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CONFIGURATION OF AN ETHYL β-NITROCINNAMATE AND ITS 1,2- AND 1,4-CYCLOADDITION TO CYCLOPENTADIENE

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In previous papers, we reported on the stereospecific formation of ethyl α,β-unsaturated β-nitrocarboxylates by the elimination reaction of ethyl α-chloro- or α-acetoxy-β-nitrocarboxylates with sodium acetate[1] and on the assignment of their configuration.[2] Although the geometric configuration of the aliphatic compounds determined to be (E)-isomer from isomerization experiments and their NMR data, that of ethyl β-nitrocinnamate (1) could not be determined. In this paper, we wish to communicate that the configuration of 1 was assigned to be (Z)-isomer, by the conversion of 1 into ethyl 3-nitro-3-phenylbicyclo[2.2.1]- and [3.2.0]hept-5-ene-2-carboxylates (2 and 3) and the subsequent formation of the corresponding tricyclic compounds containing an isoxazolidinone ring.

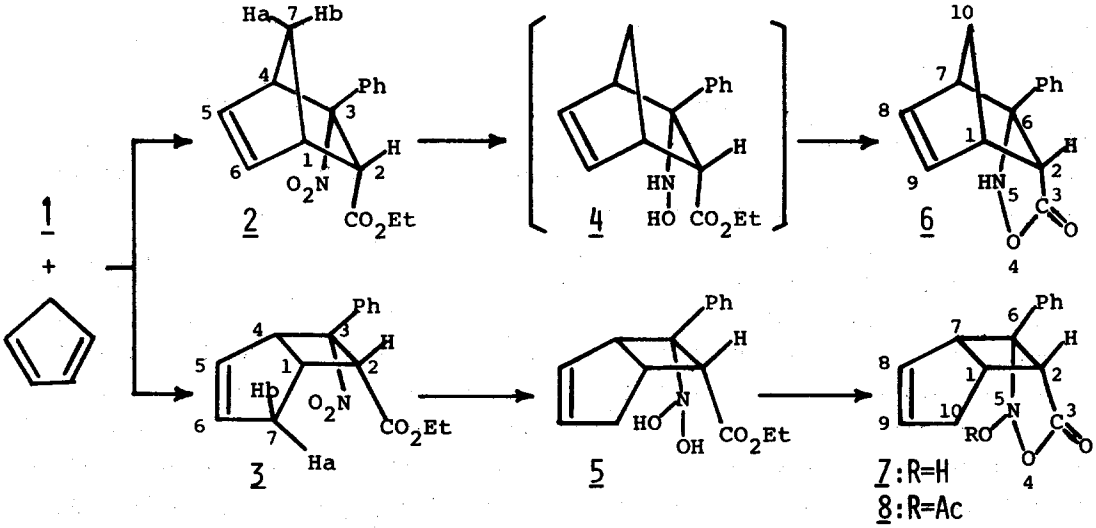
A solution of 1 (9 mmol) and cyclopentadiene (14 mmol) in dry benzene (20 ml) was heated in a sealed tube[3,4] at 100°C for 1 hr and then evaporated under reduced pressure to give a semi-solid substance. Separation of it on a silica gel column, using benzene and acetone (50 : 1 V/V) as eluent, gave two kinds of crystals in a fairly good yield.

