

2-AZABICYCLO[3.2.0]HEPTANE-3,4-DIONES (3): LEWIS ACID CATALYSED
RING EXPANSION OF 3-ETHOXY- Δ^2 -AZABICYCLO[3.2.0]HEPTAN-4-ONES:
SYNTHESIS OF 2-ETHOXY-3-AZATROPONES¹

Takehiro Sano*, Yoshie Horiguchi, and Suetaka Kambe

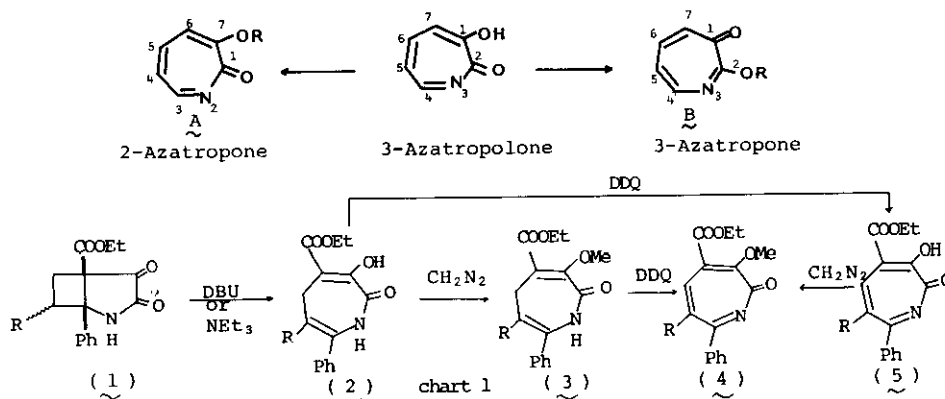
Showa College of Pharmaceutical Sciences, Setagaya-Ku, Tokyo 154, Japan.

Yoshisuke Tsuda

Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa 920, Japan.

Treatment of 2-azabicyclo[3.2.0]heptane-3,4-dione imidic ester (6) with tin(IV) chloride gave the dihydroazatropolone 2-ethyl ethers (7) in moderate yields which were also obtained by reaction of dihydroazatropolones (2) with Meerwein reagent. DDQ oxidation of 7 gave 2-ethoxy-3-azatropones (8), which rearranged, on treatment with water, into ethyl pyridine 2-carboxylate (10). Spectroscopic data of azatropolone 2-ethyl ethers were also described.

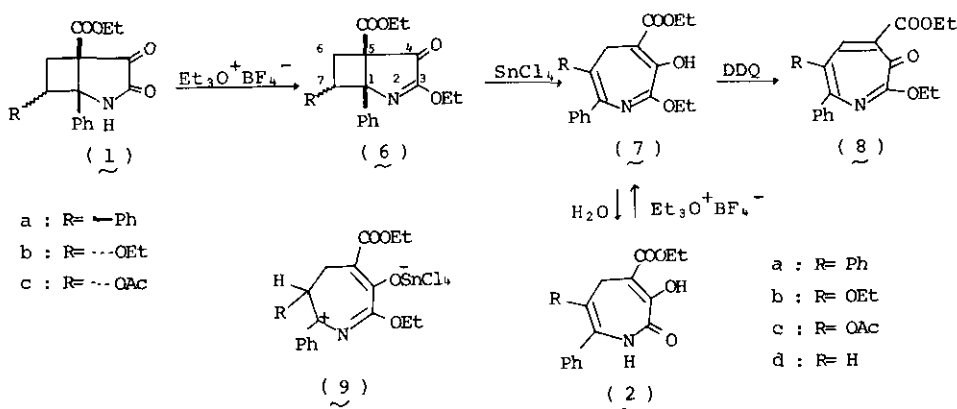
For an azatropolone two alkyl ethers, A and B, are possible. Recently, we reported base catalyzed ring expansion of 2-azabicyclo[3.2.0]heptane-3,4-diones (1) to dihydroazatropolones (2) which on methylation followed by dehydrogenation afforded 7-methoxy-2-azatropolone (4)² (type A). Methylation of 3-azatropolones (5) produced only the same ethers (4). Thus, the corresponding 2-alkyl ethers (type B) are hitherto unknown. Here we report the unequivocal synthesis of the 2-ethyl ethers, via Lewis acid catalysed ring expansion of the imidic esters of 2-azabicyclo[3.2.0]heptane-3,4-diones.



