Tetrahedron Letters No. 46, pp 4573 - 4574.
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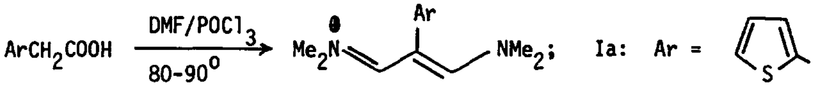
0040-4039/78/1108-4573$02.00/0

SYNTHESIS OF A 1,3-DICARBONYL EQUIVALENT VIA VILSMEIER FORMYLATION OF α-ENAMINO ESTERS

S. Liljefors* and A. Hallberg
Division of Organic Chemistry 1, Chemical Center
University of Lund
P.O. Box 740, S-22007 Lund 7, Sweden

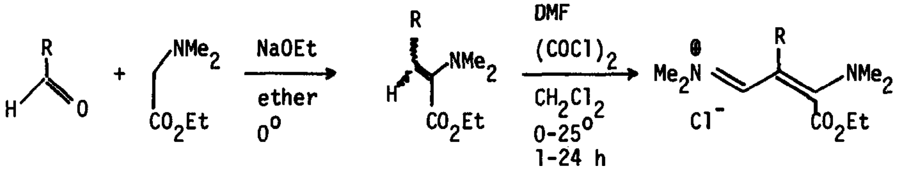
Vilsmeier formylation of arylacetic acids is an excellent method for the preparation of 2-aryl-substituted vinamidinium salts (I) (1) - important intermediates for the synthesis of aromatic and heteroaromatic compounds (2).



I

However, when applied to 2-thiopheneacetic acid, this reaction gives no yield of the corresponding vinamidinium salt Ia due to ring-formylation (3).

Searching for an alternative route to compounds of type I, we have found that α-enamino esters (II) - easily prepared from aldehydes and N,N-dimethylglycine ethyl ester (4) - smoothly undergo Vilsmeier formylation under very mild conditions (5) giving carbethoxy-substituted vinamidinium salts (III).



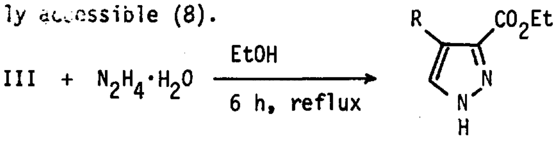
II III

For different R, see Scheme below.

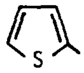
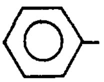
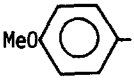
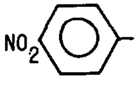
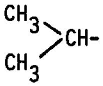
The crude product obtained after evaporation of the solvent consists of a red viscous oil, which besides III also contains an equimolar amount of hydrogen chloride. At present, we have no effective way of isolating III in a pure state. Aqueous work-up leads to hydrolysis of III. Attempts to prepare crystalline perchlorates (6) have not been successful.

However, the NMR ($CDCl_3$) spectrum of the crude product is in accordance with the proposed structure. For example, III (R = C_6H_5) gives: δ 8.65 (N=CH, s, 1H), 7.50-7.06 (C_6H_5, m, 5H), 4.03 (CH_2, q, 2H), 3.73 (NCH_3, s, 3H), 3.55 ($N(CH_3)_2$, s, 6H), 2.71 (NCH_3, s, 3H), 0.98 (CCH_3, t, 3H).

For a preliminary evaluation of the synthetic utility of III, we have reacted (7) the crude product of III with hydrazine hydrate to give pyrazoles (IV), which are otherwise not readily accessible (8).



IV

R					
M.p. °C	156-7	164-5	167-8	217-20	80-82
M.p. °C (Lit.)		162 (9)		219-221 (10)	
Yield %	58	64	60	18	42

Yields are calculated as overall yields from II to IV. All examples of IV give NMR, IR and MS spectra in accordance with the proposed structures.

The authors wish to express their sincere thanks to Professor Salo Gronowitz for his valuable criticism and kind interest in this work.

NOTES AND REFERENCES

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2. For review: LLOYD, D. and MCNAB, H., Angew. Chem. 88, 496 (1976) and JUTZ, C., Topics in Current Chemistry Vol. 73, p. 125 (1978).
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5. Oxalyl chloride (10 mmol) is added drop-wise to a solution of N,N-dimethylformamide (10 mmol) in dichloromethane (15 ml) at 0°. The white slurry formed is stirred at room temperature for 15 min and then cooled to 0°. II (10 mmol) in dichloromethane (3 ml) is added during 5 min whereby the white precipitate disappears. The mixture is then left without cooling for 1 h. Evaporation of solvent gives crude III.

   In the case of R = $(CH_3)_3CH$-, the reaction of II is very slow at 0° and was instead performed at 25° for 24 h.
6. Procedures used were analogous to JUTZ, C. and SCHWEIGER, E., Chem. Ber. 107, 2391 (1974).
7. Crude III (5 mmol) and hydrazine hydrate (5.5 mmol) were dissolved in abs. ethanol (100 ml). After reflux for 6 h and evaporation of solvent, the residue obtained was taken up in water. The dichloromethane extract of this mixture was washed (H_2O), dried ($MgSO_4$) and evaporated. From the residue, IV was isolated by column chromatography on silica gel/CH_2Cl_2,EtOAc.
8. Compare for example refs. 9 and 10 and BASTIDE, J. and LEMATRE, J., Bull. Soc. Chim. France 3543 (1970).
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(Received in UK 13 September 1978)