

CONVENIENT SYNTHESIS OF BENZO[b]TROPONES FUSED WITH INDOLIZINES
OR INDOLES BY REACTION OF 2-PHENYL-3-VINYL SUBSTITUTED
DERIVATIVES WITH POLYPHOSPHORIC ACID

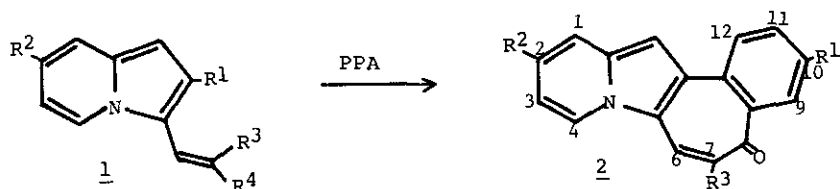
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Abstract — Reaction of 2-phenyl-3-(2-ethoxycarbonylvinyl)-indolizine derivatives with polyphosphoric acid gave 8H-benzo[6,7]cyclohept[1,2-b]indolizin-8-ones 2 by an intramolecular acylation reaction. Reaction of 2-phenyl-3-(2-ethoxycarbonylvinyl)indole derivatives gave 5H,10H-benzo[6,7]cyclohept[1,2-b]indol-10-ones 7.

Indolizines are useful starting materials to prepare a novel type of heterocycles such as cyclazines.¹ Recently, we have reported a simple synthetic method of 3-vinylindolizine derivatives 1.² These indolizines have been expected to be useful for synthesizing a new type of nitrogen-bridged heterocycles. In this connection, we have examined the reaction of the indolizines 1 with polyphosphoric acid (PPA) and found a one-pot synthetic method of benzo[b]tropones fused with indolizines.

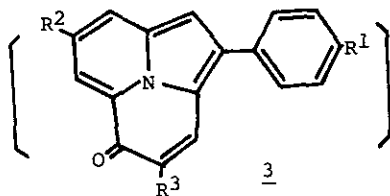
When a mixture of 3-[2,2-bis(ethoxycarbonyl)vinyl]indolizine derivatives 1a-c and PPA (1 : 10 by weight) was heated at 120-130 °C for 1 h, yellow crystals 2 [2a; mp 147-149 °C, 27 %, 2b; mp 140-150 °C (decomp), 4 %, 2c; mp 180 °C (decomp), 17 %] were obtained, respectively. The structures of the products were determined on the basis of the spectral data.³ The elemental analyses and mass spectra indicate that 2a-c are products formed by elimination of ethanol from the starting indolizines 1a-c. The UV spectra indicate the presence of a long conjugated system [for example, 2a; λ_{\max} (ethanol) 231 nm ($\log \epsilon=4.30$), 269 (4.46), 289 (4.28), 317 (4.08), 449 (4.21)]. The IR spectra strongly suggest 2 to be tropone derivatives because the characteristic $\nu_{C=C}$ and $\nu_{C=O}$ bands of tropone series are observed

[2a; ν_{\max} (KBr) 1635, 1580 cm^{-1} , 2b; ν_{\max} (KBr) 1640, 1580 cm^{-1}]. The ^1H NMR spectra are consistent with these structures 2 in which characteristic singlet peaks due to the H-6 protons appear in the lowest field (2a; δ ppm 8.49, 2b; 8.37, 2c; 8.78). The formation of 2 can be explained by an intramolecular acylation reaction. Another possible isomers 3 could not be identified. The difficulty of the acylation reaction at the C_5 -position of the indolizines was also indicated by the fact that the reaction of the methyl derivative 1d with PPA gave no clear product. On the other hand, reaction of an isomeric mixture of 3-[(2-acetyl-2-ethoxycarbonyl)vinyl]indolizines 1e and 1f (2 : 1) with PPA at 120 °C afforded 8H-benzo[6,7]cyclohept[1,2-b]indolizin-8-one (2d) (mp 166-168 °C) in 43 % yield. Similarly, reaction of a 2 : 1 mixture of 1g and 1h with PPA gave 2e (mp 200-204 °C) in 30 % yield. The structures which are deacetylated from the expected intramolecular acylated compounds were deduced from the spectral data.^{3,4} In particular, the following high resolution ^1H -NMR spectrum (200 MHz) of 2e provides convincing evidence for the structural assignment.⁵ δ ppm (CDCl_3) 2.36 (s, Me), 6.58 (dd, H-3, $J=7.0, 2.0$ Hz), 6.70 (d, H-7, $J=12.0$), 7.10 (s, H-13), 7.26 (brs, H-1), 7.58 (ddd, H-10 or H-11, $J=8.0, 8.0, 1.5$), 7.71 (d, H-6, $J=12.0$), 7.72 (ddd, H-11 or H-10, $J=$

