Synthesis of Indenes by Cyclization of 2-Allenylbenzaldehyde Dithioacetals

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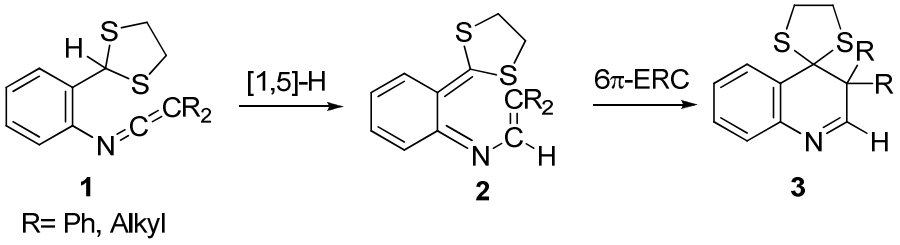
Abstract: The cyclization of dithioacetal-allenes by activating the electron-rich cumulene function with a protic acid has been studied. These reactions give rise to new indenes as reaction products. A mechanistic rationale for explaining these results will be also disclosed.

Keywords: cyclization, allene, dithioacetal, indene, protic acid

1. Introduction

We recently became engaged in the study of thermally-activated [1,5]-H shift/6π electrocyclic ring closure (6π-ERC) tandem processes in which the hydrogen atom that undergo migration in the first step is placed at the thioacetalic carbon atom of a 1,3-dithiolane fragment, whereas the migration terminus is the electrophilic central carbon atom of heterocumulenic functions such as ketenimines. Thus, the [1,5]-H shift in 1,3-dithiolane-ketenimines **1** leads to *o*-azaxylylene intermediates **2**, which undergo 6π-ERC to give quinolines **3** (Scheme 1).[1] The initial [1,5]-H shift of these conversions was characterized as an intramolecular hydride transfer by means of computational DFT studies. In fact, those calculations showed the weakening and polarization of the acetalic C-H bond by hyperconjugative interaction of its σ* C-H orbital with the lone-pair electrons of the two vicinal sulfur atoms of the acetalic function, thus facilitating the hydride transfer to the central heterocumulenic carbon atom.

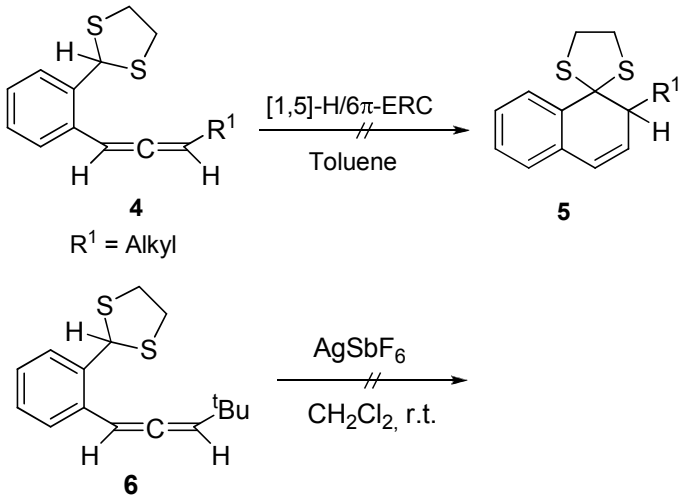


Scheme 1

We reasoned that related tandem processes are conceivable by changing the hydride-acceptor unit from heterocumulenes to other electrophilic functional groups, while keeping the dithioacetalic function as the hydride-releasing fragment. In this line, we assumed that the central carbon atom of an allene moiety may also act as the electrophilic terminus of a similar 1,5-hydride shift from an 1,3-dithiolane function, thus promoting a sequential transformation closely related with those cited above.

However, the new allenes **4** did not undergo the expected [1,5]-H/6π-ERC to give the spirodithioxolanes **5** when heated in a toluene solution for a long time.

Thus, we decided to increase the electrophilic character of the central carbon atom of the allene function with a Lewis acid such as $AgSbF_6$. Unfortunately, when allene **6** was treated with $AgSbF_6$, in dichloromethane at room temperature, a non resolvable complex mixture was obtained (Scheme 2).



Scheme 2

Next, we decided to essay the cyclization of a series of dithioacetal-allenes with similar structures to those of compounds **4** and **6** by activating the electron-rich cumulene function with Brönsted-Lowry acids. Thus, in this communication we describe the cyclization of several 2-allenylbenzaldehyde dithioacetals catalyzed by trifluoroacetic acid, which have given rise to the preparation of new indenes.

