# An Unusually Easy Retro-Thio-Claisen Rearrangement. Stereoselective Synthesis of Tetrahydrocyclopenta[*b*]thiopyran

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Although reverse-Claisen rearrangement is limited to rather unusual structures,[1-6] we have shown recently that in sulfur chemistry it may occur cleanly with appropriate simple γ-unsaturated thiones.[7,8] During an investigation of the synthesis of unsaturated thioketones,[9] we encountered another interesting example of such a reaction. For this study we needed thiones **2** in order to prepare labile conjugated thioketones **3** by a retro-Diels–Alder reaction performed in high-vacuum flash thermolysis according to Scheme I.

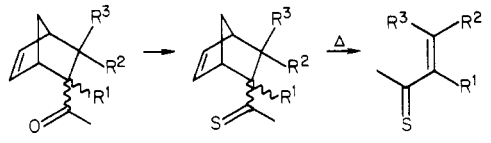
Sulfurization of the known pure endo or exo ketones **1a–d** was attempted in mildly acidic[10] conditions ($H_2S$, $HC(OEt)_3$, catalytic $ZnCl_2$) in methanol at 0 °C. In the case of the exo ketones **1a–d**, the expected exo thioketones were obtained easily.[9] With endo ketones **1a–c**, unique unexpected products **4a–c** were formed, whereas the endo ketone **1d** afforded indeed the endo thioketone **2d**. The structure of compounds **4a–c** prepared from endo **1a–c** was proved by spectral data to be a 4,4a,5,7a-tetrahydrocyclopenta[*b*]thiopyran.

These results may be interpreted as follows. In all cases the thiones **2** are formed. The non sterically hindered thiones **2a–c** then undergo a [3.3] sigmatropic shift (retro-thio-Claisen) to afford compounds **4** (see Scheme II). This reaction occurs at an exceptionally low temperature (≤0 °C) as compared to known reverse oxy-Claisen reactions. We could find no evidence of such a rearrangement reported for compounds **1**, even at high temperature.[11] The sterically hindered endo thioketone **2d** could be isolated by operating below 50 °C. Above this temperature, it is slowly transformed into **4d**. In order to explain the easy transformation **2** → **4** and avoid any possible acid catalytic effect, we studied the kinetics of this reaction with thioketone **2d** in a neutral media. We used the spectral measurement of the disappearance of thioketone **2d** at $\lambda_{max}$ = 515 nm (ε 11), where **4d** is totally transparent, in decahydronaphthalene at five different temperatures (see Table I).

The rearrangement gave good first-order kinetics. The activation energy $\Delta E^{\ddagger}$ = 22.6 kcal/mol is slightly lower than the one we observed for the related retro-thio-Claisen reaction.[7,8] Relief of strain in the bicyclo[2.2.1]heptene may account for this difference. This factor might also explain that the equilibrium is shifted toward the formation of the sulfide **4**. A highly negative activation-entropy variation is observed, in agreement with a [3.3] sigmatropic process and a high order for the tricyclic transition state (whether pseudo-aromatic or diradicaloid.[15]

In the case of the less substituted thiones **2a–c** we could not investigate the kinetics in neutral media. However, it seems reasonable to deduce from the comparison of the reaction in acidic conditions that the rearrangement of thiones **2a–c** would exhibit an even lower activation energy. This work confirms the ease of the retro-Claisen reaction in the sulfur series and opens the way to cyclopenta[*b*]-thiopyrans **4** with stereochemical control at three centers.

