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Homologation of Carboxylic Acids by Arndt-Eistert Reaction under Ultrasonic waves

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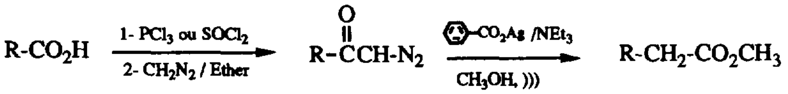
Abstract: The use of ultrasonic activation in the Arndt-Eistert reaction leads rapidly, in good yields, to the expected compounds at room temperature.

The Arndt-Eistert synthesis is a procedure for converting a carboxylic acid to its higher homolog or to a derivative of the homologous acid, such as an ester or amide[1]. It consists in the formation of an α-diazomethylketone which is converted into derivatives of an acid in the presence of solid silver oxide or silver benzoate in solution as a catalyst. This last step is known as the Wolff rearrangement.

Two methods can be used for this rearrangement [2]:

- Heterogeneous conditions, using a suspension of silver oxide in methanol, have proved to be somewhat erratic [3,4].

- On the other hand, homogeneous conditions, involving silver benzoate solubilized in triethylamine, give reproductible results [5]. However these two methods are relatively time consuming (3 or 5 hours) and carried out at 70-80°C. In this paper, we report a procedure by which the rearrangement may be carried out rapidly at room temperature. The novelty of this method lies in the use of ultrasonic waves[6] in a homogeneous medium [7]. (Scheme 1)



$$R\text{-}CO_2H \xrightarrow[\text{2- }CH_2N_2\text{ / Ether}]{\text{1- }PCl_3\text{ ou }SOCl_2} R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}CH\text{-}N_2 \xrightarrow[CH_3OH,\ )))]{C_6H_5\text{-}CO_2Ag\ /NEt_3} R\text{-}CH_2\text{-}CO_2CH_3$$

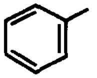
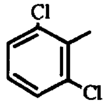
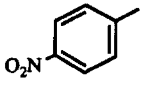
Scheme 1

These conditions have been applied to benzoic acid, 2,6-dichlorobenzoic acid, p-nitrobenzoic acid, palmitoic acid and decanoic acid.

The structure of the diazomethylketones is in accord with its infrared and ^1H NMR spectra.

The results of the second step are summed-up in Table 1.

Table 1 - Arndt-Eistert reaction under ultrasonic activation.

R	Yield %	Time reaction (min)	Temperature °C	^{1}H NMR ppm δ (OCH$_3$)	MS m/z (M+H)$^+$
	92 (88)[5]	2 (120)	RT (65)	3.7	151
	75	2	RT	3.6	226
	15 (no reaction)[5]	10	RT	3.8	-
$C_{15}H_{31}$-	90 (81)[8]	1(>60)	RT (180)	3.6	285
C_9H_{19}-	85	1.5	RT	3.6	201

The values in parenthesis are dealing with conventional thermal rearrangement found in the literature. RT: room temperature.

As it can be observed, the reaction times are always relatively short (less than ten minutes) and the yields are similar or higher than those mentioned in litterature.

In view of the conditions (room temperature and short reaction times), this method could be useful for fragile substrates.

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7- General procedure: A solution of 1g of silver benzoate in 9.1g of triethylamine was prepared and filtered to remove small amount of precipitate. The diazomethylketone (100 mg) is dissolved in 10 mL of anhydrous methanol. 1 mL of silver benzoate solution is added. The mixture was then allowed to react under sonication The rise in temperature due to the ultrasonic activation did not exceed 8°C.(Ultrasonic equipment: vibra-cell 600W, maximal power used: 360 W, reactor volume: 100 mL, sounding line diameter: 13 mm high intensity). The reaction is monitored by TLC. After filtration and concentration, the residue is purified by column chromatography (silica).

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