Chemistry of Heterocyclic Compounds, Vol. 39, No. 8, 2003

FORMATION OF HETEROCYCLIC α-OXO THIOKETONES USING N-CHLOROSULFENYLSUCCINIMIDE

Yu. G. Shermolovich, S. V. Emets, and A. A. Tolmachev

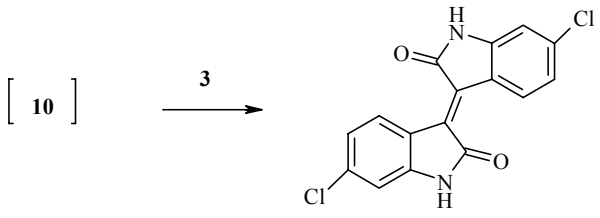
N-Chlorosulfenylsuccinimide is a suitable reagent for the generation of heterocyclic α-oxo thioketones. The latter readily undergo [4 + 2] cycloaddition with 1,3-dienes to give heterocyclic compounds containing spirocyclic thiine substituents.

Keywords: α-oxo thioketone, thiin, N-chlorosulfenylsuccinimide.

We have previously studied the synthesis of spirocyclic derivatives of 4-thioxo-2-pyrazolin-5-ones using N-chlorosulfenylphthalimide and 2-pyrazolin-5-ones [1]. We showed that this method could be used successfully for other heterocyclic systems containing an active α-methylene group to an oxo substituent. N-chlorosulfenylsuccinimide **4** can be used as well as N-chlorosulfenylphthalimide to obtain an increased yield of the desired products and to facilitate their further purification.

Chroman-2,4-dione (**1**), N,N'-dimethylbarbituric acid (**2**), and 6-chloroindolin-2-one (**3**) were used as the heterocyclic starting materials. The sulfenamides **5-7** decomposed *in situ* with pyridine to give the corresponding α-oxo thioketones **8-10**. The thiones **8-10** are highly reactive unstable compounds which cannot be isolated in the pure state. However their generation from the sulfenamides **5-7** in the presence of 2,3-dimethylbuta-1,3-diene as a dienophile trap led to the formation of products of [4 + 2] cycloaddition – spirocyclic thiines **11-13**.

