A New Redundant Rearrangement of Aromatic Ring Fused Cyclic α-Hydroxydithiane Derivatives. Synthesis of Aromatic Ring Fused Cyclic 1,2-Diketones with One-Carbon Ring Expansion

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A new reaction involving rearrangement of aromatic ring fused cyclic dithiane alcohol by *N*-chlorosuccinimide in $CH_2Cl_2-H_2O$ to the corresponding one-carbon ring expanded 1,2-diketone has been developed. A wide range of structurally varied dithiane alcohols have been found to undergo this rearrangement in high yields. The general criteria and reaction mechanism for this rearrangement have also been worked out.

Introduction

During a recent investigation we have encountered an unexpected rearrangement of dithianylcyclobutachromanol derivative **1** to 1,2,2a,8,9,9a-hexahydrocyclobuta[*b*][1]benzoxepin-8,9-dione **2** on treatment with mercuric oxide and fluoroboric acid in aqueous tetrahydrofuran[1] (Scheme 1).

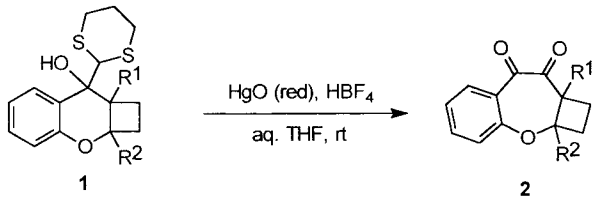
This rearrangement is unprecedented and leads to a unique system incorporating an aromatic ring fused 1,2-dione unit which is of considerable synthetic importance, being an active constituent in many natural products, e.g., carbazoquinocin C, tanshinone[1] etc.[2] This prompted us to initiate a systematic investigation to find out the generality, scope, and reaction pathways of this new rearrangement. After a detailed study we have been able to postulate the general criteria and best experimental conditions for this rearrangement, together with its possible mechanism, and these results will be presented here.

Results and Discussions

A wide range of structurally varied dithiane alcohols [**12**, **14**, **16**, **18**, **20**, **22**, **24**, **26**, **28**] have been incorporated for this study. These dithiane alcohols have been prepared by the reaction of the corresponding ketones with 2-lithio-1,3-dithiane in THF.[3] The ketones were obtained from suitable precursors primarily by Friedel−Crafts acylation followed by alkylation by standard procedures[4] as delineated in Scheme 2.

Our initial observation of this rearrangement, as represented in Scheme 1, revealed the requirement of a substituent at the ring juncture adjacent to hydroxy carbon and poses two questions: (a) whether the presence of a fused cyclobutane moiety and an aromatic ring are indispensable, and (b) whether the ring-oxygen has any role to play. It also solicits attempts for further improvement of the yield of the rearranged product.

Scheme 1



1 **2**

a. $R^1 = R^2$ = Me 60%

b. R^1=Me, R^2 = H 65%

c. $R^1 = R^2$ = H 6%

To find out the best experimental conditions, a number of other reagents such as HgO, BF_3 in aq THF; $CaCO_3$, $HgCl_2$ in aq CH_3CN; and *N*-chlorosuccinimide in $CH_2Cl_2-H_2O$ have been tried and among all these, NCS in $CH_2Cl_2-H_2O$ has been found to be the best. Thus, in a typical general procedure, the dithiane alcohol (1 mmol) was stirred with *N*-chlorosuccinimide (3.5 mmol) in CH_2Cl_2 in the presence of a few drops of water at room temperature under nitrogen, for a certain period of time as required to complete the reaction (TLC). CH_2Cl_2 was removed, and the residue was extracted with ether. Evaporation of ether followed by purification by column chromatography furnished the rearranged diketone. This procedure is followed for the rearrangement of all dithiane alcohols. All products including 1,2-diketones have been properly characterized by IR and ^1H and ^{13}C NMR spectral data and elemental analysis (Experimental Section).

The dithiane alcohol **12** containing a fused cyclopentane ring, when subjected to this procedure, underwent smooth rearrangement to produce the 1,2-diketone **13** in high yield (Scheme 3). Obviously this disproves the absolute necessity of a cyclobutane ring (Scheme 1). On the other hand, the efficient rearrangement of dithiane alcohols **14** and **16** eliminates the possibility of any role

(1) Ranu, B. C.; Bhar, S.; Patra, A.; Nayak, N. P.; Mukherjee, M. *Chem. Commun.* **1996**, 1965.

