Regioselective Aluminium Chloride-catalysed Reactions of Acetylenic Esters with 2-Bromothiazole

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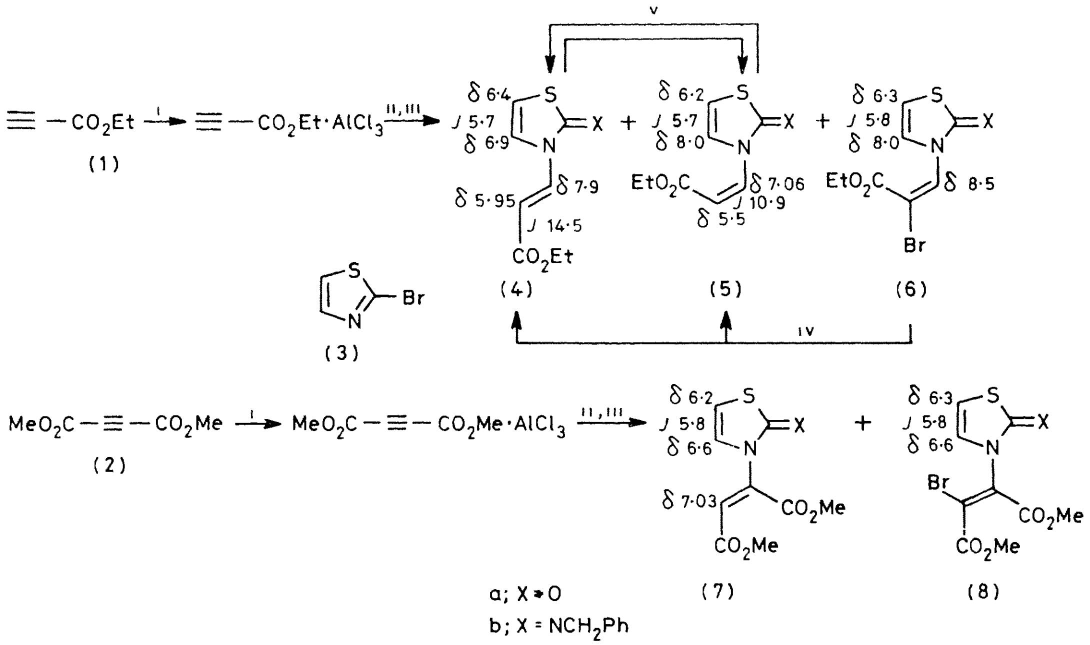
Summary Ethyl propiolate and dimethyl acetylenedicarboxylate activated by $AlCl_3$ react with 2-bromothiazole to give, after quenching with aqueous $NaHCO_3$ or $PhCH_2NH_2$, *N*-vinylthiazolin-2-ones and 2-benzylimino-*N*-vinylthiazolines respectively.

Lewis acids have been reported to promote thermal [2 + 2] cycloadditions and ene reactions of acetylenic esters with unactivated alkenes.[1] We now describe the aluminium chloride-activated additions of ethyl propiolate (**1**) and dimethyl acetylenedicarboxylate (DMAD) (**2**) to 2-bromothiazole (**3**) to give open-chain 1 : 1 adducts *via* regioselective attack by the triple bond carbon, β in the case of (**1**), at the nitrogen of the thiazole ring. In the absence of $AlCl_3$, the acetylene (**1**) was practically inert towards various thiazoles, including (**3**), and DMAD is known to require drastic conditions to give mixtures of 2 : 1 adducts.[2]



Scheme. i, 1 equiv. of $AlCl_3$; ii, 1 equiv. of (**3**); iii, aq. $NaHCO_3$ (for X = O), or 3 equiv. of $PhCH_2NH_2$ (for X = NCH_2Ph); iv, Bu_3SnH, tetrahydrofuran, room temp.; v, 0·005 M, *hν* (3000 Å), CH_2Cl_2.