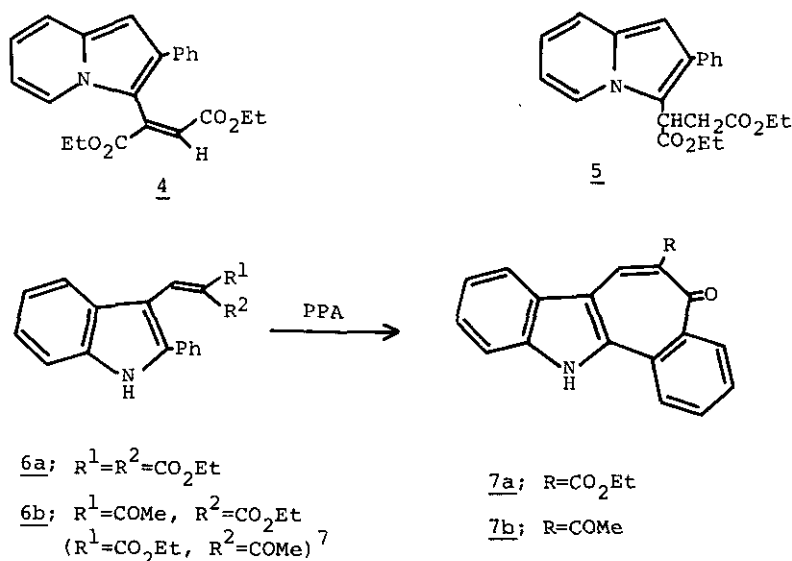


- a; $\text{R}^1=\text{Ph}, \text{R}^2=\text{H}, \text{R}^3=\text{R}^4=\text{CO}_2\text{Et}$
b; $\text{R}^1=\text{Ph}, \text{R}^2=\text{Me}, \text{R}^3=\text{R}^4=\text{CO}_2\text{Et}$
c; $\text{R}^1=\text{p-BrC}_6\text{H}_4, \text{R}^2=\text{H}, \text{R}^3=\text{R}^4=\text{CO}_2\text{Et}$
d; $\text{R}^1=\text{Me}, \text{R}^2=\text{H}, \text{R}^3=\text{R}^4=\text{CO}_2\text{Et}$
e; $\text{R}^1=\text{Ph}, \text{R}^2=\text{H}, \text{R}^3=\text{COMe}, \text{R}^4=\text{CO}_2\text{Et}$
f; $\text{R}^1=\text{Ph}, \text{R}^2=\text{H}, \text{R}^3=\text{CO}_2\text{Et}, \text{R}^4=\text{COMe}$
g; $\text{R}^1=\text{Ph}, \text{R}^2=\text{Me}, \text{R}^3=\text{COMe}, \text{R}^4=\text{CO}_2\text{Et}$
h; $\text{R}^1=\text{Ph}, \text{R}^2=\text{Me}, \text{R}^3=\text{CO}_2\text{Et}, \text{R}^4=\text{COMe}$