(2) (a) Tanaka, M.; Shin-Ya, K.; Furihata, K.; Seto, H. *J. Antibiot.* **1995**, *48*, 326. (b) Knolker, H.-J.; Frohner, W. *Tetrahedron Lett.* **1997**, *38*, 1535. (c) Danheiser, R.; Casebier, D. S.; Loebach, J. L. *Tetrahedron Lett.* **1992**, *33*, 1149. (d) Knolker, H.-J.; Frohner, W. *Tetrahedron Lett.* **1998**, *39*, 2537.

(3) Ranu, B. C.; Sarkar, D. C.; Basu, M. K. *Tetrahedron* **1989**, *45*, 3107; Chakraborty, R.; Basu, M. K.; Ranu, B. C. *Tetrahedron* **1992**, *48*, 8849.

(4) Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; Longman Group: Harlow, Essex, England, 1989. Krapcho, A. P. *Synthesis* **1974**, 383. Olson, C. E.; Bader, A. R. *Organic Syntheses*; Wiley: New York, 1963; Coll. Vol. 4, p 898.

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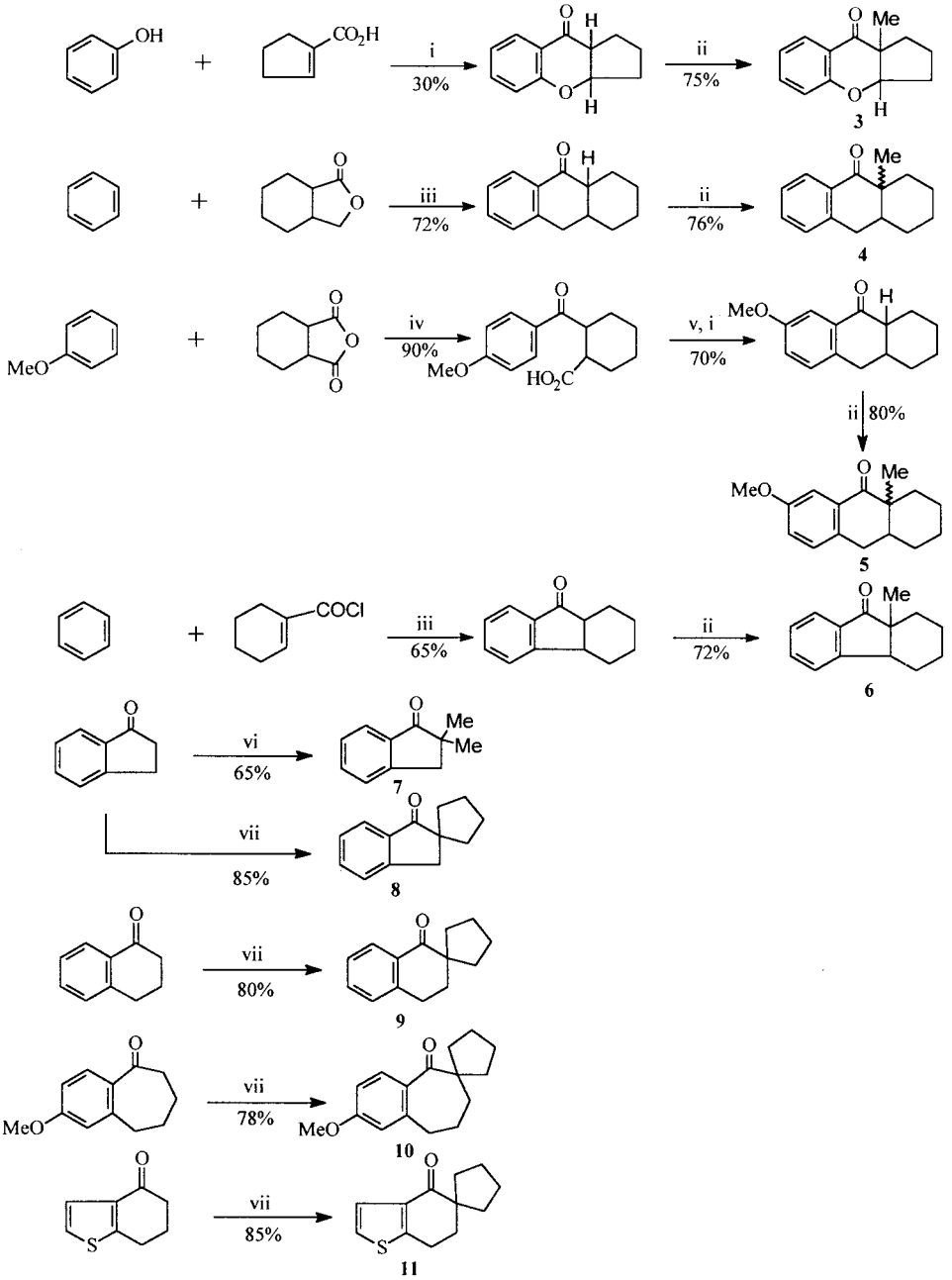
Scheme 2.[a] Preparation of Aromatic Ring Fused Ketone Substrates