2. Methods/Experimental

Preparation of methyl carbonates 10

To a mixture of 1-[2-(1,3-dioxolan-2-yl)phenyl]-3-phenyl-2-propyn-1-yl methyl carbonate **9** (1 mmol) and the corresponding thiol (2.2 mmol) or dithiol (1.1 mmol) a catalytic amount of (bromodimethyl)sulfonium bromide was added (0.023 g). The reaction mixture was stirred at room temperature for 15 min. After completion of the reaction, the mixture was neutralised by addition of two drops of saturated sodium hydrogen carbonate solution. Then, the final reaction mixture was directly purified by silica gel column chromatography.

Representative analytical and spectroscopic data

Compound 10d: yield 78%; yellow oil; eluent for column chromatography: diethyl ether/hexanes (3:2 v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.93 (dd, *J* = 1.5, 7.8 Hz, 1 H), 7.57-7.49 (m, 3 H), 7.40 (td, *J* = 1.5, 7.5 Hz, 1 H), 7.34-7.27 (m, 4 H), 6.76 (s, 1 H), 6.32 (s, 1 H), 3.83 (s, 3 H), 3.60-3.51 (m, 2 H), 3.45-3.36 (m, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 154.7 (s), 139.3 (s), 134.4 (s), 132.0, 130.2, 129.8, 128.9, 128.8, 128.3, 128.2, 121.9 (s), 88.8 (s), 84.8 (s), 68.4, 55.2, 51.8, 40.5, 40.4 ppm; IR (Neat): ν= 1750 (vs), 1490 (m), 1441 (s), 1262 (vs) cm $^{-1}$; HRMS (ESI): *m/z* calcd for $C_{20}H_{15}S_2$ $[M+H-C_2H_3O_3]^+$ 295.0615; found 295.0613.

Preparation of allenes 11.

To an ice cooled solution of CuI (9.6 g, 50 mmol) and LiBr (4.34 g, 50 mmol) in anhydrous THF (40 mL) 1.0 M *tert*-butylmagnesium bromide in THF (50 mL, 50 mmol) was added, and the resulting mixture was stirred for 30 min. Then a solution of the corresponding methyl carbonate **10** (5 mmol) in anhydrous THF (10 mL) was dropwise added, continuing the stirring at 0 ºC for 40 min. Next, saturated solution of NH_4Cl (20 mL) was added, and the suspension was extracted with diethyl ether (2 x 40 mL). The organic layers were combined, washed with brine (30 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography using hexanes/ethyl acetate (9:1 v/v) as eluent.

Representative analytical and spectroscopic data.

Compound 11d: yield 47%; yellow oil; ^{1}H NMR (400 MHz, CD_2Cl_2): δ= 7.78 (dd, *J* = 2.0, 8.0 Hz, 1 H), 7.45 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.37-7.16 (m, 7 H), 6.60 (s, 1 H), 6.01 (s, 1 H), 3.49-3.43 (m, 2 H), 3.36-3.30 (m, 2 H), 1.21 (s, 9 H) ppm; ^{13}C NMR (100 MHz, CD_2Cl_2): δ= 204.3 (s), 137.5 (s), 137.0 (s), 133.7 (s), 129.9, 128.9, 128.6, 128.4, 127.9, 127.5, 119.5 (s), 92.1, 55.1, 40.6, 40.5, 35.7 (s), 30.1 ppm; IR (Neat): ν= 1941 (s), 1596 (s), 1480 (vs) cm $^{-1}$; HRMS (ESI): *m/z* calcd for $C_{22}H_{25}S_2$ $[M+H]^+$ 353.1392; found 353.1393.

Preparation of indenes 12.

To a solution of the allene **11** (1 mmol), in dichloromethane (10 mL) at room temperature, trifluoroacetic acid (0.11 g, 1 mmol) was added. The reaction mixture was stirred at this temperature for 20 min. Then, saturated $NaHCO_3$ solution (10 mL) was added and the suspension was extracted with dichloromethane (2 x 15 mL). The organic layers were combined, washed with brine (30 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography.