From the absence of long range coupling between 7- and 2-protons according to W-letter rule[3-5] and the ring foramation between 3-ethoxycarbonyl and 2-mono- or dihydroxyamino groups, after reduction of nitro group, as shown in the following experiments, the first eluted one was assigned to be ethyl 3-endo-nitro-3-exo-phenylbicyclo[2.2.1]hept-5-ene-2-endo-carboxylate (2; colorless needles from ethanol, yield 47.3%, mp 84-85°C. IR: 1725 (ester), 1640 (C=C), 1540 and 1360 (NO_2) cm^{-1}. NMR: δ 1.46 (1H, 7b-H, dt, $J_{1,7b}$=2.0, $J_{4,7b}$=2.0Hz), 1.67 (1H, 7a-H, d, $J_{7a,7b}$=9.2Hz), 3.18 (1H, 1-H, s), 3.62 (1H, 2-H, d, $J_{1,2}$=3.0Hz), 6.10 (1H, 5-H, dd, $J_{5,6}$=5.7, $J_{4,5}$=3.0Hz), 6.73 (1H, 6-H, dd, $J_{1,6}$=3.0Hz), 7.40-7.85 (5H, C_6H_5, m). Anal; Found: C, 66.63; H, 5.93; N, 4.78%. Calcd for $C_{16}H_{17}NO_4$:C, 66.88; H, 5.96; N, 4.88%). The second eluted compound which shows considerably different pattern from 2 and two equal J values between cis protons on cyclobutane ring could be assigned to be ethyl 3-endo-nitro-3-exo-phenylbicyclo[3.2.0^{1,4}]hept-5-

ene-2-endo-carboxylate (3; colorless needles from ethanol, yield 37.5%, mp 90-91°C. IR: 1735 (ester), 1620 (C=C), 1550 and 1350 (NO_2) cm^{-1}. NMR: δ 2.12 (1H, 7b-H, dt, $J_{1,7b}$=2.0Hz), 2.66 (1H, 7a-H, dd, $J_{7a,7b}$=18.0, $J_{1,7a}$=8.3Hz), 3.86 (1H, 2-H, m, $J_{1,2}$=8.3Hz), 3.88 (1H, 1-H, m), 5.60 (1H, 4-H, d, $J_{1,4}$=8.3Hz), 5.95 (1H, 5-H, dd, $J_{5,6}$=5.7Hz), 6.08 (1H, 6-H, dd), 7.38-7.94 (5H, C_6H_5, m). Anal; Found: C, 66.92; H, 5.95; N, 4.86%. Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88%). Although many photochemical 1,2-cycloaddition between diens and dienophiles are appeared in the literatures,[6,7] thermal 1,2-cycloadducts such as 3 are scarcely known. Decoupling data (Fig 1) for the assignment and the endo-rule in Diels-Alder reaction indicates that the cycloaddition proceeds stereospecifically to yield only endo-isomer.

The structures of 2 and 3 were further proved by conversion into the corresponding tricyclic derivatives. When 2 (3.5 mmol) was reduced by aluminum-amalgam in ether (50 ml),[8] 6-exo-phenyl-endo-4-oxa-5-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3-one (6) was obtained by one step (colorless needles from ethanol, yield 31.6% from 2, mp 112-113°C. IR: 3240 (NH), 1765 (lactone), 1640 (C=C) cm^{-1}. NMR: δ 1.54 (1H, 10b-H, dt, $J_{1,10b}$=2.0, $J_{7,10b}$=2.0Hz), 1.70 (1H, 10a-H, d, $J_{10a,10b}$=9.0Hz), 3.48 (2H, 1,7-H, m), 3.76 (1H, 2-H, d, $J_{1,2}$=4.0Hz), 6.14 (1H, NH, broad s), 6.43 (1H, 8-H, dd, $J_{8,9}$=5.5, $J_{7,8}$=3.0Hz), 6.56 (1H, 9-H, dd, $J_{1,9}$=3.0Hz), 7.43 (5H, C_6H_5, m). Anal; Found: C, 73.89; H, 5.82; N, 6.14%. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16%). From the above result, it is deduced that the compound 2 was reduced to the corresponding unstable endo-hydroxyamino intermediate (4), which cyclized immediately to give 6.