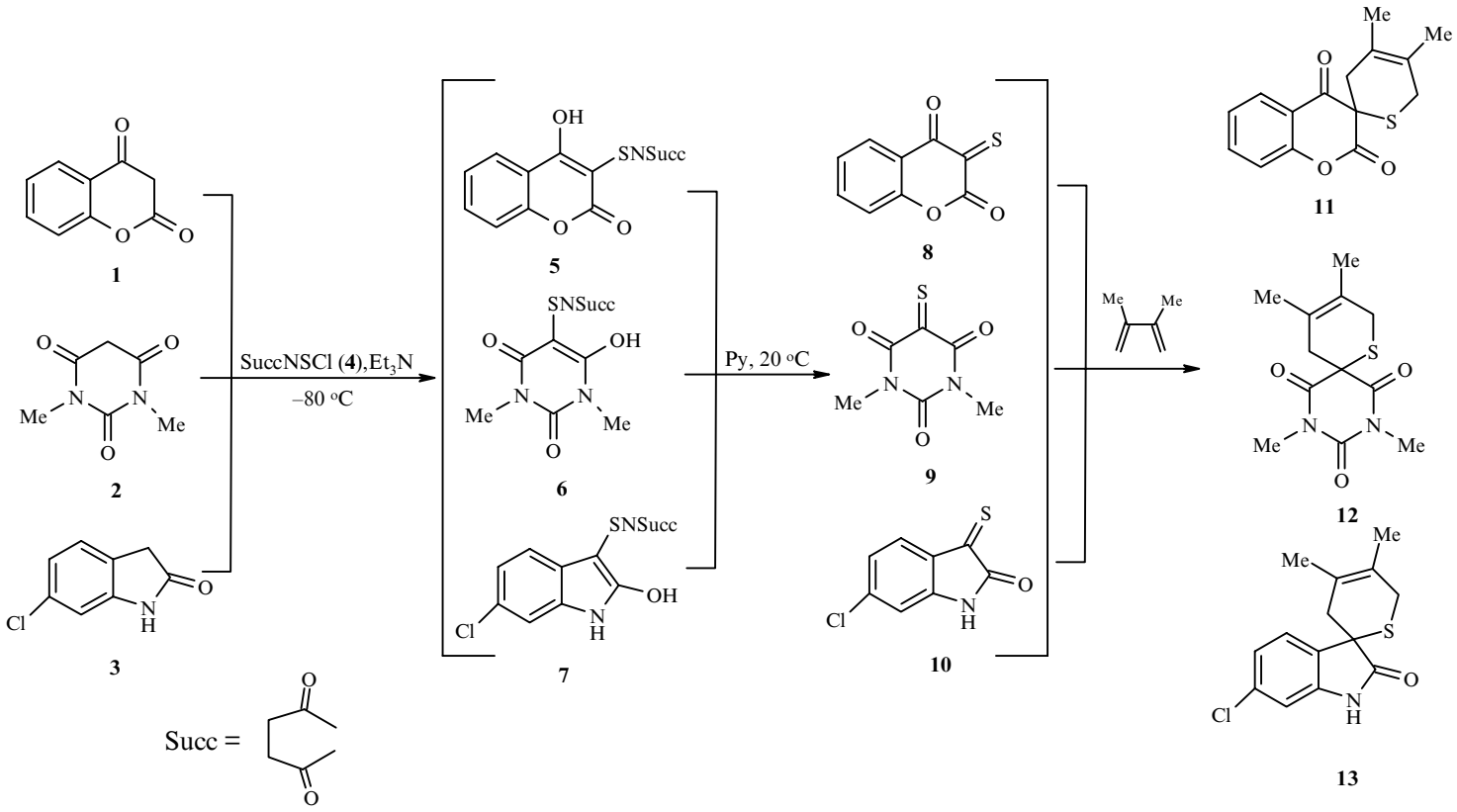
In the case of the indolinone **3** a side reaction occurred to a considerable extent to give the 6,6'-dichloro derivative **14**, evidently by condensation of the thioketone **10** with a molecule of the indolinone starting material **3**.



14

Institute of Organic Chemistry, Ukraine National Academy of Sciences, Kiev 02094; e-mail: sherm@ukrpack.net. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, 1231-1233, August 2003. Original article submitted September 3, 2001.

 0009-3122/03/3908-1076$25.00


SuccNSCl (4),Et3N
–80 °C
Py, 20 °C
Succ =

EXPERIMENTAL

IR spectra in KBr disks were recorded on a UR-10 machine, ^{1}H and ^{13}C NMR spectra were recorded with a Varian-VXR spectrometer (300 and 75 MHz respectively) in $CDCl_3$ (compounds **11-13**) and DMSO-d_6 (compound **14**) with TMS as internal standard.

Thiins 11-13. (General Method). A solution of the corresponding heterocyclic compound **1-3** (3.29 mmol) and triethylamine (3.29 mmol) in methylene chloride (20 ml) was added dropwise and with stirring over 10 min to a solution of N-chlorosulfenylsuccinimide (3.94 mmol) in methylene chloride (20 ml) at -80°C. The temperature of the solution was slowly raised to 0°C and 2,3-dimethylbuta-1,3-diene (6.58 mmol) was added. After 1 h at 20°C pyridine (9.87 mmol) was added, the reaction mixture was kept for 12 h, washed with water (5 × 50 ml), and dried with Na_2SO_4. Methylene chloride was evaporated and the raw material was dried in vacuum (0.07 mmHg).