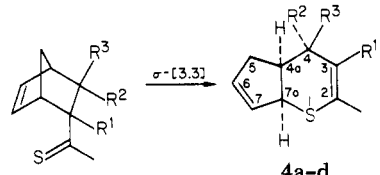
Scheme I



**1** **2** **3**

**a**, $R^1 = R^2 = R^3 = H$; **b**, $R^1 = R^2 = H$; $R^3 = CH_3$; **c**, $R^2 = R^3 = H$; $R^1 = CH_3$; **d**, $R^1 = H$; $R^2 = R^3 = CH_3$

Scheme II



*endo*-**2a–d** **4a–d**

Table I. Kinetic Data for Rearrangement 2d → 4d

| *T*, K | $k \times 10^5$, $s^{-1}$ | correlation coeff |
|---|---|---|
| 344 | 3.47 | 0.987 |
| 354 | 8.90 | 0.998 |
| 365 | 21.73 | 0.999 |
| 375 | 50.52 | 0.996 |
| 386 | 131.50 | 0.997 |
| $\Delta E^{\ddagger}$ = 22.61 kcal $mol^{-1}$ | | 0.999 |
| $\Delta S^{\ddagger}$(354 K) = −15.56 eu | | |
| log *A* = 9.90 | | |

## Experimental Section

$^1H$ and $^{13}C$ NMR spectra were recorded on Varian EM-360 and Bruker WP-60 spectrometers, respectively, with tetramethylsilane as internal standard. IR spectra were obtained with a Perkin-Elmer 225 spectrometer. Kinetics of the thermal rearrangement were studied in decahydronaphthalene solution by UV techniques on a Unicam SP-700 spectrophotometer. Elemental analyses were performed at CNRS Microanalysis Laboratory of Caen.

Endo and exo ketones **1a–d** were prepared by known procedures[12-14] and purified by preparative GLC performed on a Varian 2700 chromatograph equipped with a 0.375 in. × 20 ft 20% Carbowax 20 M Chromosorb WAW 60 column.

**General Sulfurization Method.** Hydrogen sulfide was bubbled into an ice-cooled methanol solution (5 mL) of ketone **1** (0.035 mol), trimethyl orthoformate (0.040 mol), and anhydrous zinc chloride (60 mg) at a rate of 25 mL/min. After 4–5 h of treatment at 0 °C, the mixture was poured into iced water and extracted by 3 × 50 mL of pentane. The organic layers were washed with brine, dried over $MgSO_4$, and concentrated under vacuum without heating. The crude product was purified by liquid chromatography on silica gel, eluting with petroleum ether. The yield was about 90%. Analytical samples of each product **4** were obtained by GLC at 150 °C.

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**4,4a,5,7a-Tetrahydro-2-methylcyclopenta[*b*]thiopyran (4a)** was prepared from endo ketone **1a**:[12] $^1$H NMR ($CCl_4$) $\delta$ 1.87 (s, 3 H, $CH_3C$=), 2.03-2.33 (m, 4 H, $CH_2$), 2.73 (m, 1 H, angular H on C-4a), 4 (br d, $J$ = 8 Hz, angular H on C-7a), 5.45-5.46 (m, 3 H); $^{13}$C NMR ($CDCl_3$) (C numbering of **4** in Scheme II) $\delta$ 24.5 (Me on C-2), 31 (C-4), 39 (C-4a + C-5), 51.6 (C-7a), 122.5 (C-3), 131.5 and 133 (C-6 and C-7), 134.5 (C-2); mass spectrum, $m/e$ 152 ($M^+$); IR (film) 3055, 3012, 1620 cm$^{-1}$.

Anal. Calcd for $C_9H_{12}S$: C, 70.99; H, 7.94; S, 21.06. Found: C, 71.16; H, 8.15; S, 21.26.

**4,4a,5,7a-Tetrahydro-2,4-dimethylcyclopenta[*b*]thiopyran (4b)** was prepared from endo ketone **1b**:[13] $^1$H NMR ($CCl_4$) $\delta$ 1.1 (d, $J$ = 7.5 Hz, 3 H), 1.85 (s, 3 H, $CH_3C$=), 2.05-2.33 (m, 3 H, $CH_2$, H on C-4), 2.97 (m, 1 H, angular H on C-4a), 4.1 (d, $J$ = 9, 2 Hz, angular H or C-7a), 5.32-5.47 (m, 3 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19 (Me on C-4), 24.5 (Me on C-2), 33.7 and 34.5 (C-4 and C-5), 46 (C-4a), 53.6 (C-7a), 128.5 (C-3), 131 and 134 (C-6 and C-7), 134.5 (C-2); mass spectrum, $m/e$ 166 ($M^+$); IR (film) 3060, 3010, 1625 cm$^{-1}$.