The imidic esters (6a-c) were prepared from (1a-c)^{3,4} in 65-89% yield with excess Meerwein reagent in CH₂Cl₂ at room temperature and the structures were confirmed spectroscopically.⁵ The imidic esters (6), when treated overnight with SnCl₄ (1.5 mol eq.) in CH₂Cl₂ at room temperature, gave the dihydroazatropolone 2-ethyl ethers (7) in moderate yields. The spectral data⁵ and the following transformations established their structures. They were hydrolysed by 5% HCl in tetrahydrofuran (1:1) to the known dihydroazatropolones (2) which on treatment with Meerwein reagent yield the 2-ethyl ethers identical with the compounds obtained above.

Interestingly, the 2-azabicyclo[3.2.0]heptane-3,4-diones (1) were not affected under similar acidic condition (SnCl₄ in CH₂Cl₂ at r.t.), and the imidic esters were stable to base. We therefore assume that the reaction of 6 proceeds through a cationic intermediate 9.

DDQ oxidation of 7 to the 2-ethoxy-3-azatropone (8) was achieved more readily than that of 2 to 5 or that of 3 to 4. Thus a mixture of 7 and DDQ (1.3 mol eq.) in benzene was heated in a sealed tube, and the resulted product was purified by rapid chromatography on SiO₂ to give the 2-ethoxy-3-azatropone (8), in satisfactory yield. Attempt to direct preparation of 8b from 5b with Meerwein reagent was unsuccessful, only a complex mixture being obtained.



All 2-ethoxy-3-azatropolones (8) prepared above were yellow gum and had $\lambda_{\max}$ around 370~400 nm in their electronic spectra. The maximum is red-shifted relative to the corresponding 3-azatropolones (5) and 7-methoxy-2-azatropolones (4)² (see Fig 1).

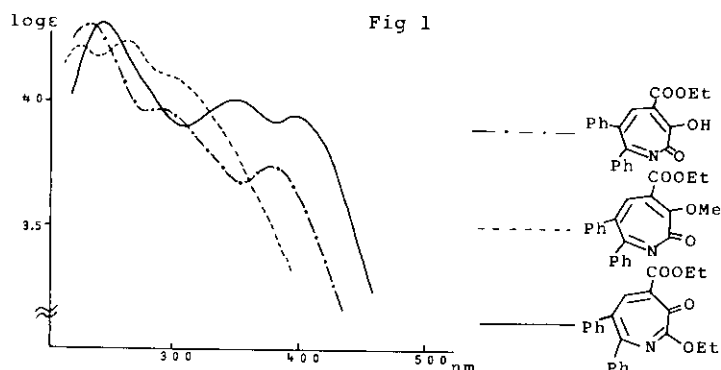


Table 1. Preparation of Dihydroazatropolone 2-Ethyl Ethers (7) and 2-Ethoxy-3-Azatropones (8).

R	Dihydroazatropolone 2-Ethyl Ether (7)			2-Ethoxy-3-Azatropone (8)		
	Yield (%)			Condition		
	from 6	from 2	m.p.	temp.	time	Yield (%)
a: ph	69	94	114-115°	105°	8 min.	77
b: OEt	12 ^{a)}	65	yellow gum	25°	spontaneous	43
c: OAc	43	82	73- 75°	110°	20 min.	60
d: H		50	colorless gum	25°	1~2 min.	82

a) 7_b was vulnerable to air oxidation

Table 2. Spectral Data of 2-Ethoxy-3-Azatropones (8).

Comp.	NMR (δ, ppm)				UV λ _{max} ^{dioxane} (ε)
	IR (cm ⁻¹)	C ₆ -H	C ₅ -H		
8 _a :	1720 1655 1620	8.17 (s)			240 (21,200) 349 (9,800) 398 (8,600)
8 _b :	1723 1660 1640	8.00 (s)			247 (10,600) 355 (5,100) 395 (5,300)
8 _c :	1765 1725 1660 1620	7.88 (s)			225 (11,500) 258sh (9,500) 345 (7,300) 385sh (6,100)
8 _d :	1725 1660 1620	8.03 (d, J=10 Hz)	6.90 (d, J=10 Hz)		240 (10,400) 258sh (9,000) 370 (12,500)