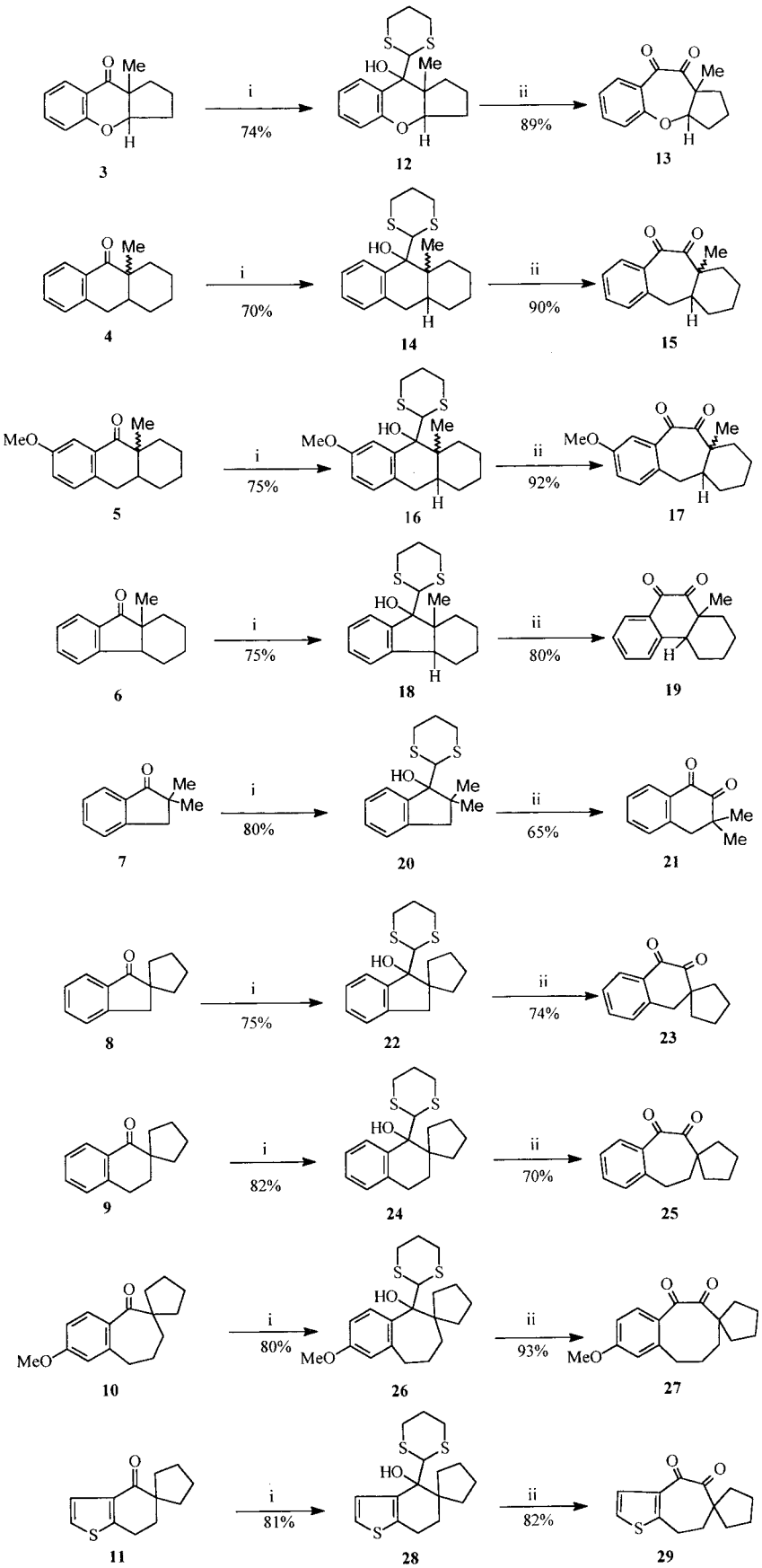
[a] Reagents and conditions: (i) PPA, 100 °C; (ii) LDA, THF, MeI; (iii) $AlCl_3$, reflux; (iv) $AlCl_3$, CH_2Cl_2, 0 °C; (v) $NH_2NH_2{\cdot}H_2O$, KOH, diethylene glycol, 180 °C; (vi) MeI, DMF, benzene, reflux; (vii) $Br(CH_2)_4Br$, $KOBu^t$, benzene, reflux.

