THE REACTION OF 1-PHENYLMETHYL-4N-ACETYLIMINO-1*H*-1,2,4-TRIAZOLIUM BETAIN WITH BUTYNEDIOIC ACID DIMETHYL ESTER

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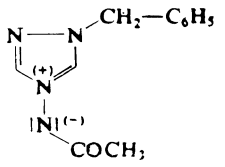
The reaction between 1-phenylmethyl-4N-acetylimino-1*H*-1,2,4-triazolium betain(I) and dimethyl butynedioate is described. By performing the reaction at ration 1 : 1 the enamide *III* is formed. With a fivefold excess of the dipolarophile, except *III*, also pyrrolo[1,2-*d*]-triazole *XII* and pyridine derivative *XV* were obtained.

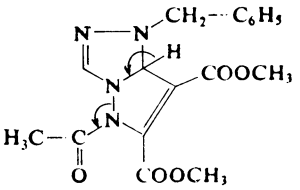
Although the behaviour of azomethine ylides, especially heterocyclic ones, in cycloaddition and cyclization reactions is well known[1-3] their reactions with acetylenic dipolarophiles with their plethora of addition and cyclization modes still offer new possibilities[4]. In view of our previous finding[5] that 1-phenylmethyl-4N-acetylimino-1*H*-1,2,4-triazolium betain (*I*) can undergo a cyclization reaction in its extended form of 1,5-dipole[6], we explored its reactions with butynedioic acid dimethyl ester in polar and nonpolar solvents. Besides well known mechanisms, such as Michael addition, [2 + 2] addition, 1,3-dipolar cycloaddition[4], we expected products also of extended 1,5-dipole.

When equimolar amounts of dimethyl butynedioate and the betain *I* were solved in toluene and kept at 40°C for 15 h, rather complex reaction mixture resulted, containing besides unreacted starting material and polymers enamide *III* as the main product. The structure of *III* has long been ambiguous. Since its IR spectrum showed bands corresponding to amide group the product of extended dipole was excluded. There still remained, however, alternatives to choose from. ^{1}H NMR spectrum of *III* shows two singlets at low field which can be interpreted as triazole protons (11·06 and 8·15δ). This seemed at first to support the linear Michael adduct structure *IV* (ref.[8]). This adduct, although a zwitterion, refused to behave appropriately. Attempts to convert it to salts using acetic acid, HBF_4, or CF_3COOH or to cyclize it thermally or photochemically failed. The only change observed was its conversion to enamine *V* upon heating or irradiation in methanol. *V* can be regarded as a solvolysis product of enamide *III*, suggesting that the primary product of the reaction between *I* and dimethyl butylenedioate is in fact a cycloadduct *II* (Scheme 1) which, being unstable, rearomatizes in a known manner[4] to *III*.

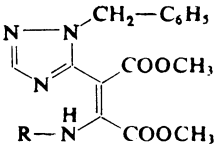
Spectral data not being conclusive, we tried to substitute dimethyl butynedioate with its synthon – acetylene masked as its adduct with furan, dimethoxycarbonyloxabicycloheptadien[7]. Indeed, by reaction with *I* at room temperature the cycloadduct *VI* has been obtained. By performing the reaction at 110°C or heating of *VI*,



