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ULTRASOUND IN ORGANIC SYNTHESIS 15[1]. RADICAL CYCLISATION OF O-ALLYL BENZAMIDES VIA THE SONOCHEMICALLY GENERATED RADICAL ANIONS

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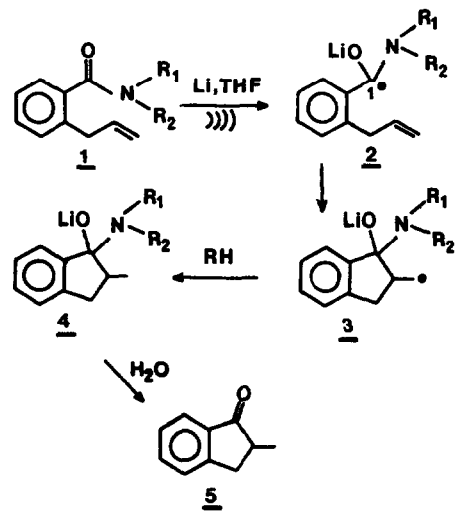
Abstract : By reaction with lithium metal in THF under sonochemical activation, o-allyl tertiary benzamides are easily cyclised to 2-methyl-indanone. Yields strongly depend on the substitution pattern of the nitrogen atom.

Synthetic methods based on carbon-carbon bond formation by radical pathways are of increasing importance in organic chemistry[2]. In the most general case, free radical chain processes are involved, requiring a catalytic initiation step. The less common reactions involving radical anions have been studied e.g. in the case of ketyl radical anions produced by electroreduction[3], dissolving metal reduction[4-6] or photochemically induced electron transfer[7]. While trying to extend Bouveault type sonochemical reactions, we noticed that delocalised radical anions are very efficiently formed from tertiary benzamides and alkali metals in etheral solvents, under ultrasound activation. Such species which have already been prepared by electroreduction and studied by EPR[8] appear to be valuable synthetic intermediates and we describe now a new radical cyclisation of o-allyl benzamides, summarized in the following scheme.

Table

Entry	$N\begin{smallmatrix}R^1\\R^2\end{smallmatrix}$	Sonication time (min)[a]	yield of 5[b]%
1	$N(CH_3)_2$	10	25
2	$N(C_2H_5)_2$	15	34
3	$N(i\text{-}C_3H_7)_2$	15	60.
4	$N(CH_3)(t\text{-}C_4H_9)$	10	95(84)[c]

[a]Given for optimal yields. [b]Determined by GC with n-tetradecane as standard. [c] Isolated yield in parentheses.



The results shown in the table indicate that the yield of 2-methyl indanone 5 depends highly on the nature of the substituents R^1 and R^2 on the nitrogen atom, as it increases along the

sequence $R^1=R^2=CH_3$, $R^1=R^2=C_2H_5$, $R^1=R^2=iC_3H_7$. This observation, in a first approach, seems to be correlated with the spin density on the primarily formed radical anion 2 (scheme). Analogously, spin densities at C-1 on the ortho unsubstituted benzamides, determined by EPR studies[8] of the delocalized radical anions follow the same sequence.

Steric crowding, which increases in the same order, becomes unfavorable to cyclisation only in the case of very congested amides as 2,2,6,6-tetramethyl-piperidide and no methyl-indanone is obtained. An optimum substitution is reached with $R^1=tC_4H_9$, $R^2=CH_3$ (table) which gives an excellent yield of 5. Other substituents ($R^1=CH_3$, $R^2=C_6H_5, CH_2C_6H_5$) are much less effective.

Few other products of low molecular weight are formed in this reaction : traces of o-allyl benzaldehyde and minor amounts of 1-tetralone formed by 6-endo trig[9] radical cyclisation. 1-Naphthol may also be present, especially for $R^1R^2=(CH_2)_4$ (yield up to 90%). It should result from an ionic reaction pathway as recently described by Snieckus at al[10]. Besides these identified by-products, variable amounts of highly polar polymeric material are formed in each case, corresponding to the material balance.

The reaction is carried out in a common laboratory ultrasonic cleaner or, preferably, in the reactor described previously[11], using 1 mmole of o-allyl amide, in 30 ml of anhydrous THF under argon, and excess lithium, at -20°C. The reaction was monitored by GC (SE 30 column, 10% on Chromosorb) and TLC. The mixture is hydrolysed (aq. NH_4Cl) and worked up as usual. Without ultrasound the reaction starts after erratic induction periods and proceeds slowly, giving very poor yields of cyclisation products and larger amounts of oligomeric material.

The chemical evolution of radical anions derived from aldehydes, ketones and esters has been the subject of many studies[12], but only a few studies with no synthetic applications have been developed in the case of amides.

The cyclisation reaction described here may offer, coupled with ortho allylation of benzamides[13], a fast and regiospecific access to 1-indanones, some of them being of biological interest[14]. The scope and limitations of this reaction such as the possible extensions to other types of radical anions are currently under study.

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