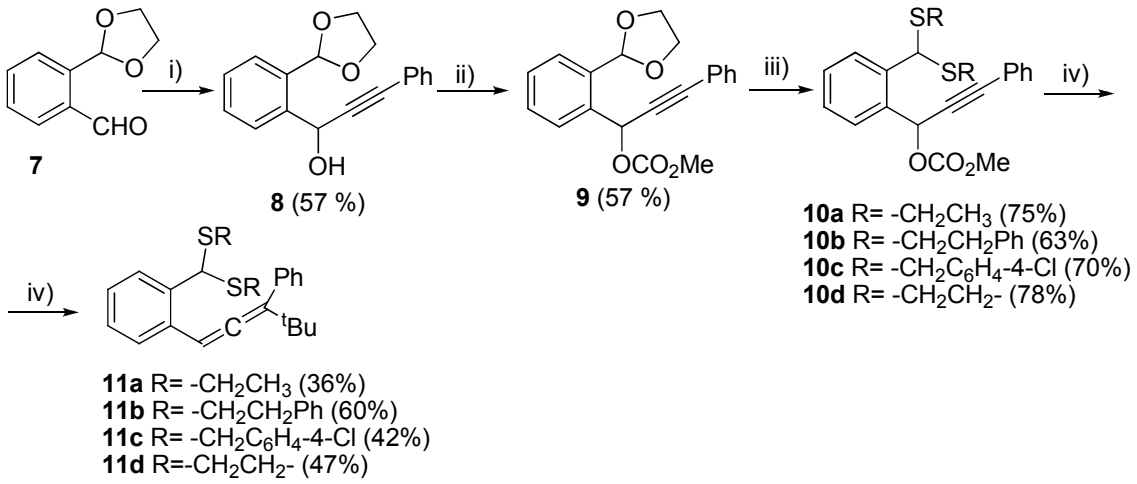
Representative analytical and spectroscopic data.

Compound 12d: yield 50%; pale yellow oil; eluent for column chromatography: hexanes/diethyl ether (4:1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.38-7.26 (m, 5 H), 7.22 (td, *J* = 1.2, 7.2 Hz, 1 H), 7.17 (td, *J* = 1.2, 7.2 Hz, 1 H), 7.08 (d, *J* = 7.6 Hz, 1 H), 6.95-6.93 (m, 1 H), 6.41 (s, 1 H), 4.26 (s, 1 H), 3.13 (dd, *J* = 8.8, 14.8 Hz, 1 H), 3.00 (dd, *J* = 8.8, 14.4 Hz, 1 H), 2.79 (dd, *J* = 8.8, 14.8 Hz, 1 H), 2.58 (dd, *J* = 8.8, 14.4 Hz, 1 H), 1.27 (s, 9 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 148.0 (s), 144.3 (s), 142.2 (s), 141.5 (s), 136.2 (s), 130.1, 128.2, 128.1, 128.0, 127.9, 127.2, 126.5, 123.5, 123.4, 52.6, 48.4, 37.8 (s), 34.1, 33.0, 31.0 ppm; IR (Neat): ν= 1730 (w), 1474 (m), 1460 (m), 439 (m) cm $^{-1}$; HRMS (ESI): *m/z* calcd for $C_{22}H_{25}S_2$ $[M+H]^+$ 353.1392; found 353.1395.

3. Results and Discussion

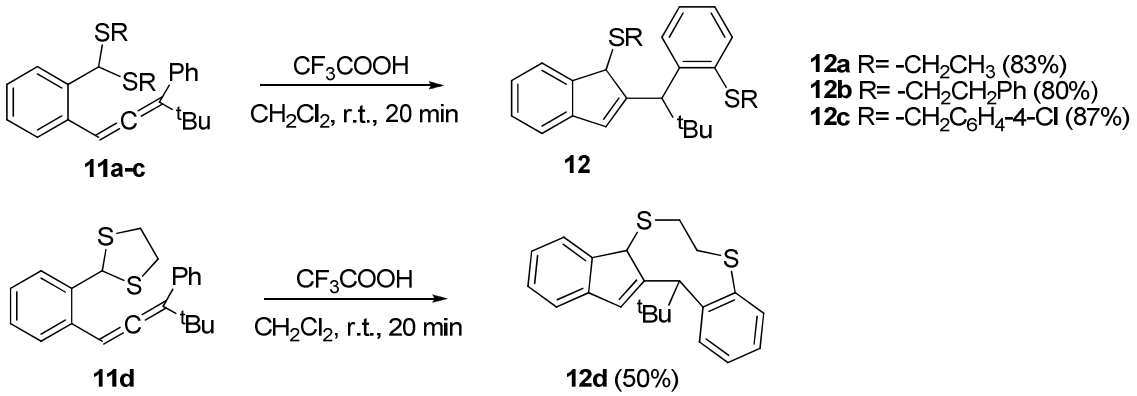
The reaction of 2-(1,3-dioxolan-2-yl)benzaldehyde **7** with (phenylethynyl)magnesium bromide provided the propargylic alcohol **8**, which was