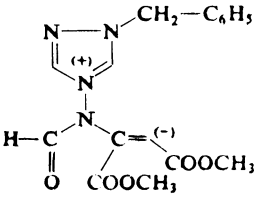
I



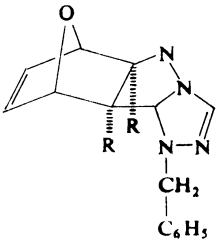
II



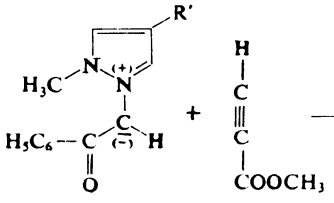
III, R = CH_3CO
V, R = H



IV

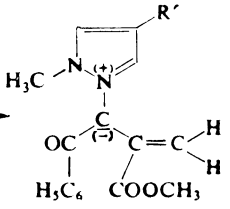


VI, R = $COOCH_3$



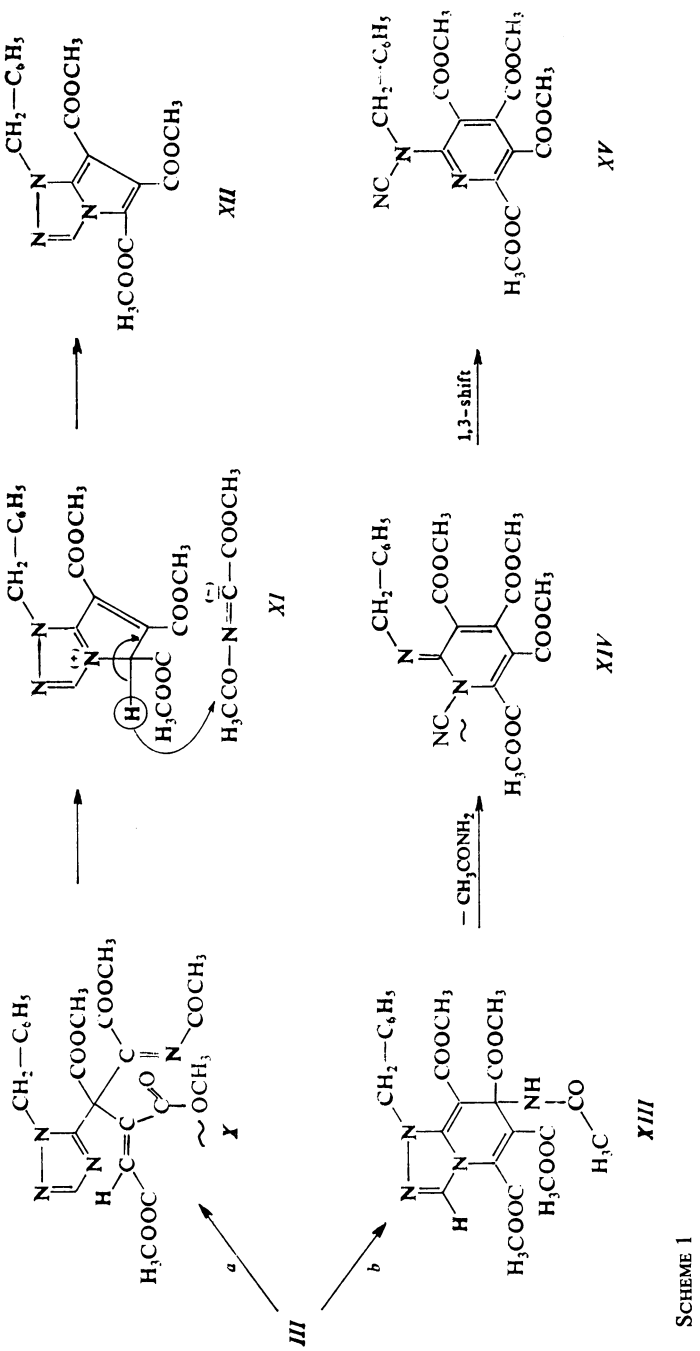
VII

VIII



IX

at this temperature the *III* has unambiguously been found[7]. Though these experiments clinched the second alternative, explaining the origin and the structure of *III*, there still remained the singlet at 11δ in the ^{1}H NMR spectrum of *III* to be accounted for. By coincidence it is found in the region, where normally the signal of H_5 proton of the starting betain is located. Moreover, the singlet at 11δ could not be moved either by addition of ^2H_2O, acid or by heating the sample, making its amidic character hard to believe. The only reasonable interpretation compatible with the structure *III* seems to be the assumption of strong intramolecular hydrogen bonding between the amidic NH and a carbonyl group of the nearest ester group.



SCHEME 1

The reason why linear Michael adduct did not form is probably the absence of hydrogen on the terminal nitrogen atom of the imine. In that case Michael adducts can be stabilized by hydrogen shift as in the pyrazolium ylid *IX* (ref.[8,9]).

Enamide *III* was found to be the main product of the reaction between *I* and dimethyl butynedioate when used in 1 : 1 ratio in benzene, toluene, dimethylformamide, in methanol enamine *V* resulted. The yields ranged from 6–72%. When fivefold excess of dimethyl butynedioate was used, besides forming *III*, the betain *I* added subsequently two molecules of acetylene derivative, giving rise to pyrrolo[1,2-*d*]-triazole (*XII*) and phenylmethyl-2-[3,4,5,6-tetramethoxycarbonyl]cyanamide (*XV*). The structure elucidation was based on spectral data. Mass spectrum of *XII*, showed $M^{+\bullet}$ peak at *m/z* 371, indicating that it is neither 1 : 1, nor 1 : 2 adduct. The precise mass of $M^{+\bullet}$ measured 271·1117 alowing us to calculate the molecular formula $C_{18}H_{17}N_3O_6$. Combined with the ^{1}H NMR spectrum showing a singlet at 8·57δ (H_3), aromatic multiplet, singlet for methylene at 5·9δ and three methyl singlets at around 3·9δ, one could put the structure of *XII* together.

To rationalize the origin of this unexpected structure one has to assume stepwise addition of the two molecules of dimethyl butynedioate, the first one in 1,3-dipolar cycloaddition manner, followed by the N–N bond cleavage to give *III*. In the second step enamide *III* acts as a nucleophile adding to the triple bond of acetylenic ester giving *X* (path *a*, Scheme 1). Zwitterion *X* cyclizes under expulsion of anionic fragment $H_3COOC—C=N—COCH_3$ which helps in its turn to aromatize the molecule by hydrogen abstraction.