Anal. Calcd for $C_{10}H_{14}S$: C, 72.23; H, 8.48; S, 19.28. Found: C, 72.25; H, 8.28; S, 19.29.

**4,4a,5,7a-Tetrahydro-2,3-dimethylcyclopenta[*b*]thiopyran (4c)** was prepared from ketone **1c**:[13] $^1$H NMR ($CCl_4$) $\delta$ 1.85 (br s, 6 H, $CH_3C$=), 2.1-2.4 (m, 4 H, $CH_2$), 2.7-2.9 (m, 1 H, angular H on C-4a), 4 (br d, $J$ = 8.5 Hz, angular H on C-7a), 5.4-5.7 (m, 2 H, CH=CH); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.5 and 21.8 (Me on C-2 and C-3), 39, 39.3, and 40 (C-4, C-4a, and C-5), 53 (C-7a), 124.5 (C-3), 131 and 132 (C-6 and C-7), 132.5 (C-2); mass spectrum, $m/e$ 166 ($M^+$); IR (film) 3055, 1620 cm$^{-1}$.

Anal. Calcd for $C_{10}H_{14}S$: C, 72.23; H, 8.48; S, 19.28. Found: C, 72.21; H, 8.63; S, 19.08.

**4,4a,5,7a-Tetrahydro-2,4,4-trimethylcyclopenta[*b*]thiopyran (4d)** was prepared from endo thioketone **2d** by heating at 100 °C for 1 h: $^1$H NMR ($CCl_4$) $\delta$ 1.02 (s, 3 H, $CH_3$ on C-4), 1.17 (s, 3 H, $CH_3$ on C-4), 1.8 (s, 3 H, $CH_3C$=), 2.1-2.3 (m, 3 H, $CH_2$ and H on C-4a), 4.1 (br d, $J$ = 8.5 Hz, angular H on C-7a), 5.1 (br s, 1 H, H on C-3), 5.65 (br s, 2 H, CH=CH); $^{13}$C NMR ($CDCl_3$) $\delta$ 24 (Me on C-2), 27.5 and 29 (Me on C-4), 33.5 (C-4), 34.5, 47 (C-4a), 51.5 (C-7a), 124.5 (C-3), 131.3 and 132 (C-6 and C-7), 134.5 (C-2); mass spectrum, $m/e$ 180 ($M^+$); IR (film) 3050, 1620 cm$^{-1}$.

Anal. Calcd for $C_{11}H_{16}S$: S, 17.18. Found: S, 17.89.

**(*endo*-3,3-Dimethylbicyclo[2.2.1]hept-5-en-2-yl)ethanethione (2d)** was prepared by sulfurization of endo ketone **1d**:[14] yield 95%; $^1$H NMR $\delta$ 0.78 (s, 3 H, endo Me), 1.12 (m, 1 H), 1.47 (s, 3 H, exo Me), 1.62 (m, 1 H), 2.30 (m, 1 H), 2.6 (s, 3 H, CSMe), 3.03 (m, 1 H), 3.35 (m, 1 H), 5.95-6.5 (m, 2 H); $^{13}$C NMR $\delta$ 23.3 and 32 (2 Me), 42.8, 44.3, 47.6, 50, 55.2, 55.5, 135.3 and 135.9 (C=C), 261.4 (C=S); mass spectrum, $m/e$ 180 ($M^+$); UV (cyclohexane) $\lambda_{max}$ 510 nm ($\epsilon$ 11). Anal. Calcd for $C_{11}H_{16}S$: C, 73.25; H, 8.94; S, 17.78. Found: C, 72.91; H, 8.82; S, 17.51.

**Registry No.** *endo*-**1a**, 824-60-2; *endo*-**1b**, 31062-12-1; *endo*-**1c**, 31062-15-4; *endo*-**1d**, 15780-45-7; *endo*-**2d**, 73367-89-2; **4a**, 73367-90-5; **4b**, 73367-91-6; **4c**, 73367-92-7; **4d**, 73367-93-8.