of ring oxygen in this rearrangement. The *cis,trans*-stereoisomers of **15** and **17** were separated by fractional crystallization and identified by spectral and analytical data. The ^1H and ^{13}C NMR spectra of *cis*- and *trans*-isomers are conclusively distinct. The structure of **15a** (*cis*-isomer) was also confirmed by single-crystal X-ray analysis (Figure 1).[5]

The dithiane alcohol **18**, where the central ring is five-membered, also underwent rearrangement to provide the corresponding diketone **19**. To find out the necessity of a fused cyclic unit adjacent to the ring bearing the dithiane moiety, the dithiane alcohol **20** was subjected to this rearrangement. Interestingly, the rearranged diketone **21** was isolated, although the yield is relatively low because of the simultaneous deprotection of the dithiane alcohol **20** to the corresponding hydroxyaldehyde. As an obvious extrapolation, the dithiane alcohols **22**, **24**, **26**, and **28** bearing a five-membered spiro unit, when treated with *N*-chlorosuccinimide under identical conditions, produced the respective diketones **23**, **25**, **27**, and **29** in good yields. The compound **27** constitutes a unique

(5) Crystal data for **15a**. $C_{16}H_{18}O_2$, $M = 242.30$. Monoclinic, space group $P2_1/c$, $Z = 4$, $a = 14.537(11)$ Å, $b = 8.149(7)$ Å, $c = 11.183(6)$ Å, $\beta = 101.79\ (5)°$, $V = 1297(2)$ Å^3, $D_c = 1.241$ mg/m^3, μ (Mo-Kα) = 0.80 cm^{-1}. Crystal size = 0.3 × 0.25 × 0.2 mm, $T = 293(2)$ K. Siemens R_3m/V diffractomer, $\lambda = 0.7173$ Å, was used to record 1846 reflections ($-15 \le h \le 15$, $-8 \le k \le 0$, $0 \le l \le 12$). θ Range 2.86 to 22.55°. Unique reflections 1692 ($R_{int} = 0.0231$) and observed reflections 1389 [$I > 2\sigma(I)$]. The structure was solved by direct methods (SHELXTL − 93 V 5.03) and refined by full-matrix least-squares on F^2 with anisotropic thermal parameters to non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms. Final R indices: R1(F) = 0.0468, w$R2$(F^2) = 0.1277, R1 (all data) = 0.0595, w$R2$ (all data) = 0.1385. Largest diff. peak and hole = 0.195 and −0.226 eÅ^{-3}, respectively.

Scheme 3.[a] Rearrangements



[a] Reagents and conditions: (i) n-BuLi, 1,3-dithiane, THF, −25 °C; (ii) *N*-chlorosuccinimide, CH_2Cl_2, H_2O.

system bearing an eight-membered diketone fused with an aromatic ring and a spiro carbocycle.

Now, to ascertain the requirement of a fused aromatic ring, a nonaromatic dithiane alcohol **31** was subjected

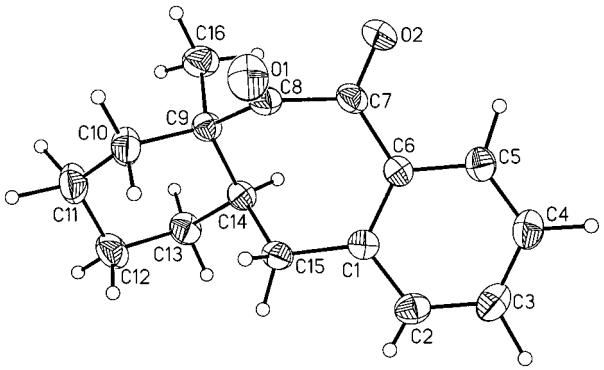


Figure 1. X-ray crystal structure of *cis*-isomer of 15 (**15a**).

