2-AZABICYCLO[3.2.0]HEPTANE-3,4-DIONES (5). STEREODEPENDENCY IN THERMAL REARRANGEMENT OF 7-VINYL-2-AZABICYCLO[3.2.0]HEPTANE-3,4-DIONES AND THEIR IMIDATES[1]

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The thermal reaction of the 7-vinyl-2-azabicyclo[3.2.0]heptane-3,4-dione yielded different products depending on the stereochemistry of 7-vinyl group. The *endo* isomer, either the lactam (3) or the imidates (8) afforded a Cope product (5 or 9) (3,3-sigmatropic shift) exclusively. On the other hand, the *exo* isomer gave rather complex results. The lactam (2) afforded a hydroindole (4) (1,3-shift) and the Cope product (5) suggesting the formation of a biradical species as an intermediate. The imidate (10) yielded a dihydropyridine (11) (1,3-sigmatropic shift followed by cheletropic loss of CO) as a major product.

Previously, Sano and Tsuda[2] reported the thermal rearrangement of 5-ethoxycarbonyl-1-phenyl-7-*exo*-vinyl-2-azabicyclo[3.2.0]heptane-3,4-dione (2b) to a hydroindole derivative (4b). Recent separation[3] of both the 7-*exo* (2b) and 7-*endo* (3b) isomers from the photo-cycloadduct of butadiene to a dioxopyrroline (1b) prompted us to reinvestigate this thermolysis in relation to the stereochemistry of 7-vinyl group, since formation of the hydroindole (4b) from 2b, if the reaction proceeds in a concerted manner, requires antarafacial 1,3-shift with retention of the configuration of the migrating center, and this is, however, highly difficult by geometrical reasons. Epimerization of 7-substituent during thermolysis was also suggested to be possible.[3,4]

Therefore, thermolyses of two sets of stereoisomers of 7-vinyl group, 2a,b[5] and 3a,b, were examined.

The *exo* isomer (2a), on heating in xylene at 140° for 4 hr, afforded two crystalline products, A: $C_{17}H_{17}NO_6$, mp.222-224°, (20%),[6] and B: $C_{17}H_{17}NO_6$, mp.178-183°, (21%),[6] which were separated by repeated fractional crystallizations. The NMR spectrum of the reaction mixture revealed that the product is a 1:1 mixture of

A and B. A had two olefinic protons (δ~6.0) in the NMR spectrum and was identical with the Diels-Alder product of the dioxopyrroline (1a) with butadiene.[7] It was thus elucidated as the hydroindole (4a). B had two olefinic protons (δ~5.50) in the NMR spectrum. Its IR spectrum showed the absorptions of a C=N (1580 cm^{-1}) and an OH (3120 cm^{-1}), in addition to a five membered-ring ketone (1785 cm^{-1}) and an ester carbonyl (1740 cm^{-1}), but no band of a lactam carbonyl being observed. The UV spectrum (λ_{max} 309 nm, ε 8,500) indicated the presence of an Ar-C=N- chromophor. Thus it was elucidated as 5a, 4-ethoxycarbonyl-1-hydroxy-3-(3',4'-methylenedioxyphenyl)-2-azabicyclo[4.2.1]nona-2,6-dien-9-one.

In contrast to 2a, the *endo* isomer (3a) yielded 5a (40%, after purification) as an only isolable product on a similar thermolysis. The NMR spectrum of the reaction mixture was almost superimposable with that of 5a, indicating no formation of 4a.

Re-investigation of the thermolysis of the *exo* isomer (2b) at a similar condition described above afforded a 2:1 mixture (NMR spectrum) of 4b (A) and 5b (B), from which the previously reported hydroindole (4b)[2], mp.228-230°, was isolated in 40% yield after chromatography (B was unstable under hydrolytic condition and easily decomposed on chromatography).

Thermolysis of the *endo* isomer (3b) again afforded 5b (gum)[6] as a sole product, whose structure was assigned by spectral resemblance with 5a.

Formation of 5 from the *endo* isomer (3) appeared to be a result of [3,3]-sigmatropic rearrangement of the enol form (7) (a Cope product). In cases of the *exo* isomer (2), direct formation of 5 is geometrically impossible. It was shown, however, that an equilibration of 7-*exo* and 7-*endo* substituent can occur under a thermal condition and that the 7-*endo* isomer was thermodynamically more stable than the 7-*exo* isomer.[3,4] We therefore consider that the thermolysis of 2 proceeds as follows. Homolytic fission of C_1-C_7 bond produces a biradical species (6) which then collapses into either the *endo* isomer (3) or the hydroindole (4) by recombination or by combination at the methylene terminus accompanying with [1,3]-shift, the former product then rearranges into 5.

