-methylthiocyclohexanone : To a mechanically stirred suspension of $NaNH_2$ (450 mmol) in THF (50 ml), under a nitrogen atmosphere, was added dropwise $Et(OCH_2CH_2)_2OH$ (150 mmol) in THF (20 ml) and the mixture was heated at 45°C for 2 h. Cyclohexanone (100 mmol) in THF (20 ml) was then added dropwise at room temperature and the mixture stirred for 2 h. After cooling to 0°C, dimethyl disulfide (100 mmol) in THF (10 ml) was slowly added (0.5 h) and the reaction was complete at the end of the addition. After classical work-up, the product was distilled at 85°C/7 mm (Lit.[9b] : 83-84°C/7 mm) to yield 12.98 g (90 %) of 2-methylthiocyclohexanone which had spectra identical with those reported elsewhere.

In conclusion, C.B. allow the generation of a number of carbanions associated with a sodium cation. Moreover, very easily prepared from commercial starting materials which are less sensitive to air and moisture and less expensive than lithium reagents, they allow large scale preparation.

Note that by removing the solvent from a C.B., Solid Complex Bases are obtained and may be kept as such under an inert atmosphere[3b,7a] or in an inert adjuvant such as mineral oil and used (after washing) by simple addition of a suitable solvent. C.B. may therefore be as easily handled as any water-sensitive solid reagent.

Substrate (mM)	Complex Base (mM of constituents)	Solvent (ml)	Preparation of carbanion T(°C)	t(h)	Condensed electrophile (mM)	Condensation temperature (°C)	Product (isolated yield %)
Pr-CH=N ⸺ C_6H_{11} (20)	$NaNH_2$-Et$(OCH_2CH_2)_2$ONa (60) (30)	THF (100)	50	3	Ph-CH_2Cl (20)	-30	Ph-CH_2-CH(Et)CHO (55)[a]
 (20)	$NaNH_2$-Bu^tONa or (60) (30) $NaNH_2$-R$(OCH_2CH_2)_2$ONa (60) (30) (R=Et,Bu)	THF (100)	60	5	Ph-CH_2Cl (20) CH_2=CH-CH_2Br (20)	-30 -35	 R=CH_2Ph (80)[a] Disubstituted (traces) R =  (85)[a] Disubstituted (traces)
Me_2CH-CHO (20)	$NaNH_2$-Bu^tONa (60) (30)	DME (100)	0	3	Ph-CH_2Br (20)	0	$Me_2C(CH_2$-Ph)CHO (85)
Me(Pr)CH-CHO (20)	$NaNH_2$-Bu^tONa (60) (30)	DME (100)	0	3	Ph-CH_2Br (20)	-10	MeC(CH_2-Ph)(Pr)CHO (84)
 n=2,3,4,5 (100)	$NaNH_2$-Et$(OCH_2CH_2)_2$ONa (300) (150)	THF (100)	0 (n=2) 25 (n=3,4,5)	2 2	Me-S-S-Me (100)	0-5	 n=2 (70) n=3 (90) n=4 (70) n=5 (86)
Et_2CO			25	2			Me(MeS)CH-CO-Et (70)
α-Tetralone			0	2			2-Methylthio-1-tetralone (80)
α-Benzosuberone (25)	$NaNH_2$-Et$(OCH_2CH_2)_2$ONa (75) (37.5)	THF (50)	25	2	Me-S-S-Me (25)		2-Methylthio-1-benzosuberone (72)
$C_6H_5CH(SEt)_2$ (20)	$NaNH_2$-Et$(OCH_2CH_2)_2$ONa (60) (30)	THF(50) or DME(50)	25	2	MeI (40)	0	Me$(C_6H_5)C(SEt)_2$ (80-85)
		DME(50)	25	2	RBr (40) R=Et,iPr,PhCH_2, 	0	$C_6H_5(R)C(SEt)_2$ R=Et (76); iPr (82); PhCH_2 (86);  (76)
$CH_2(SEt)_2$ (20)	$NaNH_2$-Et$(OCH_2CH_2)_2$ONa (120) (60)	DME (50)	25	3	MeI (40)	0	$MeCH(SEt)_2$ (70)[b]
			25	5	C_6H_{13}Br (40)	0	$(C_6H_{13})CH(SEt)_2$ (86)
 (20)	$NaNH_2$-Et$(OCH_2CH_2)_2$ONa (80) (40)	DME (50)	25	3	RBr (40) R=Et,C_6H_{13}	0	 R=Et (82); C_6H_{13} (86)

a) After hydrolysis
b) In mixture with 10 % of unreacted starting material (ratio determined by ^{1}H NMR).

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