In the similar reduction, compound 3 gave unexpected product, ethyl 3-endo-dihydroxyamino-3-exo-phenylbicyclo[3.2.$0^{1,4}$]hept-5-ene-2-endo-carboxylate (5; colorless fibrous crystals from benzene, yield 48.8%, mp 97-98°C. IR: 3450 and 3225 (OH, strong), 1738 (ester), 1640 (C=C) cm^{-1}. NMR: δ 2.41 (1H, 7b-H, dd, $J_{1,7b}$=2.0Hz), 2.77 (1H, 7a-H, dd, $J_{7a,7b}$=17.5, $J_{1,7a}$=8.0Hz), 3.46 (1H, 1-H, m), 3.64 (1H, 2-H, d, $J_{1,2}$=8.0Hz), 5.66 (1H, 4-H, d, $J_{1,4}$=8.0Hz), 5.88 (1H, 5-H, dd, $J_{5,6}$=6.0Hz), 6.04 (1H, 6-H, dd, $J_{6,7}$=3.0Hz), 2.05-3.00 and 7.20-7.70 (2H, $N(OH)_2$), 7.40 (5H, C_6H_5, m). Anal; Found: C, 66.35; H, 6.63; N, 4.78%. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84%). Because of the high unstability of 5 in the presence of water, the attempt to prove the presence of two active hydrogens by deuterium exchange in D_2O was unsuccessful. However, from the fact obtained in following experiment, it was found that 5 is the first example in which a nitro group was reduced into a dihydroxyamino group. When 5 (0.6 mmol) was heated in dry benzene (10 ml) at 50°C for 1 hr, the expected 6-exo-phenyl-endo-4-oxa-5-azatricyclo[5.3.$0^{1,7}0^{2,6}$]dec-8-ene-3-one-5-ol (7) was obtained (colorless prisms from hexane and ethanol, yield 52.5%, mp 118-119°C. IR: 3340 (OH, strong), 1745 (lactone), 1620 (C=C) cm^{-1}. NMR: δ 2.38 (1H, 10b-H, $J_{1,10b}$=2.5Hz), 2.74 (1H, 10a-H, $J_{10a,10b}$=18.0, $J_{1,10a}$=8.0Hz), 3.43 (1H, 1-H, octet), 3.74 (1H, 2-H, d, $J_{1,2}$=8.0Hz), 5.64 (1H, 7-H, $J_{1,7}$=8.0Hz), 5.79 (1H, 8-H, dd, $J_{7,8}$=3.0, $J_{8,9}$=6.0Hz), 6.12 (1H, 9-H, $J_{9,10}$=3.0Hz), 7.20-7.70 (1H, N(OH)), 7.40 (5H, C_6H_5, m). MS: m/e



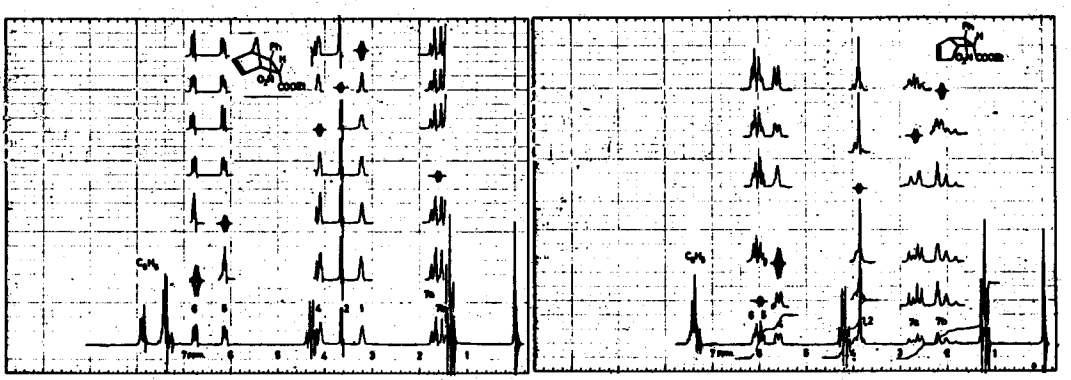


Fig 1. NMR spectrum of 2 and 3.

