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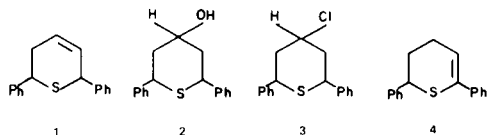
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Synthesis of 5,6-dihydro-2*H*-thiopyrans by mild dehydromesylation of the corresponding tetrahydro-4*H*-thiopyran-4-mesyates using commercial grade Woelm W-200 (activity, Super 1) neutral alumina is described. *Cis*- and *trans*-stereoisomers of 2,6-diphenyl-5,6-dihydro-2*H*-thiopyrans were prepared for the first time without isomerization.

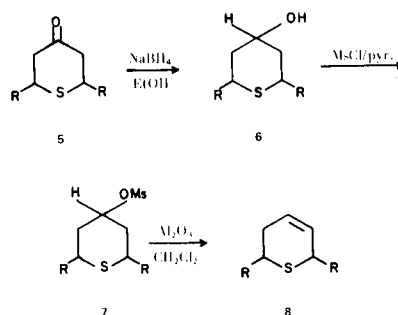
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In the course of our study of thiopyran chemistry (1), we required a substantial amount of the hitherto unknown 2,6-diphenyl-5,6-dihydro-2*H*-thiopyran (1). A literature survey (2) has produced few syntheses which are efficient enough for our purpose. Most synthetic approaches reported were essentially following the original work of Arndt and Schauder (3), *via* a direct dehydration of the corresponding 4*H*-thiopyran-4-ols either under acid catalysis (4) or by pyrolysis in the presence of anhydrous magnesium sulfate (5). Both of these methods, however,



failed to dehydrate the alcohol 2. Neither the dehydrochlorination of 3 nor the pyrolysis of the acetate or benzoate of 2 led to olefins (6). A Bamford-Stevens reaction on the *p*-toluenesulfonylhydrazone of *cis*-2,6-diphenyltetrahydro-4*H*-thiopyran-4-one (5, R = Ph) produced in low yield only the isomeric 3,4-dihydro-2*H*-thiopyran (4) (6) instead of the desired 5,6-dihydro-2*H*-thiopyran (1).

In seeking a mild elimination procedure for the synthesis of 1, we found that the dehydromesylation reaction recently developed by Posner and coworkers (7) using activated neutral alumina afforded good yields of the required olefins. Thus, a simple synthesis of 5,6-dihydro-2*H*-thiopyrans can be readily realized from the corresponding tetrahydro-4*H*-thiopyran-4-ones (1) by the synthetic sequence shown. The alcohols 6 were readily obtained by



sodium borohydride reduction of the corresponding ketone 5 in ethanol. Due to the conformational mobility of *trans*-2,6-diphenyl (5, R = Ph), there is, as expected, only one alcohol (equatorial) formed by the reduction. The rigid *cis*-isomer 5 (R = Ph), when treated with lithium aluminum hydride, gave two diastereoisomeric alcohols in a 10:1 ratio with the equatorial predominant (6). By increasing the reaction temperature (refluxing ethanol) and using sodium borohydride, an equatorial-to-axial ratio of alcohols of 7.7:2.3, as determined by silylation and glc analysis, was obtained. Mesylation in the usual manner using methanesulfonyl chloride and pyridine in methylene chloride gave 7 in nearly quantitative yields. Dehydromesylation was accomplished by stirring an 8- to 10-fold excess of Woelm W-200 (activity Super 1), neutral alumina in methylene chloride at ambient temperature. Removal of alumina by filtration produced the desired olefins 8 in good yields (Table I). The structures were fully supported by their ir, nmr, and high-resolution mass spectra as well as elemental combustion analyses. Another dehydromesylation reaction using sodium acetate and hexamethyl-

Table I

Synthesis of 5,6-Dihydro-2*H*-thiopyrans

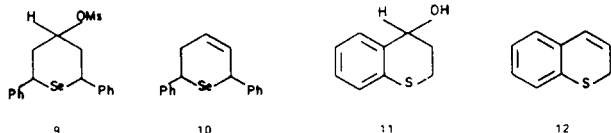
R	6		7		8	
	M.p., °C	Yield %	M.p., °C	Yield %	M.p. (B.p.)	Yield %
H	53 (5)	95 (a)	--	100 (a)	(76-78°/62 mm) (9)	55 (a,b)
<i>trans</i> -Ph	142-143 (6)	85	82	96 (a)	34.1° (104-115°/1 μ)	75 (c)
<i>cis</i> -Ph (eq. OH)	155-156 (6)	70	97.1	85	74°	62 (b)
Anisyl (d)	190-193	71	141-143	97	(192-194°/5 μ) (e)	51 (a)

(a) Yield of sufficiently pure material suitable for subsequent reaction. (b) Yield based on the starting alcohol. (c) Pure sample obtained by distillation. (d) Stereochemistry is not fully established (nmr spectrum suggested a *cis* configuration). (e) Decomposition and compositional changes occurred during the distillation since a major new spot was found on the tlc plate.

phosphoramidate (8) also has been tried, but the results were somewhat inferior.