If the above argument is correct, formation of the imidate (8) will facilitates the Cope rearrangement. In fact, the *endo* isomers (3a,b), on treatment with excess Meerwein reagent in CH_2Cl_2 at room temp. for 20 hr, directly afforded the Cope product (9) in a quantitative yield. 9a: $C_{19}H_{21}NO_6$, mp.91-93°[6], and 9b: $C_{18}H_{21}NO_4$, mp.99-101°.[6] In contrast to 5, they were stable to chromatographic purification.

The NMR spectra of 9a,b were almost superimposable with those of 5a,b respectively, except for the signals due to OEt group, supporting the assigned structures. Apparently, fixation of the C=N double bond greatly reduced the activation energy of the Cope rearrangement.

Similar treatment of the *exo* isomer (2b) with Meerwein reagent gave the corresponding imidate (10b), mp.96-97°, in 80% yield. Thermolysis of 10b gave a different result from that of the lactam (2b). On heating under reflux in toluene for

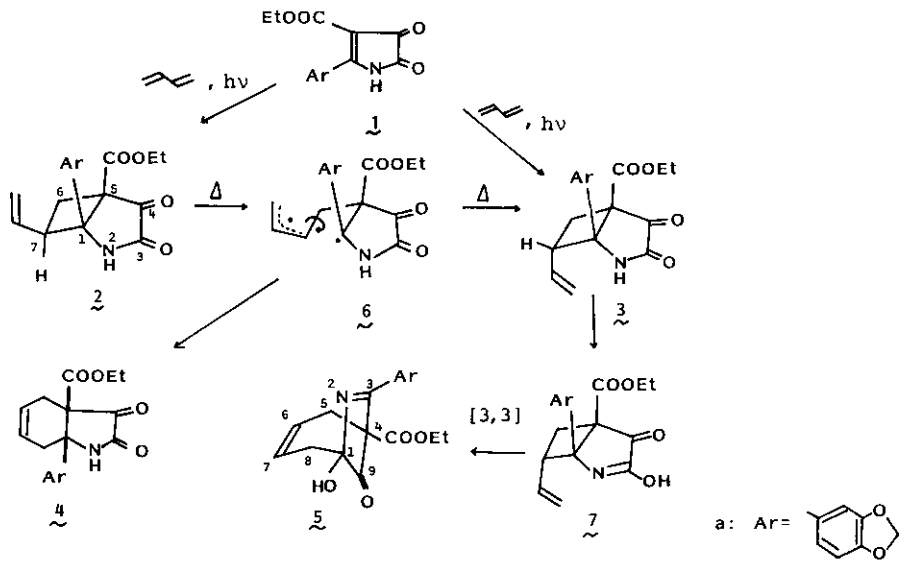

chart 1

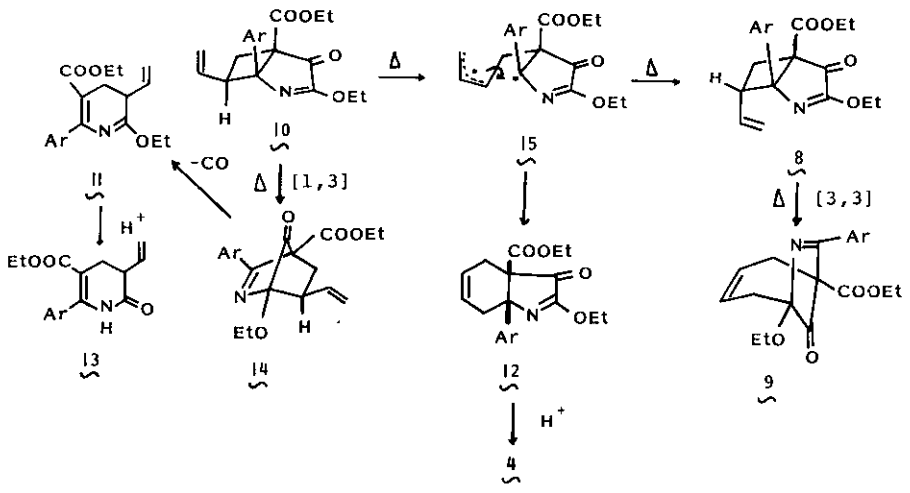

chart 2

30 min. followed by mild acid hydrolysis (5%HCl, r.t., 30 min.), it afforded a dihydropyridone (13b), mp.112-114° (60%), the hydroindole (4b)(4%), and the Cope product (9b)(10%). The structure of 13b was elucidated by comparisons of the spectral data with those of the known 3,4-dihydro-α-pyridones.[8] This result indicates that the thermolysis products of 10b are 11, 12 and 9. The major path (formation of a dihydropyridine) is explained by [1,3] sigmatropic shift of C_7 to C_3 followed by cheletropic elimination of CO from an intermediary 2-azabicyclo-[2.2.1]heptan-7-one (14).[9] However, the fact that the *exo* isomer (10b) yielded the Cope product (9b), though in minute amount, again suggested that a biradical species (15) by homolytic cleavage of C_1-C_7 bond would partially participate, since the *exo* isomer (10) is geometrically impossible to give the Cope product (9). The biradical (15) would collapse into either the hydroindole (12) or the *endo* isomer (8), the latter then being rearranged into the Cope product (9).

