Reaction of 2-Chlorotropone with Enamines. Synthesis of 2-(2-Oxocycloalkyl)-tropones

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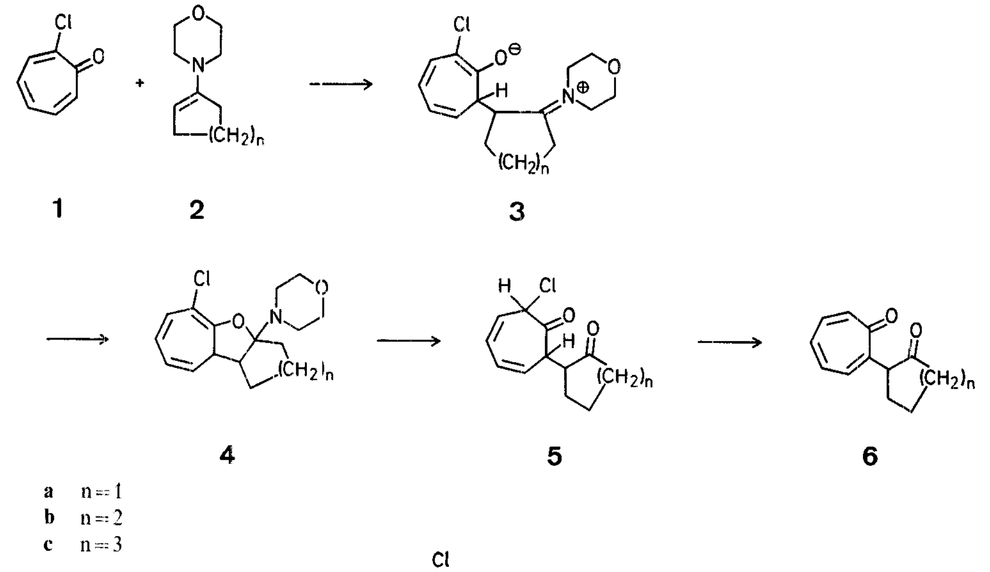
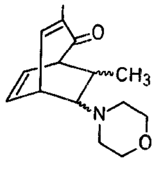
In a previous communication[1], we described cycloaddition reactions of tropone with enamines. We now report a similar cycloaddition of 2-chlorotropone (**1**) with enamines (**2**), giving either 1,8- or 1,4-cycloadducts. The former are easily converted into 2-(2-oxocycloalkyl)-tropones (**6**).

Reactions of **1** with 1-morpholinocyclopentene (**2**, n = 1), -cyclohexene (**2**, n = 2), and -cycloheptene (**2**, n = 3) in ethanol readily proceed at room temperature (slightly exothermally) to give the corresponding crystalline 1,8-cycloadducts **4a** (m.p. 98–98.5°), **4b** (m.p. 86–87°), and **4c** (m.p. 74–74.5°) in 62, 73, and 58% yield, respectively. The reaction of **1** with 1-morpholinopropene, an acyclic enamine, gave rise to a 1,4-cycloadduct (**7**; m.p. 115–118°, dec; $\nu_{C=O}$: 1672 cm^{-1}). The N.M.R. data of **4** (the integral area of the olefinic protons corresponds to 4H) and the result of the hydrolysis of **4** described below indicate that the enamines initially attacked the C-7 position of the tropone[2].

The reactions also proceeded without a solvent. The I.R. and N.M.R. spectra of the reaction mixtures indicate that the reactions are complete within 30 min. and the formation of adducts is quantitative.

Adduct **4b** was easily hydrolyzed by 2*N* hydrochloric acid to give 5-chloro-6-oxo-7-(2-oxocyclohexyl)-cyclohepta-1,3-diene (**5b**) in 84% yield. Compound **5b** is unstable and decomposes even at room temperature. Treatment of **5b** with triethylamine in dichloromethane at room temperature gave 2-(2-oxocyclohexyl)-tropone (**6b**) in high yield. Similar hydrolysis of **4a** did not yield the corresponding chlorodiketone (**5a**) but directly 2-(2-oxocyclopentyl)-tropone (**6a**). However, similar hydrolysis of the adduct **4c** yielded





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neither the chlorodiketone **5c** nor the tropone derivative **6c** but rather unstable and yet unidentified solids which contain a morpholino group.

For the purpose of syntheses of compounds **6a** and **6b**, a one-step process, without isolation of the intermediates, was successfully used.

6-Chloro-4a-morpholino-1,2,3,4,4a,10b-hexahydro-10a*H*-benzo[*b*]-cyclohepta[*d*]furan (4b), by Reaction of 2-Chlorotropone (1) with 1-Morpholinocyclohexene (2, n = 2):

To a solution of 1-morpholinocyclohexene (1.32 g) in absolute ethanol (4 ml) at room temperature was added 2-chlorotropone (1.00 g). When the reaction mixture was allowed to stand at room temperature, colorless crystals separated. After 5 hr, the mixture was cooled in an ice-bath for 30 min.; the product was then collected by filtration and washed with a small amount of cold ethanol; yield: 1.615 g (73.5%); colorless prisms, m.p. 86–87° (from dichloromethane/methanol).