By this method we were able to synthesize, for the first time, the pure *cis*- and *trans*-2,6-diphenyl-5,6-dihydro-2*H*-thiopyrans (1) from the corresponding *cis*- and *trans*-ketone 5 (R = Ph) and to study their nmr spectra in detail with respect to their preferred conformation in solution. The conformation of the 5,6-dihydro-2*H*-thiopyran ring system has been the subject of much interest. A quasi-boat conformation was recently proposed to explain the formation of the kinetically favored *trans*-2,6-diphenyl-tetrahydro-4*H*-thiopyran-4-one (5, R = Ph) from the hydrogen sulfide cyclization of dibenzalacetone (6). Study of the nmr spectra of *cis*- and *trans*-1 in relation to their conformations is being pursued and the results will be published later. Contrary to an earlier observation (6), the *cis*- and *trans*-olefin 1 are remarkably stable to thermal rearrangement. In fact, the *trans*-1 can be distilled *in vacuo* without change.

Following the same procedure, we also prepared the selenium analog 10 from the corresponding mesylate 9.



The structure was fully supported by nmr and high-resolution mass spectra. Attempts to prepare the mesylate of thiochroman-4-ol (11) under a variety of conditions were not satisfactory, presumably due to the unstable nature of the mesylate formed under basic reaction conditions. 2*H*-Thiochromen (12) (10) can, however, be prepared in low yield by direct dehydration of 11 with alumina.

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## EXPERIMENTAL

### 4-Mesyloxytetrahydro-4*H*-thiopyran (7, R = H).

To a solution of 7 g. (0.059 mole) of tetrahydro-4*H*-thiopyran-4-ol (6, R = H) (5) and 5 g. (1.1 equiv) of pyridine in 100 ml. of methylene chloride at room temperature was added dropwise 7.5 g. (1.1 equiv) of methanesulfonyl chloride. The solution was kept at ambient temperature for two days, then poured into water and ice; the organic phase was separated, dried (magnesium sulfate), and concentrated giving 12 g. (~100%) of an oil: (<sup>1</sup>H nmr): δ 2.1 (m, 4H), 2.5 (m, 4H), 2.9 (s, 3H, CH<sub>3</sub>SO<sub>3</sub>-), and 4.5 (m, 1H, methine) ppm; HRMS: m/e 196.0230 (M<sup>+</sup>, Calcd. for C<sub>16</sub>H<sub>12</sub>O<sub>3</sub>S<sub>2</sub>: 196.0228).

### 5,6-Dihydro-2*H*-thiopyran (8, R = H).

A mixture of 12 g. (0.059 mole) of crude 7 (R = H) and 80 g. of Woelm W-200 (Super I) alumina in 200 ml. of methylene chloride was stirred at ambient temperature for 1-2 days and the

reaction was followed by tlc until the disappearance of starting material. The mixture was filtered and the filtrate was concentrated *in vacuo* giving 3.2 g. (55%) of crude 8 (R = H) which was purified by distillation, b.p. 76-78° (62 mm) [lit. (9) b.p. 75° (58 mm)]; ir (neat): 1650 (C=C); <sup>1</sup>H nmr: δ 2.3 (m, 2H, -CH<sub>2</sub>CH=), 2.7 (t, 2H, -CH<sub>2</sub>CH<sub>2</sub>S-), 3.1 (m, 2H, -SCH<sub>2</sub>CH=), and 5.7 (m, 2H, olefinic) ppm.

### *trans*-2,6-Diphenyl-4-mesyloxytetrahydro-4*H*-thiopyran (7, R = Ph).

To a cooled solution of 36.4 g. (0.135 mole) of *trans*-2,6-diphenyltetrahydro-4*H*-thiopyran-4-ol (6, R = Ph) (6) and 13 g. (0.165 mole) of pyridine in 250 ml. of methylene chloride was added dropwise 19 g. (0.165 mole) of methanesulfonyl chloride. The mixture was allowed to stir at ambient temperature until a tlc (dichloromethane) assay showed the disappearance of starting alcohol. Workup in the same manner described for 7 (R = H), gave 44.8 g. (96%) of a solid which was shown by tlc and <sup>1</sup>H nmr to be one isomer. A high resolution mass spectrum showed M<sup>+</sup> at m/e 348.0838. An analytical sample was obtained by recrystallization from benzene and hexanes, m.p. 82°; <sup>1</sup>H nmr: δ 2.85 (s, 3H, CH<sub>3</sub>SO<sub>3</sub>-), 4.92 (septet, 1H, methine), 4.39 (t, J = 4.3 Hz, 1H, benzylic), 4.00 (d, d, J = 10.8 and 3.4 Hz, 1H, benzylic), 2.3-3.2 (m, 4H, ring methylene), and 7.4 (m, 10, ArH) ppm.