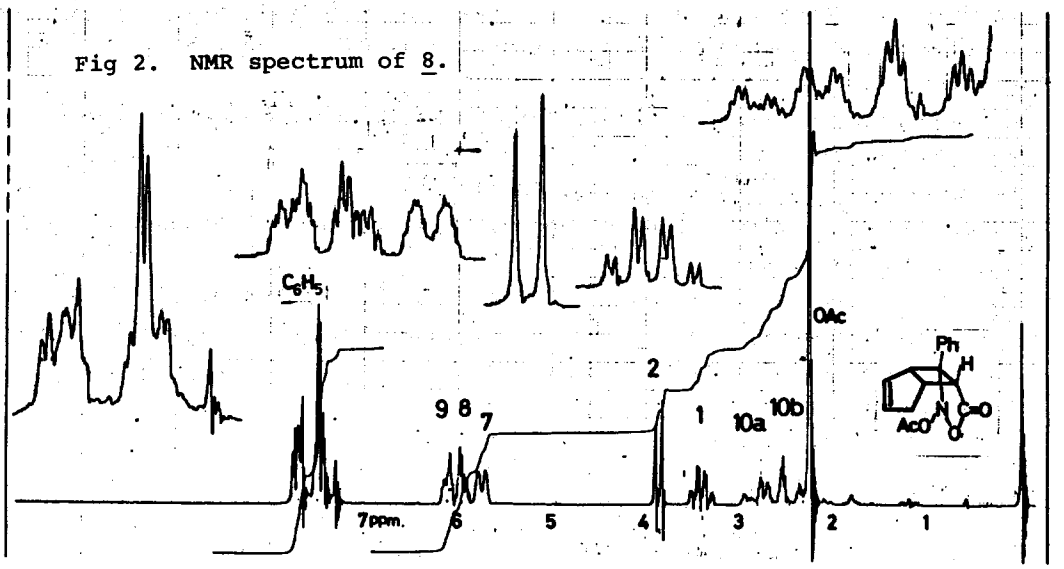


Fig 2. NMR spectrum of 8.

244 (M^+). Anal; Found: C, 68.72; H, 5.39; N, 5.75%. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76%).

Furthermore, the structure of 7 was supported that the acetylation of 7 (0.5 mmol) with acetic anhydride (10 ml) in the presence of pyridine (3 ml) gave the corresponding O-acetyl derivative (8; colorless prisms from ethanol, yield 48.5%, mp 107~108°C. IR: 1775 (acetyl), 1755 (lactone), 1630 (C=C) cm^{-1}. NMR: δ 2.26 (3H, $OCOCH_3$, s), 2.46 (1H, 10b-H, $J_{1,10b}$=2.0Hz), 2.80 (1H, 10a-H, $J_{10a,10b}$=18.8, $J_{1,10a}$=8.1Hz), 3.40 (1H, 1-H, octet), 3.85 (1H, 2-H, d, $J_{1,2}$=8.1Hz), 5.73 (1H, 7-H, d, $J_{1,7}$=8.1Hz), 5.95 (1H, 8-H, dd, $J_{7,8}$=3.5, $J_{8,9}$=6.0Hz), 6.12 (1H, 9-H, $J_{9,10}$=3.0Hz), 7.45-7.69 (5H, C_6H_5, m), as shown in Fig 2. Anal; Found: C, 67.33; H, 5.11; N, 5.03%. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91%).

Consequently, the isoxazolidinone ring formation in 5 and 7 indicated clearly the configuration of 1 to be (Z)-isomer. Moreover, from the chemical shifts, 1,4- and 1,2-cycloaddition products were distingiushed from $J_{7a,7b}$ or $J_{10a,10b}$ values, which showed 9.0-9.2Hz in the former adduct[4,9] and 17.5-18.0Hz region in latter, respectively.

It will be note worthy that two J values between cis protons on cyclobutane ring of 3, 5, 7 and 8 are always equal.

Further works including the analogous study are now in progress.

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IR spectra were taken in KBr and NMR spectra in $CDCl_3$ at 100 MHz; s; singlet, d; doublet, t; triplet, m; multiplet.

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