to this rearrangement and found to furnish only the deprotected hydroxyaldehyde **32** (Scheme 4). No rearrangement has been observed to occur under varied experimental conditions also. The acyclic dithiane alcohol **34** also did not produce any rearranged diketone; only the hydroxyaldehyde **35** was obtained. So, from this study it appears that this rearrangement is a general one for aromatic ring fused cyclic dithiane alcohols bearing no hydrogen at the position α to the carbon containing hydroxy and dithiane moieties. A possible mechanism has been delineated in Scheme 5. Obviously, the key step is the conversion of the intermediate II to III involving the migration of bond "a".[6] This bond migration is greatly facilitated by the electron density on the adjacent carbon, which plays a vital role in guiding this rearrangement. Thus, this rearrangement does not occur at all when there is no substitution at this center[7] and proceeds marginally with monosubstitution (**1c** to **2c**). When this rearrangement is carried out with *N*-chlorosuccinimide in dry CH_2Cl_2, the intermediate monoketone **36** (IR 1680 cm^{-1}) has been isolated in high (75%) yield. Treatment of **36** with NCS in H_2O produced the diketone **25** almost quantitatively. Formation of the monoketone **36** certainly substantiates the migration of bond "a" and rules out aryl migration. Similar observations were also made with another substrate **1b**. Obviously, the presence of H_2O in the reaction medium from the start pushed the reaction to the final product in a single operation.

Conclusion

This rearrangement of aromatic ring fused cyclic dithiane alcohols by *N*-chlorosuccinimide to the one-carbon ring expanded 1,2-diketone constitutes a very novel fundamental reaction. It makes an easy access to the basic skeleton of many complex natural products,[2] including aryl taxoids.[8] The reaction is simple, general, fast, and high yielding. The presence of two distinct keto carbonyl functionalities and the aromatic ring with high potential for various manipulations make this system more synthetically useful. Further investigations to broaden the scope of this rearrangement will constitute our next endeavor.

(6) This type of bond migration is very facile and follows the conventional migratory aptitude: Carruthers, W. *Modern Methods of Organic Synthesis*, 3rd ed.; Cambridge University Press: New York, 1996.

(7) The corresponding dithiane alcohols from 1-indanone and 1-tetralone did not undergo this rearrangement.

(8) Nicolaou, K. C.; Claiborne, C. F.; Paulvannan, K.; Postema, M. H. D.; Guy, R. K. *Chem. Eur. J.* **1997**, *3*, 399.

Experimental Section

General. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 300 and 75 MHz, respectively. Analyses were done on a Perkin-Elmer 240C autoanalyzer. Tetrahydrofuran (THF) was distilled over potassium−benzophenone immediately before use. Methylene chloride (CH_2Cl_2) was dried over P_2O_5. *N*-Chlorosuccinimide was used as supplied (E. Merck).

Preparation of Ketones. Ketone 3. To polyphosphoric acid (10 g), prepared by heating a mixture of P_2O_5 (5 g) and H_3PO_4 (2.5 mL) at 100 °C for 5 h, was added a mixture of phenol (941 mg, 10 mmol) and cyclopentene carboxylic acid (1.12 g, 10 mmol). The reaction mixture was agitated by mechanical stirrer at 100 °C for 4.5 h. The reaction mixture was cooled and quenched by ice−water. The resulting aqueous suspension was extracted with ether. The ether extract was washed successively by water, 10% KOH, and brine and dried over Na_2SO_4. The extract was evaporated and purified by silica gel column chromatography to afford the intermediate cyclic ketone (564 mg, 30%) as a colorless liquid; IR (neat) 1680, 1605 cm^{-1}; ^1H NMR δ 1.74−2.20 (m, 6H), 2.69−2.73 (m, 1H), 4.92 (t, J = 3 Hz, 1H), 6.91 (d, J = 9 Hz, 1H), 6.98 (t, J = 9 Hz, 1H), 7.44 (t, J = 9 Hz, 1H), 7.87 (d, J = 9 Hz, 1H); ^{13}C NMR δ 22.4, 27.5, 33.0, 51.1, 83.3, 118.0, 119.1, 121.2, 127.0, 136.6, 160.6, 194.6. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.65; H, 6.66.