*Anal.* Calcd. for C<sub>18</sub>H<sub>20</sub>O<sub>3</sub>S<sub>2</sub> (348.0854): C, 62.0; H, 5.8; S, 18.4. Found: C, 62.2; H, 6.0; S, 18.3.

### *cis*-2,6-Diphenyl-4-*cis*-mesyloxytetrahydro-4*H*-thiopyran (1, R = Ph).

The procedure described for the preparation of *trans*-7 (R = Ph) was applied to 16.53 g. (0.061 mole) of the *cis*-alcohol 6 (R = Ph), m.p. 155-156° (lit. (6) m.p. 155-156°) yielding 24 g. of solid which was recrystallized from benzene and hexane giving 13.6 g. (85%) of pure *cis*-mesylate, m.p. 97.1°; <sup>1</sup>H nmr: δ 2.0-2.9 (m, 4H, ring methylene), 3.02 (s, 3H, CH<sub>3</sub>SO<sub>3</sub>-), 4.17 (d, d, J = 11.7 and 2.2 Hz, 2H, benzylic), 4.90 (m, 1H, methine), and 7.37 (m, 10H, ArH) ppm.

*Anal.* Calcd. for C<sub>18</sub>H<sub>20</sub>O<sub>3</sub>S<sub>2</sub> (348): C, 62.0; H, 5.8; S, 18.4. Found: C, 61.8; H, 5.6; S, 18.5.

### *cis*-2,6-Diphenyl-5,6-dihydro-2*H*-thiopyran (8, R = Ph).

To a solution of 13 g. (0.0374 mole) of *cis*-7 (R = Ph) in 250 ml. of methylene chloride was added 130 g. of Woelm W-200 alumina (neutral, Super I). The reaction was worked up in the manner described above, giving 5.8 g. (62%) of pure solid product. The structure was fully supported by <sup>1</sup>H nmr. An analytical sample was obtained by recrystallization (benzene and hexanes), m.p. 74°; ir (potassium bromide): 1600 (C=C) and 2860 (HC=) cm<sup>-1</sup>; <sup>1</sup>H nmr: δ 2.3-3.0 (m, 2H, methylene), 4.26 (d, d, J = 10.3 and 5.0 Hz, 1H, benzylic C-5 protons), 4.97 (m, 1H, C-2 benzylic), 5.97 (m, 2H, olefinic), and 7.35 (m, 10H, ArH) ppm.

*Anal.* Calcd. for C<sub>17</sub>H<sub>16</sub>S (252): C, 80.9; H, 6.4. Found: C, 80.9; H, 6.2.

### *trans*-2,6-Diphenyl-5,6-dihydro-2*H*-thiopyran (8, R = Ph).

To a solution of 22.4 g. (0.0643 mole) of *trans*-7 (R = Ph) in 300 ml. of methylene chloride at room temperature was added 220 g. of Woelm W-200 alumina (neutral, Super I). The suspension was stirred until a tlc assay of the mixture showed the disappearance of the starting mesylate. The mixture was filtered and the filtrate was concentrated *in vacuo* giving 12.5 g. (77%) of pure product in the form of an oil. The structure was fully supported by <sup>1</sup>H nmr and high-resolution mass spectrum (m/e = M<sup>+</sup>, 252.0959). An analytical sample was purified by vacuum distillation (b.p. 104-115°/1 μ). The pure sample slowly solidified on keeping in the cold, m.p. 34.1°; ir (film): 1600 (C=C) and 2810 (HC=) cm<sup>-1</sup>; <sup>1</sup>H nmr: δ 2.64 (m, 2H, methylene), 3.93

(t,  $J = 5.9$  Hz, 1H, benzylic C-5 proton), 4.3 (d,  $J = 1.8$  Hz, 1H, benzylic C-2 protons), 6.09 (m, 2H, olefinic), and 7.3 (m, 10, ArH) ppm.

*Anal.* Calcd. for  $C_{17}H_{16}S$  (252.0971): C, 80.9; H, 6.4; S, 12.7. Found: C, 81.1; H, 6.3; S, 13.1.

2,6-Bis(4-Methoxyphenyl)-4-hydroxytetrahydro-4*H*-thiopyran (**6**, R = *p*-anisyl).