converted into the carbonate **9** by treatment with methyl chloroformate in the presence of pyridine. The transthioacetalization reaction of this carbonate with different thiols and a dithiol afforded the carbonates **10**. Then, the allenes **11** were obtained by a copper-mediated S_N2' substituion reaction at the carbonates **10** by *t*-butylmagnesium cuprate (Scheme 3).



Scheme 3. *Reagent and conditions:* i) PhC≡CMgBr, THF, 0 ºC, 40 min; ii) $ClCO_2Me$, pyridine, DCM, 0 ºC, 1 h; iii) HSR, Me_2SBr_2, r.t., 15 min; iv) ^tBuMgCl, CuI, LiBr, THF, 0 ºC, 40 min.

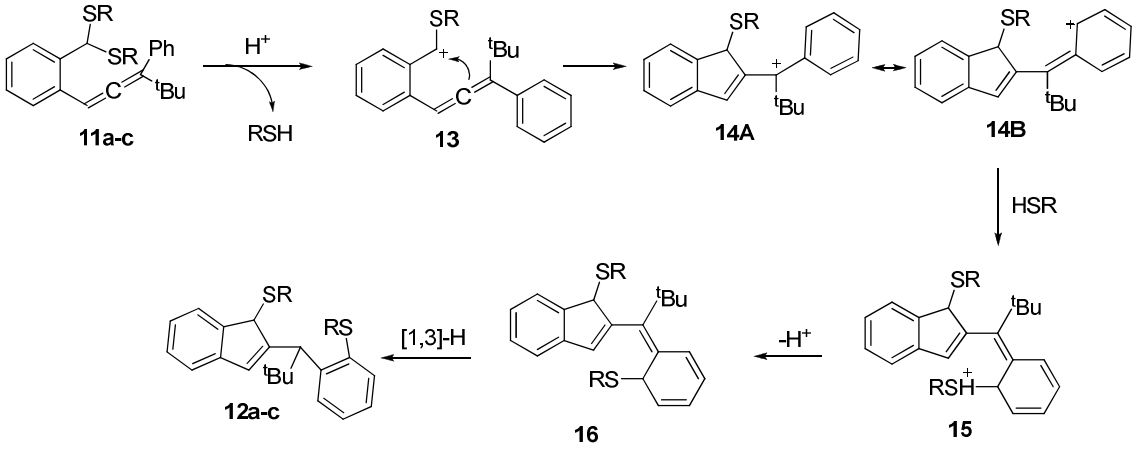
The treatment of allenes **11a-c**, supporting acyclic dithioacetalic functions, with trifluoroacetic acid, in dichloromethane at room temperature, yielded the indenes **12a-c**. The cyclic anologue **11d** by similar treatment provided the fused indene **12d** (Scheme 4).



Scheme 4

The conversion **11a-c→12a-c** could proceed by a mechanism involving as the first step the protonation/fragmentation of the dithioacetal function to give the carbocationic intermediate **13**. Cyclization of species **13** by involving the formation of a new bond between the central carbon atom of the cumulene moiety and the carbocationic centre should provide the (terc-butyl)(inden-2-yl)(phenyl) methyl cation

14. A successive intermolecular nucleophilic addition of a molecule of the thiol eliminated in the first step to the carbocation **14** via its canonical form **14B** would yield the indene **12a-c**, through intermediates **15** and **16**. The conversion **11d→12d** should occur by a similar mechanism sequence, although in this case the second mechanistic step is an intramolecular process (Scheme 5).



Scheme 5

4. Conclusions

In this communication we have described the synthesis of new indenes by cyclization of 2-allenylbenzaldehyde dithioacetals with trifluoroacetic acid. We have also given a reasonable explanation of the mechanistic course of these processes.

5. Acknowledgements

This work was supported by the MCYT (Project CTQ2008-05827/BQU) and Fundación Séneca-CARM (Project 08661/PI/08).

5. References

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