Reference and Notes

1. Dioxopyrrolines XIX. Part XVIII : T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, preceding paper.
2. T. Sano and Y. Tsuda, Heterocycles, 1976, 4, 1361.
3. T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, 1981, 16 in press (Part XVI).
4. T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, 1981, 16 in press (Part XV).
5. Prepared in the manner as described in ref. 3.
   2a: mp.175-177°. 3a: mp.172-174°. They gave satisfactory spectral data.
6. 4a: IR(Nujol): 1775, 1735, 1720 cm^{-1}. NMR($CDCl_3$): 0.83(3H, t, J=7 Hz), 2.6-3.0 (4H, m), 3.60(2H, m), 6.00(2H, bs, olefinic H), 6.00(2H, s), 6.6-7.1(3H, m).
   5a: IR(Nujol): 3120, 1785, 1740, 1580 cm^{-1}. UV λ_{max}^{EtOH} (ε): 228(12,900), 274(7,600), 309(8,500). NMR($CDCl_3$): 1.03(3H, t, J=7 Hz), 2.2-3.1(4H, m), 4.17(2H, q, J=7 Hz), 5.50(2H, bs, olefinic H), 6.0(2H, s), 6.9-7.5(3H, m).
   5b: IR(Nujol): 3400-3200, 1780, 1740, 1600, 1570 cm^{-1}. NMR($CDCl_3$): 1.00(3H, t, J=7 Hz), 2.6-3.1(4H, m), 4.13(2H, q, J=7 Hz), 5.40-5.63(2H, m), 7.0-8.0 (5H, m).
   9a: IR(Nujol): 1780, 1730, 1580 cm^{-1}. NMR($CDCl_3$): 1.10(3H, t, J=7 Hz), 1.25(3H, t, J=7 Hz), 2.67(2H, m), 2.90(2H, m), 3.55(2H, qd, J=2 and 7 Hz), 4.2(2H, q, J=7 Hz), 5.45(2H, m, olefinic H), 6.05(2H, s), 6.80(1H, d, J=8 Hz), 7.22(1H, dd, J=2 and 8 Hz), 7.53(1H, d, J=2 Hz).
   9b: IR(Nujol): 1785, 1740, 1605 cm^{-1}. NMR ($CDCl_3$): 1.07(3H, t, J=7 Hz), 1.30 (3H, t, J=7 Hz), 2.3(1H, m), 2.6-3.0(3H, m), 3.67(2H, q, J=7 Hz), 4.17(2H, q, J=7 Hz), 5.57-5.37(2H, m), 7.0-8.0(5H, m).
   13b: mp.112-114°. IR(Nujol): 1715, 1660, 1640 sh, 1600 cm^{-1}. NMR($CDCl_3$): 0.9 (3H, t, J=7 Hz), 2.7-2.95(2H, m), 3.1-3.4(1H, m), 3.95(2H, q, J=7 Hz), 5.1-5.4(2H, m), 5.8-6.35(1H, m), 7.35(5H, m).
7. In acetic anhydride, 160°C, 2 hr, followed by acid hydrolysis(5%HCl-MeOH), 6% yield.
8. T. Sano, Y. Horiguchi, Y. Tsuda, and Y. Itatani, Heterocycles, 1978, 9, 161.
9. See Part XVIII.

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