$C_{17}H_{22}NO_2Cl$	calc.	C 66.35	H 7.20	N 4.55
	found	66.40	7.37	4.50

I.R. (KBr): ν_{max} = 1632, 1621, 1558, 1207, 1118, 860, 834, 788 cm^{-1}.

U.V. (isooctane): λ_{max} = 213 (log ε = 4.34), 317 nm (3.55).

N.M.R. ($CDCl_3$): δ = 6.36–5.85 (m, 3H), 4.98 (ddd, 1H, J = 8.5, 3.3, 1.5 Hz), 3.62 (m, 4H), 3.00–2.40 (m, 5H), 2.17 (m, 1H), 1.88–1.27 (m, 8H).

5-Chloro-6-oxo-7-(2-oxocyclohexyl)-cyclohepta-1,3-diene (5b):

To a suspension of the adduct **4b** (1.00 g) in ethanol (4 ml) was added 2*N* hydrochloric acid (10 ml) with stirring in an ice-bath. The reaction mixture became a clear solution whereupon colorless crystals separated. After 30 min., the crystals were collected by filtration; yield: 0.651 mg (84%); colorless prisms, m.p. 89° (dec.), from dichloromethane/methanol.

$C_{13}H_{15}O_2Cl$	calc.	C 65.42	H 6.33
	found	65.59	6.41

I.R. (KBr): ν_{max} = 1723, 1700 cm^{-1}.

U.V. (isooctane): λ_{max} = 235 (log ε = 3.73), 285 nm (2.92).

N.M.R. ($CDCl_3$): δ = 6.16 (d-like, 2H), 5.66 (m, 2H), 5.29 (d, 1H, J = 5.6 Hz), 3.72 (t, 1H, J = 6 Hz), 3.30 (m, 1H), 2.4–1.4 (m, 8H).

2-(2-Oxocyclohexyl)-tropone (6b):

To a solution of compound **5b** (0.270 g) in dichloromethane (6 ml) was added triethylamine (0.3 ml) at room temperature. After 15 min., the reaction mixture was twice washed with water and dried over sodium sulfate. Evaporation of the solvent under reduced pressure afforded almost pure **6b** as a yellowish liquid which on seeding crystallized; yield: 225 mg (99%); pale yellowish crystals, m.p. 57–59°.

$C_{13}H_{14}O_2$	calc.	C 77.20	H 6.98
	found	77.63	7.16

I.R. (KBr): ν_{max} = 1693, 1625, 1568, 788 cm^{-1}.

U.V. (isooctane): λ_{max} = 226 (log ε = 4.40), 305 (3.77), 316 nm (sh, 3.74).

N.M.R. ($CDCl_3$): δ = 7.0 (br., 5H), 3.92 (br., 1H), 2.46 (m, 2H), 2.3–1.5 (m, 6H).

2-(2-Oxocyclopentyl)-tropone (6a):

To a suspension of the adduct **4a** (1.00 g) in ethanol (3 ml) was added 2*N* hydrochloric acid (10 ml) at room temperature. Analysis by T.L.C. of the reaction mixture indicated the formation of **6a**. After 15 min., a saturated aqueous solution of sodium hydrogencarbonate (5 ml) was added to the yellowish reaction mixture, which then changed to a pinkish suspension. The reaction mixture was extracted five times with dichloromethane (a total of 50 ml). The organic layer was washed twice with water, dried over sodium sulfate, and the solvent evaporated. The reddish oily residue was chromatographed on silica gel, using benzene/ethyl acetate (4:1) as eluent. From the pale yellow fractions, 0.353 g (55%) of pale yellowish crystals (**6a**) were obtained; m.p. 74.5–76°.

$C_{12}H_{12}O_2$	calc.	C 76.57	H 6.43
	found	76.47	6.38

I.R. (KBr): ν_{max} = 1724, 1624, 1574, 783 cm^{-1}.

U.V. (ethanol) λ_{max} = 228 (log = 4.36), 312 (3.87), 320 nm (3.86).

N.M.R. ($CDCl_3$): δ = 7.43 6.88 (m, 5H), 3.22 (t, 1H, J = 9.0 Hz), 2.87–1.83 (m, 6H).

A One-Step Synthesis of 2-(2-Oxocyclohexyl)-tropone (6b):

To a solution of 1-morpholinocyclohexene (0.703 g) in absolute ethanol (2 ml) at room temperature was added 2-chlorotropone (0.560 g). After 30 min., 2*N* hydrochloric acid (10 ml) was added to the reaction mixture. The mixture was then stirred for another 30 min., dichloromethane (15 ml) was added to dissolve the separated solid, and the layers were separated. The organic layer was once washed with water, and the triethylamine (0.605 g) was added. After stirring for 5 min., the reaction mixture was washed twice with water, and dried with sodium sulfate. Evaporation of the solvent afforded 0.805 g of crude **6b** which contained a small amount of cyclohexanone.

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