Slow addition (2 h) of the ethyl propiolate–$AlCl_3$ complex† in ethyl ether (100 ml) to 1 equiv. of 2-bromothiazole (**3**) in the same solvent (100 ml) at room temperature with vigorous stirring for 60 h, followed by aqueous work-up, filtration through Celite, and extraction with ether, gave a mixture‡ (*ca.* 50% yield) of *N*-vinylthiazolin-2-ones (**4a**), m.p. 93—95 °C, (**5a**), m.p. 42—44 °C, and (**6a**), m.p. 64—66 °C in a 5 : 1 : 0·14 ratio (Scheme). Reactions in benzene or methylene dichloride were faster, taking 4—5 h at room temperature, but gave lower yields and irreproducible ratios of the products. The configuration about the *N*-vinyl group of (**4a**) and (**5a**) was assigned on the basis of the ^{1}H n.m.r. ($CDCl_3$) coupling constants between the corresponding vicinal protons, whereas the conformation about the N–C (vinyl) single bond was inferred from the low-field resonance of 4-H in (**5a**) and (**6a**) which can be attributed to deshielding by the carbonyl of the β-ethoxycarbonyl group. That compounds (**4a**) and (**5a**) are (*E*)- and (*Z*)-isomers was confirmed by the photochemical conversion of one into the other,§ while the ready debromination of (**6a**) by Bu_3SnH to both (**4a**) and (**5a**) supports the close structural relation between these products. Compounds (**4a**), (**5a**), and (**6a**) were stable in the presence of $AlCl_3$ (ether, 4 days).

Quenching the mixture from the reaction between the ethyl propiolate–$AlCl_3$ complex and the thiazole (**3**) with 3

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† Prepared from the acetylene (5 mmol) and $AlCl_3$ in 1 : 1 ratio (ref. 1b).

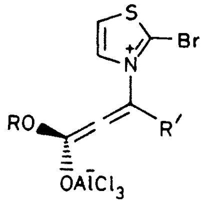
‡ Yields calculated with respect to 2-bromothiazole (**3**). All new compounds gave satisfactory elemental analyses and their mass spectra showed the molecular ion. N.m.r. data in the Scheme refer to compounds (**4a**), (**5a**), (**6a**), (**7a**), and (**8a**).

§ Irradiation (4 h) of either (**4a**) or (**5a**) produced mixtures where the (*E*)-isomer [(**4a**)] prevailed over the (*Z*)-[(**5a**)].

equiv of benzylamine gave (40% yield) the 2-benzylimino-(*E*)-*N*-vinylthiazoline (**4b**), m p 64—66 °C [J_{HH} (*N*-vinyl) 14·8 Hz, δ 6·8 (4-H)] and the bromovinyl derivative (**6b**), m p 68—71 °C, [δ 7·97 (4-H)] in a 36 : 1 ratio The formation of the (*Z*)-isomer (**5b**) could not be detected in this reaction

Further, the DMAD–$AlCl_3$ complex, prepared in the same way as the corresponding ethyl propiolate complex, reacted with the thiazole (**3**) in ether at room temperature over 48 h to give (*ca* 50% yield) after quenching with aqueous $NaHCO_3$ the (*E*)-*N*-vinylthiazolin-2-one (**7a**) (oil) and the bromo derivative (**8a**), m p 90—91 °C in a 10 : 1 ratio, whose stereochemistries were assigned on the basis of ^1H n m r spectra (Scheme) Quenching with $PhCH_2NH_2$ did not afford the expected 2-benzylimino-derivatives (**7b**) and (**8b**) but gave back 2-bromothiazole (**3**) and tarry material

Regioselective nucleophilic attack by the thiazole (**3**) at the β-carbon of the complexes resulting from co-ordination[1] of $AlCl_3$ with the ester group of acetylenes (**1**) and (**2**) may be envisaged This would produce the zwitterion (**9**) as an intermediate which, by substitution of bromine by water or benzylamine accompanied by removal of $AlCl_3$ from the ester group and protonation, would lead to the *N*-vinylthiazolines (**4**), (**5**), and (**7**) The allenic structure of the zwitterion (**9**), which appears particularly favoured owing to co-ordination of the carbonyl with $AlCl_3$, accounts for the preferential *cis* addition[3] by the thiazole (**3**) and proton to the $AlCl_3$–acetylene complexes to give prevailing or exclusive formation of (*E*)-isomers (**4**) and (**7**) On the other hand, the mechanism of formation of the bromovinyl derivatives (**6**) and (**8**) is at present unclear



(9)

R = Me, Et

R′ = H, CO_2Me

The synthetic value of the sequences in the Scheme, whose key step is the activation of the acetylenic esters by $AlCl_3$, is evident since it affords stereoselectively *N*-vinylthiazolines which are synthetic intermediates hitherto unknown and probably not readily accessible by other routes

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