The 2-ethoxy-3-azatropones, similar to the 3-azatropolones, were unstable in aqueous solvent. When 8 was treated with silica gel-H₂O or heated in aqueous acetone in presence of catalytic amount of sodium acetate, it quantitatively changed into the ethyl pyridine 2-carboxylate (10)⁵, identical with that obtained on treatment of 2 or 4 with ethanol⁶, no pyridine 2-carboxylic acid being formed. The conversion of 8 to 10 is explained by hydration to -C=N- double bond, benzylic acid type rearrangement followed by dehydration, thus supporting our proposed mechanism of an azatropolone to pyridine 2-carboxylate.²

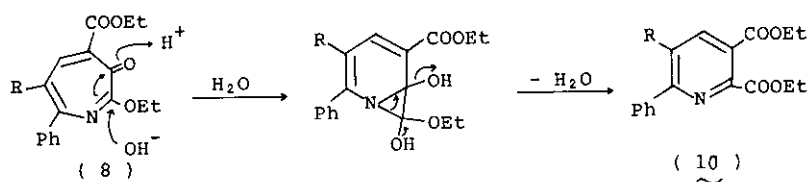


chart 3

References and Note

1. Dioxopyrrolines XVII, Part XVI: T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, in press.
2. T. Sano, Y. Horiguchi and Y. Tsuda, Heterocycles, 1979, 12, 1427.
3. T. Sano and Y. Tsuda, Heterocycles, 1976, 4, 1229.
4. see Part XVI.
5. 6a: mp.137-139°; IR: 1760, 1740, 1640 cm⁻¹; NMR:δ 2.38(1H, dd, J=6, 4 Hz, C₆-H), 3.58(1H, dd, J=4, 6 Hz, C₆-H), 3.78(1H, t, J=6 Hz, C₇-H).
6b: mp.68-71°; IR: 1770, 1760, 1735 cm⁻¹; NMR:δ 1.93(1H, dd, J=14, 5 Hz, C₆-H), 3.37(1H, dd, J=14, 8 Hz, C₆-H), 4.71(1H, dd, J=5, 8 Hz, C₇-H).
6c: mp.106-108°; IR: 1759, 1750, 1630 cm⁻¹; NMR:δ 2.05(1H, dd, J=14, 5 Hz, C₆-H), 3.57(1H, dd, J=14, 9 Hz, C₆-H), 5.85(1H, dd, J=5, 9 Hz, C₇-H).
7a: IR: 1665, 1630, 1600 cm⁻¹; NMR:δ 2.90(2H, s, C₅-H); λ_{max}^{dioxane} 234(ε 20,600), 268(ε 17,800), 345sh(ε 2,100)nm.
7b: IR: 1730, 1660, 1620 cm⁻¹; NMR:δ 2.90(2H, s, C₅-H); λ_{max}^{dioxane} 255sh(ε 10,700) nm.
7c: IR: 1765, 1660, 1630 cm⁻¹; NMR:δ 2.97(2H, s, C₅-H); λ_{max}^{dioxane} 228sh(ε 12,000), 253(ε 16,500), 335sh(ε 1,500)nm.
7d: IR: 1658, 1620 cm⁻¹; NMR:δ 2.68(2H, d, J=7 Hz, C₅-H), 5.85(1H, t, J=7 Hz, C₆-H); λ_{max}^{dioxane} 223(ε 13,600), 258(ε 17,300), 335sh(ε 1,300)nm.
10b: mp.84-85°; IR: 1745, 1725 cm⁻¹; NMR:δ 7.57(1H, s, C₄-H); λ_{max}^{EtOH} 239(ε 14,800), 264sh(ε 10,100), 315(ε 12,500)nm.
10c: gum; IR: 1765, 1725, 1600 cm⁻¹; NMR:δ 8.0(1H, s, C₄-H); λ_{max}^{EtOH} 262(ε 9,500), 293(ε 10,600)nm.
10d: gum; IR: 1740, 1730 cm⁻¹; NMR:δ 8.28(1H, d, J=9 Hz, C₅-H), 7.82(1H, d, J=9 Hz, C₄-H); λ_{max}^{EtOH} 268sh(ε 15,000), 290(ε 18,900)nm.
6. Y. Tsuda, N. Kaneda, T. Sano, Y. Horiguchi, and Y. Iitaka, Heterocycles, 1979, 12, 1423.

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