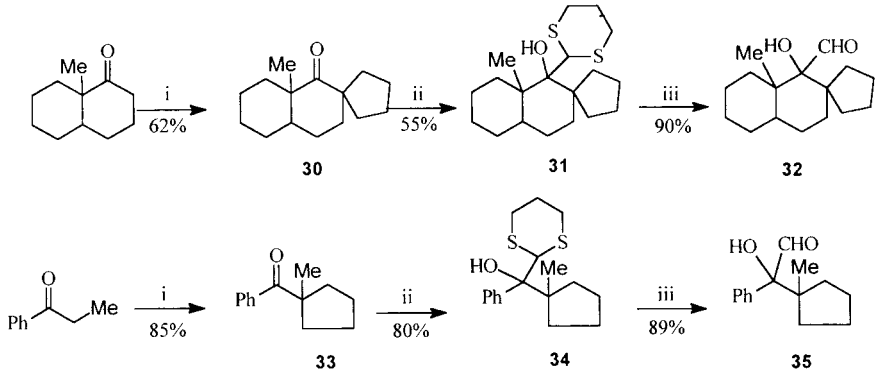
A solution of the ketone, prepared in the earlier step, (300 mg, 1.59 mmol) in THF (2 mL) was added to a stirred solution of LDA in THF at −78 °C under argon. The reaction mixture was slowly warmed to −25 °C and stirred at that temperature for 1.5 h. The temperature of the reaction mixture was again brought down to −78 °C and HMPA (2 mL) followed by methyl iodide (0.31 mL, 5 mmol) was added dropwise. The reaction mixture was allowed to attain room temperature and left overnight. After quenching with ice cold water, the reaction mixture was extracted with ether. The ether extract was washed successively by water and brine and dried over Na_2SO_4. The extract was evaporated, and the residue was purified by silica gel column chromatography to furnish ketone **3** (241 mg, 75%) as a colorless viscous oil; IR (neat) 1680, 1600 cm^{-1}; ^1H NMR δ 1.20 (s, 3H), 1.58−2.17 (m, 6H), 4.55 (d, J = 3.3 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 6.98 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.88 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 16.9, 19.2, 30.9, 33.7, 52.1, 87.9, 117.9, 121.1, 121.5, 127.3, 135.7, 159.6, 196.5. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.39; H, 6.70.

Ketone 4. To a stirred solution of lactone (1.40 g, 10 mmol) in dry benzene (50 mL) was added aluminum chloride (3.99 g, 30 mmol) over a period of 15 min. The reaction mixture was then heated under reflux for 10 h. It was then cooled to room temperature and poured into crushed ice followed by acidification with concentrated HCl. The product was extracted with ether, and the ether extract was washed successively by water, saturated $NaHCO_3$ solution, and brine and dried over Na_2SO_4. Evaporation of solvent and purification of the residue by silica gel column chromatography provided the intermediate cyclic ketone (1.44 g, 72%) as a solid (mp 100−103 °C); IR (KBr) 1680, 1600 cm^{-1}; ^1H NMR δ 1.39−1.67 (m, 9H), 2.69−2.71 (m, 1H), 2.96−3.03 (m, 2H), 7.21−7.31 (m, 2H), 7.46 (dt, J = 9, 3 Hz, 1H), 8.03 (dd, J = 9, 3 Hz, 1H); ^{13}C NMR δ 23.4, 23.7, 25.3, 28.82, 33.8, 35.7, 48.2, 126.4, 127.1, 129.2, 131.7, 133.3, 142.8, 200.3. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.98; H, 8.16.

Methylation of this intermediate ketone following the same procedure as in the preparation of **3** produced the ketone **4** as a colorless liquid (76%, as a 1:1 mixture of *cis*−*trans* isomers); IR (neat) 1675, 1605 cm^{-1}; ^1H NMR δ 1.05 (s, 1.5 H), 1.17 (s, 1.5 H), 1.25−1.97 (m, 9H), 2.63−2.73 (m, 2H). Anal. Calcd for $C_{15}H_{18}O$: C, 84.06; H, 8.47. Found: C, 84.36; H, 8.63.

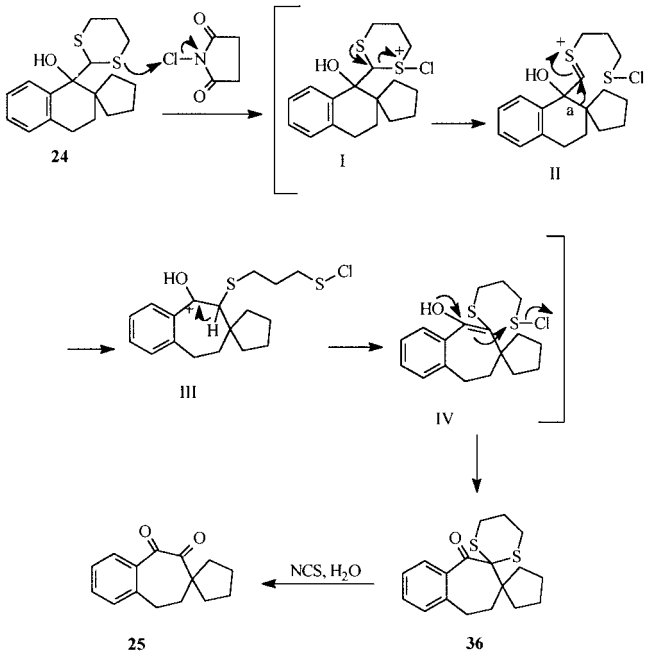
Ketone 5. To a cold (0 °C) stirred solution of anisole (2.40 g, 20 mmol) and $AlCl_3$ (6.66 g, 50 mmol) in dry CH_2Cl_2 (25 mL), was added 1,2-*cis*-cyclohexanecarboxylic anhydride (3.08 g, 20 mmol) in CH_2Cl_2 (6 mL). The mixture was vigorously stirred, and the temperature of the reaction was maintained at 0 °C for 3 h; then the reaction mixture was kept frozen