- a; $\text{R}^1=\text{R}^2=\text{H}, \text{R}^3=\text{CO}_2\text{Et}$
b; $\text{R}^1=\text{H}, \text{R}^2=\text{Me}, \text{R}^3=\text{CO}_2\text{Et}$
c; $\text{R}^1=\text{Br}, \text{R}^2=\text{H}, \text{R}^3=\text{CO}_2\text{Et}$
d; $\text{R}^1=\text{R}^2=\text{R}^3=\text{H}$
e; $\text{R}^1=\text{R}^3=\text{H}, \text{R}^2=\text{Me}$



8.0, 8.0, 1.5), 8.19 (d, H-4, J=7.0), 8.30 (dd, H-9 or H-12, J=8.0, 1.5), 8.61 (dd, H-12 or H-9, J=8.0, 1.5). The deacetylation is an unusual reaction and the mechanistic details are under investigation. For comparisons, reaction of indolizine derivatives 4 and 5⁶ with PPA was attempted. Under the same conditions of those of 1, indolizines 4 and 5 were almost recovered unchanged. This result shows that two carbonyl substituents at the 2,2-position in the vinyl group are needed for the smooth acylation reaction.



The reaction found in indolizine derivatives could be applied to indole derivatives. 2-Phenyl-3-vinylindole derivatives 6a,b were prepared by reaction of 3-formyl-2-phenylindole with diethyl malonate and ethyl acetoacetate, respectively. Reaction of 6a with PPA under the same conditions as those described for indolizines 1 afforded an expected benzo[b]troponone derivative fused with indole 7a (mp 243-245 °C, 30 %). The spectral data are consistent with this structure.⁸ On the other hand, the reaction of 6b was complex and a troponone derivative 7b (mp 256-258 °C) was isolated in 3 % yield, in which a deacetylated product, such as 2d,e in the previous case, could not be identified.

The reaction found here provides a facile entry to benzo[b]tropones fused with indolizines or indoles, and their chemical and physical properties are currently under investigation.

REFERENCES AND NOTES

1. A. Galbraith, T. Small, R. A. Barnes, and V. Boekelheide, *J. Am. Chem. Soc.*, 1961, 83, 453, V. Boekelheide and K. Fahrenholts, *ibid.*, 1961, 83, 458, A. Kakehi, S. Ito, B. Wada, K. Watanabe, K. Nishimura, and A. Kumagai, *Bull. Chem. Soc. Jpn.*, 1982, 55, 3590.
2. Y. Yamashita, D. Suzuki, and M. Masumura, *Heterocycles*, 1981, 16, 1499.
3. All new compounds obtained here showed satisfactory elemental analyses and spectral data.
4. The characteristic UV and IR spectra are as follows. 2d; λ_{\max} (ethanol) 262 nm ($\log \epsilon=4.49$), 271 (4.60), 283 (4.41), 313 (3.93), 336 (3.93), 353 (3.97), 447 (4.13), ν_{\max} (KBr) 1630, 1600 cm^{-1} , 2e; λ_{\max} (ethanol) 273 (4.63), 286 (4.39), 300 (4.24), 314 (4.19), 337 (3.95), 354 (3.96), 457 (4.21), ν_{\max} (KBr) 1640, 1600 cm^{-1} .
5. We thank Professor Toshio Mukai at Tohoku University for providing the NMR measurements.
6. Indolizine 4 was prepared by reaction of 2-phenylindolizine with dimethyl acetylenedicarboxylate. Indolizine 5 was obtained by reduction of 4 with NaBH_4 .
7. 6b is a mixture of stereoisomers (4 : 1) and the stereochemistry could not be unambiguously determined.
8. UV λ_{\max} (ethanol) 208 nm ($\log \epsilon=4.63$), 224 sh (4.32), 253 (4.18), 281 (4.22), 300 sh (3.99), 452 (4.39), IR ν_{\max} (KBr) 1730, 1627, 1555 cm^{-1} , ^1H NMR δ_{ppm} (CDCl_3) 1.32 (t, 3H, $J=7.0$ Hz), 4.28 (q, CH_2 , $J=7.0$), 7.50-7.80 (m, 4H), 7.82-8.10 (m, 4H), 8.50 (s, 1H), 12.78 (s, NH).

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