A mixture of 19 g. (0.06 mole) of **5** (R = *p*-anisyl) (**1**) in 800 ml. of boiling alcohol was stirred and 2 g. (0.052 mole) of sodium borohydride was added in portions, and the heating and stirring were continued until the solid dissolved (about 30 minutes). The hot solution was diluted with water and chilled, and the solid (13.5 g.) was collected. The ir spectrum was similar to that of the corresponding *cis*-diphenyl derivative **6**, and this material was used for subsequent mesylation without further purification.

2,6-Diphenyl-4-hydroxytetrahydro-4*H*-selenopyran.

A solution of 4 g. (0.0127 mole) of crude 2,6-diphenyl-4*H*-selenopyran-4-one (**12**) in 100 ml. of alcohol was stirred and 0.5 g. (0.013 mole) of sodium borohydride was added. The solution was stirred for 1 hour, diluted with water, and chilled giving 2 g. of the alcohol, m.p. 130-140°, which was used directly without further purification.

2,6-Bis(4-Methoxyphenyl)-4-mesylytetrahydro-4*H*-thiopyran (**7**, R = *p*-anisyl).

The procedure described for the preparation of **7** (R = Ph) was repeated using 13.5 g. (0.041 mole) of **6** (R = *p*-anisyl) giving 16 g. of solid which was recrystallized from benzene and hexane, m.p. 141-143°. The stereochemistry was found to be *cis-cis* by comparing the  $^1H$  nmr of this sample with that of the *cis*-2,6-diphenyl-*cis*-4-mesyl isomer **7** (R = Ph) in the benzylic regions:  $^1H$  nmr:  $\delta$  2-2.9 (m, 4H), 3.04 (s, 3H, Ms), 3.81 (s, 6H,  $CH_3O$ ), 4.13 (d, d,  $J = 12$  and 2.6 Hz, 2H, benzylic), 4.87 (m, 1H, methine), and 6.88, 7.34 (d, d of  $A_2B_2$ , 8H, ArH) ppm.

*Anal.* Calcd. for  $C_{20}H_{24}O_5S_2$  (408): C, 58.8; H, 5.9; S, 15.7. Found: C, 58.9; H, 5.8; S, 15.5.

2,6-Bis(4-Methoxyphenyl)-5,6-dihydro-2*H*-thiopyran (**8**, R = *p*-anisyl).

The procedure described for the preparation of **8** (R = Ph) was used with 15 g. (0.0368 mole) of **7** (R = *p*-anisyl) giving 6 g. of **8** (R = *p*-anisyl) which gave a single spot on a tlc (benzene) plate. The splitting pattern of  $^1H$  nmr spectrum of the benzylic protons region is identical to that of the *cis*-2,6-diphenyl-**8** (R = Ph) suggesting the same *cis* stereochemistry;  $^1H$  nmr:  $\delta$  2.58 (m, 2H), 3.71 (s, 6H,  $CH_3O$ ), 4.2 (d, d,  $J = 9.8$  and 5.0 Hz, 1H, C-5 benzylic), 4.92 (m, 1H, C-2 benzylic), 5.94 (m, 2H, olefinic), and 6.83, 7.28 (d, d, 8H, ArH) ppm.

*Anal.* Calcd. for  $C_{19}H_{20}O_5S$  (312): C, 73.0; H, 6.5. Found: C, 72.7; H, 6.3.

2,6-Diphenyl-4-mesylytetrahydro-4*H*-selenopyran (**9**).

The mesylation procedure described for the other examples was repeated with 2 g. (6.3 mmoles) of crude 2,6-diphenyl-4-hydroxytetrahydro-4*H*-selenopyran (m.p. 130-140°) giving 2.3 g. (~100%) of **9** which gave a single spot on tlc (dichloromethane):  $^1H$  nmr:  $\delta$  2.6 (m, 4H), 3.4 (s, 3H, Ms), 4.2 (m, 2H, benzylic), 4.5 (m, 1H, methine), and 6.9 (m, 10H, ArH) ppm.

2,6-Diphenyl-5,6-dihydro-2*H*-selenopyran (**10**).

Demesylation of 2.3 g. (6.32 mmoles) of crude **9** in the usual manner gave 1.5 g. (79%) of **10** as a pale yellow oil showing a single spot on tlc (benzene). A high-resolution mass spectrum showed  $M^+$  at  $m/e$  300.0395 (Calcd. for  $C_{17}H_{16}Se$ : 300.0415). The structure is supported by  $^1H$  nmr:  $\delta$  2.73 (m, 2H), 4.55 (d, d,  $J = 11$  and 4.2 Hz, 1H, C-6 benzylic), 5.23 (m, 1H, C-2 benzylic), 6.04 (m, 2H, olefinic), and 7.3 (m, 10H, ArH) ppm.

*Anal.* Calcd. for  $C_{17}H_{16}Se$  (300): C, 68.0; H, 5.3. Found: C, 67.7; H, 5.0.

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