Scheme 4[a]



[a] Reagents and conditions: (i) $Br(CH_2)_4Br$, $KOBu^t$, benzene, reflux; (ii) n-BuLi, 1,3-dithiane, THF, −25 °C; (iii) *N*-chlorosuccinimide, CH_2Cl_2, H_2O.

Scheme 5



overnight. The whole mass was poured into ice−water followed by acidification with concentrated HCl. The product was extracted with CH_2Cl_2, and the organic layer was washed successively by water and brine and dried over Na_2SO_4. The extract was evaporated, and the solid residue was crystallized to produce the corresponding keto acid (4.72 g, 90%), mp 105 °C; IR (KBr) 3600−3500, 1710−1720,1600 cm^{-1}; ^1H NMR δ 1.28−2.25 (m, 9H), 2.64−2.68 (m, 1H), 3.88 (s, 3H), 6.91 (dt, J = 9, 3 Hz, 2H), 7.85 (dt, J = 9, 3 Hz, 2H). This keto acid (4 g, 15.26 mmol) was added to a hot solution of KOH (4 g, 41.3 mmol) in diethylene glycol (20 mL) followed by hydrazine hydrate (1.5 mL). The mixture was heated at 180 °C under stirring with continuous removal of water formed over a period of 2 h. After being cooled, it was poured into ice−water and acidified by HCl. The product was extracted with ether, and the ether extract was successively washed by water and brine and dried over Na_2SO_4. The extract was evaporated, and the solid residue was crystallized to afford the intermediate acid (2.87 g, 76%), mp 90−92 °C; IR (KBr) 3500−3600, 1700−1710, 1600 cm^{-1}; ^1H NMR δ 0.85−2.28 (m, 11H), 2.79−2.81 (m, 1H), 3.77 (s, 3H), 6.81 (d, J = 9 Hz, 2H), 7.07 (d, J = 9 Hz, 2H). This acid (1 g, 4.02 mmol) was then cyclized by stirring in PPA for 2 h at 90 °C. Usual workup and purification by silica gel column chromatography yielded the corresponding cyclic ketone (656 mg, 71%) as a solid, mp 109−110 °C; IR (KBr) 1670, 1600 cm^{-1}; ^1H NMR δ 1.19−2.11 (m, 9H), 2.37−2.41 (m, 1H), 2.62−2.85 (m, 2H), 3.81 (s, 3H), 7.00−7.12 (m, 2H), 7.49 (d, J = 2.7 Hz, 1H); ^{13}C NMR δ 25.4, 25.8, 26.0, 34.0, 36.5, 40.3, 51.8, 55.5, 109.2, 121.4, 129.7, 133.1,136.1, 158.2, 199.8. Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.30; H, 7.95.

Methylation of this intermediate ketone was performed by LDA and methyl iodide by the same procedure as in the preparation of **3**. Ketone **5** was obtained in 80% yield as a pale yellow liquid [*cis*−*trans* (1:1)]; IR (neat) 1670, 1600 cm^{-1}; ^1H NMR δ 1.05 (s, 1.5 H), 1.18 (s, 1.5 H), 1.23−1.96 (m, 9H), 2.57−2.70 (m, 2H), 3.81 (s,1.5 H), 3.82 (s, 1.5 H), 7.00−7.10 (m, 2H), 7.52 (m, 1H). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.92; H, 8.43.

Ketone 6. To a solution of 1-cyclohexenoyl chloride (1.44 g, 10 mmol) in dry benzene (30 mL) was added $AlCl_3$ (2.66 g, 20 mmol) over a period of 10 min. The mixture was then refluxed for 5 h, cooled to room temperature, and poured into ice water followed by acidification with concentrated HCl. The product was extracted with ether, and the ether extract was successively washed with water and brine and dried over Na_2SO_4. The solvent was evaporated off, and the residue was purified by silica gel column chromatography to produce a cyclic ketone (1.21 g, 65%) as a colorless liquid; IR (neat) 1705, 1600 cm^{-1}; ^1H NMR δ 1.14−2.10 (m, 8H), 2.69−2.75 (m, 1H), 3.32−3.39 (m, 1H), 7.15−7.74 (m, 4H); ^{13}C NMR δ 22.4, 22.6, 23.1, 31.3, 38.7, 48.4, 123.8, 123.8, 124.0, 127.3, 135.5, 158.3, 207.8. Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.90; H, 7.62.