The pyridine derivative *XV* on the other hand with its $M^{+\cdot}$ peak at *m/z* 441 was clearly an 1 : 2 adduct. Its ^{1}H NMR spectrum displayed besides aromatic multiplet only singlets for the methylene and methyl groups. IR spectrum showed strong cyano peak at 2 200 cm^{-1}. *XV* can be seen to arise from the Diels–Alder addition of dimethyl butynedioate and enamide *III*, followed by ring opening of the triazole, expulsion of acetamide molecule and 1,3- shift of the cyano group to furnish pyridine derivative (path *b*, Scheme 1). This mechanism is supported by the fact that acetamide was found in the reaction mixture, as well as by independent experiments aimed at production of *XV* from *III* and dimethyl butynedioate.

In conclusion, our assumption about the participation of the 1,5-dipolar structure of 1-phenylmethyl-4N-acetylimino-1*H*-1,2,4-triazolium betain in the reaction with dimethyl butynedioate has not been validated. By far the most reactive moiety of the betain seems to be the azomethine imine, despite the fact that it is a part of the aromatic ring. In contrast to the reactions of *I* with heterocumulenes[5] dimethyl butynedioate, being more reactive and less selective reagent, does not form products from 1,5-dipole stable enough to be identified.

EXPERIMENTAL

All melting points are uncorrected, determined on Kofler hot stage. Infrared spectra were taken on UR-20 Zeiss Jena in chloroform. ^{1}H NMR spectra were obtained on a 80 MHz Tesla BS 487 C with tetramethylsilane as internal standard. ^{13}C NMR spectra were measured on a JEOL FX-100 in deuteriochloroform with tetramethylsilane as internal standard. High resolution mass spectra were obtained on AEI 902 S spectrometer (70 eV). All solvents were dried and distilled before use. N,N-dimethylformamide was distilled from phosphorus pentoxide. In experiments carried out above the boiling point of the solvent thick-walled glass reactors with magnetic stirrer were used. For TLC, home-made 20 × 20 plates, coated with 2 mm layer of silica gel containing fluorescent indicator were used.

Reactions of *I* with Dimethyl Butynedioate

a) Equimolar amounts of *I* (3 g, 13·8 mmol) and dimethyl butynedioate (2 g, 13·8 mmol) in 150 ml of toluene were heated to 40°C for 15 h. Shortly after the addition of ester the solution turned orange, later red. In the course of reaction the betain gradually dissolved. The concentrated mixture was separated using preparative TLC (cyclohexane–ethyl acetate 5 : 1) using one plate loaded with 100 mg. The rest of the mixture was put on the silica gel column. TLC yielded 230 mg (4·6%) of *III*, m.p. 129–130°C, ref.[7] m.p. 129–130°C.

b) the reaction of *I* with fivefold excess of dimethyl butynedioate, reaction conditions as in the preceding example gave compound *XII*, m.p. 148–149°C, yield 11%. For $C_{18}H_{17}N_3O_6$ (371·1) calculated: 58·20% C, 11·31% N, 4·58% H; found: 58·32% C, 11·22% N, 4·68% H. IR spectrum: 1 670, 1 700 1 725 (s) cm^{-1}. ^{13}C NMR spectrum: 164·1, 162·5, 159·7δ (ester carbonyl) 54·1δ (methylene), 52·9, 52,1, 51·7δ (ester methyl groups). Mass spectrum: $M^{+\cdot}$ measured 371·1117, calculated for $C_{18}H_{17}N_3O_6$ 371·1117, *m/z* 312 $M^{+\cdot}-\dot{C}OOCH_3$, *m/z* 253 312–$\dot{C}OOCH_3$. Further compound *XV* was isolated in 7% yield, m.p. 102–103°C. For $C_{18}H_{17}N_3O_6$ (351·1) calculated: 57·14% C, 4·31% H, 9·52% N; found: 57·24% C, 4·21% H, 9·57% N. IR spectrum (KBr): 1 720 (s), 2 200 (m) cm^{-1}. 1^1 NMR spectrum: 5·15δ (2 H, s), 3·93δ, 4·03δ (12 H, s, s).

c) The reaction of equimolar amounts of *I* and dimethyl butynedioate gave at room temperature (24 h) the compound *XII* in 13% yield (toluene).

d) The product *III* was also obtained under the same ratio of starting materials using benzene (reflux), benzene (r.t.), dimethylformamide (40°C) in 6, 33 and 38% yields respectively.

e) By performing the reaction in methanol at 110°C for 3 h after separation compound *V* was obtained in 27% yield, m.p. 182–184°C, ref.[7] m.p. 182–183°C.

Reactions of Dimethyl 1-(1′-phenylmethyl-1′,2′,4′-triazolyl)-2-[N-acetamino]butanedioate (*III*) with Dimethyl Butynedioate

0·93 mmol of *III* and an equivalent of dimethyl butynedioate were heated 17 h at 110°C in methanol, benzene or toluene. The mixture was evaporated to small volume and *XII* precipitated with ether, recrystallized from ethanol, yield 38–43%. The rest of the mixture was filtered through a short Al_2O_3 column, evaporated, the solid crystallized from dioxane to give 14% of *XV*.

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