## Reaction of Diphenylketene with 1-Methylbenzimidazole. A Reinvestigation

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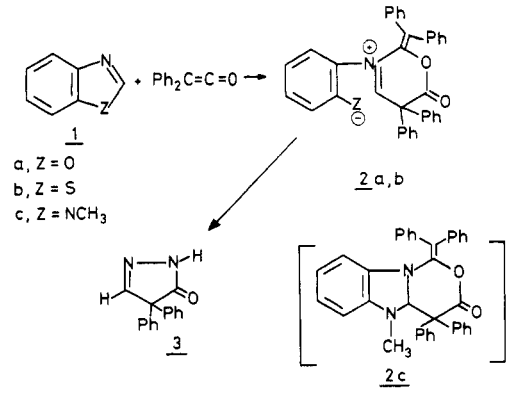
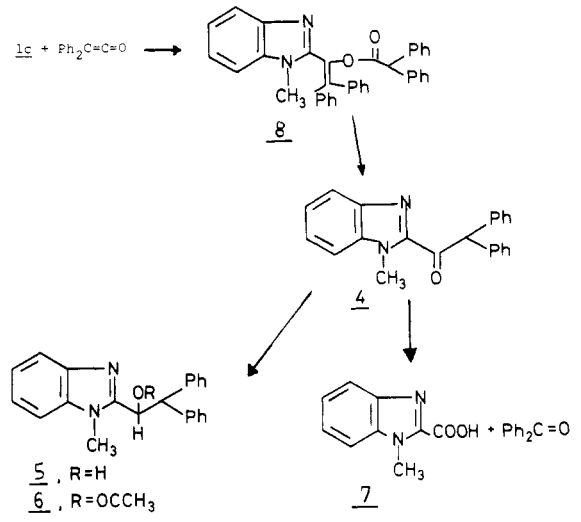
The reactions of diphenylketene with benzoxazole (**1a**), benzothiazole (**1b**), and 1-methylbenzimidazole (**1c**) were described first by Kimbrough.[1] The structures of these 1:2 adducts were revised later by Hassner and Haddadin,[2] who assigned them structures **2a-c**, respectively. We now present evidence that the adduct from **1c** has the enol acetate structure **8**.

**Scheme I**




**Scheme II**




Adducts **2a,b** were found to yield 4,4-diphenyl-5-pyrazolone (**3**) upon treatment with hydrazine[2] (Scheme I). We have now found that the adduct from **1c** gives a different product with hydrazine, which shows a strong carbonyl band at 1680 cm$^{-1}$ and no infrared absorption in the N-H region. The NMR spectrum of the hydrazinolysis product consisted of two singlets at $\delta$ 3.88 (3 H) and 6.69 (1 H, exchangeable in $CDCl_3/D_2O$) in addition to the aromatic multiplet (14 H). The parent peak in the mass spectrum, $m/e$ 326, corresponds to a molecular formula of $C_{22}H_{18}N_2O$. The same compound is obtained by the treatment of the adduct from **1c** with methanolic potassium hydroxide. Further evidence is presented in support of structure **4** for this product.

Reduction of ketone **4** with $NaBH_4$ gave alcohol **5** ($m/e$ 328) (Scheme II) which displayed a broad band at 3100-3000 cm$^{-1}$ and no carbonyl absorption; its NMR spectrum showed a singlet at $\delta$ 3.09 (3 H), two doublets at $\delta$ 4.47 and 5.32 (1 H each), and a multiplet at $\delta$ 6.6-7.1 (14 H). Acetylation of alcohol **5** with acetic anhydride yielded acetate **6** which, with base, was hydrolyzed to **5**. Oxidation of either ketone **4** or alcohol **5** with either chromic anhydride or manganese dioxide gave benzophenone as a major product. Ketone **4** was found to be sensitive to air oxidation, especially under basic conditions, and gave benzophenone. A Baeyer-Villiger oxidation of ketone **4** with *m*-chloroperbenzoic acid in acetic acid

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