(5,6-Dihydro-3,4-dimethyl-2H-thiin)-6-spiro-3'(chroman-2',4'-dione) (11). Yield of the solid brownish raw material 83%. Colorless crystals were obtained after recrystallization from ethyl acetate, yield 40%; mp 131-134°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.80 (3H, s, CH_3); 1.84 (3H, s, CH_3); 2.65, 2.99 (2H, $^2J_{AB}$ = 17.7, CH_2); 2.99, 3.21 (2H, $^2J_{AB}$ = 16.8, CH_2); 7.19 (1H, d, ^3J = 7.7, Ar); 7.29 (1H, t, ^3J = 7.7, Ar); 7.65 (1H, t, ^3J = 7.7, Ar); 7.93 (1H, d, ^3J = 7.7, Ar). ^{13}C NMR spectrum, δ, ppm: 19.33 (CH_3), 20.03 (CH_3), 30.80 (CH_2), 31.23 (CH_2), 54.87 (spiro C), 117.05, 118.31, 121.31, 124.87, 126.39, 127.64, 136.53 (C=C, Ar), 165.58 (COO), 186.55 (C=O). IR spectrum, ν, cm^{-1}: 1680 (C=O), 1750 (COO). Found: *m/z* 268 (M^+). $C_{15}H_{14}O_3S$. Calculated: M = 274.34. Found, %: C 65.03; H 5.03; S 11.88. $C_{15}H_{14}O_3S$. Calculated, %: C 65.67; H 5.14; S 11.69.

(5,6-Dihydro-3,4-dimethyl-2H-thiin)-6-spiro-5'-(1',3'-dimethylperhydropyrimidine-2',4',6'-trione (12). The orange oily raw material (yield 91%) was dissolved in ether (10 ml). The ether solution was evaporated and the residue dried in vacuum (0.07 mm Hg). The light colored oil solidified on standing in air, yield 68%; mp 61-65°C. ^{1}H NMR spectrum, δ, ppm:, 1.81 (6H, s, 2CH_3); 2.73 (2H, s, CH_2); 3.14 (2H, s, CH_2); 3.32 (6H, s, 2NCH_3). Found: *m/z* 268 (M^+). $C_{12}H_{16}N_2O_3S$. Calculated: M = 268.34. Found, %: C 53.44; H 6.09; N 10.01; S 11.88. $C_{12}H_{16}N_2O_3S$. Calculated, %: C 53.71; H 6.01; N 10.44; S 11.95.

(5,6-Dihydro-3,4-dimethyl-2H-thiin)-6-spiro-3'-(6'chloroindolin-2'one) (13). The raw material was a mixture of isoindigo **14** and the spiro compound **13**. It was treated with chloroform (15 ml) and the reddish violet insoluble compound **14** was filtered off (47%). The chloroform solution was evaporated and the oily solid was chromatographed on a silica gel column (eluent chloroform) to give compound **13** (yield 47%); mp 193-196°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.76 (3H, s, CH_3); 1.89 (3H, s, CH_3); 1.86 (2H, s, CH_2); 3.05, 3.75 (2H, $^2J_{AB}$ = 17.2, CH_2); 6.94 (1H, d, ^4J = 1.8, Ar); 7.01 (1H, dd, ^3J = 8.1, ^4J = 1.8, Ar); 7.11 (1H, d, ^3J = 8.1, Ar); 8.63 (1H, s, NH). IR spectrum, ν, cm^{-1}: 1700 (C=O), 3200 (NH). Found: *m/z* 280 [M^+]. $C_{14}H_{14}ClNOS$. Calculated: M = 279.29. Found, %: N 5.00; S 11.08. $C_4H_{14}ClNOS$. Calculated, %: N 5.01; S 11.46.

6,6'-Dichloro-3,3'-biindolinilidene-2,2'-dione (14) , was recrystallized from DMSO to give red-violet crystals, yield 35%; mp 360°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.85 (2H, d, ^4J = 1.5, Ar); 7.00 (2H, dd, ^3J = 8.7, ^4J = 1.5, Ar); 9.05 (2H, d, ^3J = 8.7, Ar); 10.92 (2H, s, 2 NH). IR spectrum, ν, cm^{-1}: 1680 (C=O), 3180 (NH). Found, %: C 57.97; H 2.52; N 8.11. $C_{16}H_8Cl_2N_2O_2$. Calculated, %: C 58.03; H 2.44; N 8.46.

REFERENCE

1. Yu. G. Shermolovich and S. V. Emets, *Khim. Geterotsikl. Soed.,* 187 (2000).