REACTIONS OF INDOLIZINES WITH TROPONE

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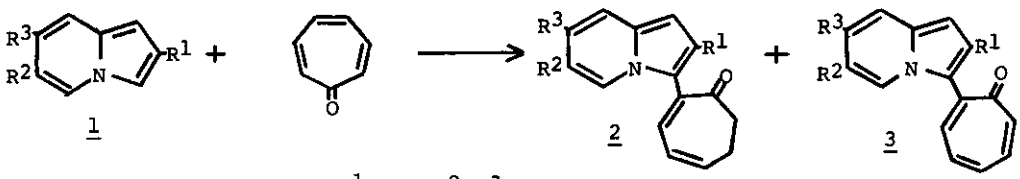
Abstract —— Reactions of indolizine derivatives with tropone gave the Michael type adducts 2 and 2-indolizin-3-yltropone derivatives 3. The tropones 3 were formed by dehydrogenation of the adducts.

Indolizines are well known to undergo the Michael type addition reactions with electron deficient olefins such as tetracyanoethylene or diethyl azodicarboxylate.[1] These reactions are of interest from the viewpoint of the reaction mechanism and also provide useful methods to prepare indolizine derivatives which are potential starting materials for synthesis of functionalized nitrogen-bridged heterocycles. In this connection, we have examined the addition reactions of indolizines with several olefins.[2] We report here the Michael type addition reactions of indolizines with tropone.

When a mixture of indolizines 1a-d and tropone (1.0 ; 2.0 equiv) in xylene was refluxed under N_2 atmosphere for 7 h, two products 2 and 3 were obtained in the yields shown in Table 1. These were purely separated by column chromatography



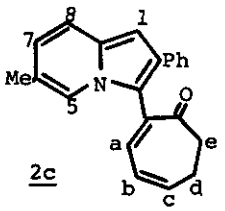
1 + tropone → 2 + 3

a; R^1=Me, R^2=R^3=H
b; R^1=Ph, R^2=R^3=H
c; R^1=Ph, R^2=Me, R^3=H
d; R^1=Ph, R^2=H, R^3=Me

Table 1. Yields and Melting Points of the Products 2 and 3

Compd	Yield, %	M.P., °C	Compd	Yield, %	M.P., °C
2a	18	oil	3a	26	oil
2b	17	128-132	3b	10	oil
2c	20	122-124	3c	15	156-158
2d	21	oil	3d	39	oil

on silica gel. The structures of the products 2 were determined mainly on the basis of the spectral data. The elemental analyses and mass spectra indicate that the products 2 are 1 : 1 adducts of indolizines 1 and tropone.[3] The UV spectra of 2 indicate the presence of the indolizine skeletone [2b; λ_{max} (ethanol) 252 nm (logε = 4.62)]. The IR spectra of 2 exhibit peaks due to a conjugated carbonyl group [ν (KBr) 1650 cm^{-1} (C=O)]. The NMR spectra strongly support the structures of 2 to be 2-indolizin-3-yldihydrotropones. The NMR spectrum of 2c, for example, is shown as follows.



2c

δppm (200 MHz, $CDCl_3$) 1.88 (Me, 3H), 1.84-1.98 (m, 2H, Hd), 2.52-2.60 (m, 2H, He), 5.49 (dddd, Hb), 5.82 (ddd, Hc), 6.34 (dd, H_7), 6.37 (d, Ha), 6.72 (s, H_1), 7.08-7.32 (m, 4H), 7.45 (brs, H_5), 7.60-7.70 (m, 2H),

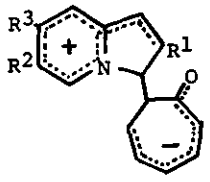
Coupling constants; $J_{a,b}$ = 7.5 Hz, $J_{b,c}$ = 11.0, $J_{c,d}$ =6.0, $J_{b,d}$ = 1.0, $J_{5,7}$ =1.2, $J_{7,8}$ = 9.0

These proton assignments based on the decoupling experiments clearly indicate that the addition reaction occurred at the C-3 position of the indolizine and the C-2 position of tropone.

On the other hand, the structures of the products 3 were also determined on the basis of the spectroscopic data along with chemical evidence. The elemental analyses and mass spectra show that 3 are dehydrogenated products of the 1 : 1 adducts 2.[3] In fact, heating the adduct 2b in refluxing toluene in the presence of 10 % Pd-C gave 3b in 55 % yield. The color of the product 3 is red violet [3b, λ_{max} (ethanol) 246 nm (logε = 4.61), 340 sh (3.77), 500 (3.54)], indicating the presence of a long conjugated system. The IR spectra strongly suggest 3 to be tropone derivatives because the characteristic $\nu_{C=C}$ and $\nu_{C=O}$ bands of the

tropone series are observed [3b; ν_{max} (CCl_4) 1618, 1570 cm^{-1}, 3c; ν_{max} (KBr) 1622, 1580 cm^{-1}]. The NMR spectra are consistent with the structures of 3 in which methylene protons observed in 2 disappeared [3a; δppm ($CDCl_3$) 2.25 (s, Me), 6.26-7.25 (m, 10H), 3c; δppm ($CDCl_3$) 2.18 (s, Me), 6.5-7.5 (m, 14H)].

The formation of the 1 : 1 adducts 2 can be explained by the Michael type addition reactions to give intermediates 4 followed by hydrogen shifts in which the initial adducts 5 undergo a 1,5-hydrogen shift to give the final products 2.[5] These Michael type addition reactions reflect the large nucleophilicity of indolizines. The selectivity of the reaction sites found in these addition reactions is in accord with the reported results that the electrophilic substitution reactions of indolizines occur at the C-3 position [1, 6] and nucleophilic reactions of tropones proceed mainly at the C-2 position.[7]



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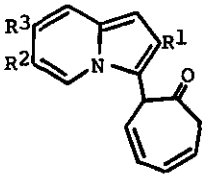

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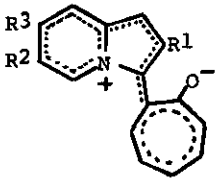

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The indolizinyltropones obtained here are expected to have the resonance contribution of the delocalized structures 6. The absorption bands in the longer wavelength region observed in the UV spectra of the tropones 3 may be attributed to the contribution of 6.[8] Further studies are in progress to investigate the chemical reactivities of these tropone derivatives 3.

References and Notes

1. O. Ceder and B. Hall, J. Heterocyclic Chem., 1978, 15, 1471; W. Flitsch and J. Heinrich, Tetrahedron Lett., 1980, 21, 3673; For reviews of indolizines, F. J. Swinbourne, J. H. Hunt and G. Klinkert, Adv. Heterocyclic Chem., 1978, 23, 103.
2. M. Masumura and Y. Yamashita, Heterocycles, 1979, 12, 787; Y. Yamashita, D. Suzuki, and M. Masumura, ibid., 1981, 16, 1499.

3. All new compounds obtained here showed satisfactory elemental analyses and spectral data.
4. We thank Professor Toshio Mukai at Tohoku University for providing the measurements.
5. The reactions of 2-chlorotropone and 2-methoxytropone with indolizines were examined for comparisons, but complex reaction occurred and no product was isolated.
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7. C. A. Cupas, W. E. Heyd, and M. -S. Kong, J. Am. Chem. Soc., 1971, 93, 4623; T. Nozoe, T. Mukai, and T. Tezuka, Bull. Chem. Soc. Japan, 1961, 34, 619.
8. These bands may be attributed in part to the intramolecular charge-transfer bands.

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