Ketone **6** was then obtained by methylation of this ketone following the same procedure as mentioned earlier, as a colorless liquid (72%); IR (neat) 1710, 1605 cm^{-1}; ^1H NMR δ 1.22 (s, 3H), 1.42−1.96 (m, 8H), 3.00−3.02 (m, 1H), 7.34−7.75 (m, 4H); ^{13}C NMR δ 21.0, 21.1, 26.2, 31.5, 45.7, 49.6, 124.4, 127.2, 134.3, 135.2, 155.7, 210.9. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.02; H, 8.35.

Ketone 7. A solution of indanone (3.96 g, 30 mmol) in benzene (20 mL) was added dropwise to a stirred suspension of NaH (3.65 g, 152 mmol) in benzene (30 mL), and stirring was continued for 5 h. To this solution was added dry DMF (20 mL), and the mixture was left overnight. Next day the reaction mixture was cooled to 0 °C, and methyl iodide (1.77 g, 12.46 mmol) was added dropwise and heated to reflux for 8 h. Again, another batch of methyl iodide (1.77 g, 12.46 mmol) was added and reflux was continued for another 8 h. Then the mixture was cooled to 0 °C and quenched by ice−water. The product was extracted with ether, and the ether extract was washed successively by water and brine and dried over Na_2SO_4. The extract was evaporated, and the crude residue was purified by vacuum distillation (120 °C/15−20 mm) to afford the 2,2-dimethylindanone **7** as a liquid (3.12 g, 65%); IR (neat) 1710, 1600 cm^{-1}; ^1H NMR δ 1.23 (s, 6H), 3.00 (s, 2H), 7.36 (m, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 26.9, 44.5, 47.1, 126.1, 128.3, 129.1, 136.5, 153.9, 213.2. Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.50. Found: C, 82.62; H, 7.64.

Ketone 8. A solution of indanone (462 mg, 3.5 mmol) in benzene (2 mL) was added to a magnetically stirred suspension

of potassium *tert*-butoxide (897.6 mg, 8 mmol) in benzene (20 mL) under nitrogen, and the mixture was refluxed for a period of 2.5 h. After being cooled to room temperature, this was quenched with ice−water and extracted with ether. The ether extract was washed throughly with water and brine and dried over Na_2SO_4. Evaporation of solvent and purification by silica gel column chromatography afforded pure spiro ketone **8** (438 mg, 85%) as an oil; IR (neat) 1705, 1600 cm^{-1}; ^1H NMR δ 1.58−2.00 (m, 8H), 3.02 (s, 2H), 7.34−7.42 (m, 2H), 7.56 (t, J = 6 Hz, 1H), 7.75 (d, J = 9 Hz, 1H); ^{13}C NMR δ 25.6, 38.3, 43.0, 56.9, 123.8, 126.0, 126.3, 127.2, 134.5, 152.7, 211.0. Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 75.80. Found: C, 83.95; H, 77.79.

This procedure is followed for the preparation of spiroketones **9**−**11**, **30**, **33**. Ketone **9**, oil (80%), IR (neat) 1680, 1600 cm^{-1}; ^1H NMR δ 1.51−1.55 (m, 2H), 1.69−1.78 (m, 4H), 2.03−2.14 (m, 4H), 2.98 (t, J = 6.2 Hz, 2H), 7.20 (d, J = 7.65 Hz, 1H), 7.28 (t, J = 7.70 Hz, 1H), 7.44 (dt, J = 7.4, 1.3 Hz, 1H), 8.04 (d, J = 7.78 Hz, 1H); ^{13}C NMR δ 25.9, 27.0, 35.6, 53.6, 126.9, 128.3, 133.3, 144.0, 202.9. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.03. Found: C, 83.90; H, 8.00.

Ketone **10**, viscous oil, yield 78%; IR (neat) 1660, 1600 cm^{-1}; ^1H NMR δ 1.50−1.88 (m, 10H), 2.08 (t, J = 6 Hz, 2H), 2.76 (t, J = 6 Hz, 2H), 3.80 (s, 3H), 6.63 (s, 1H), 6.75 (d, J = 9 Hz, 1H), 7.34 (d, J = 9 Hz, 1H); ^{13}C NMR δ 24.1, 25.2, 33.5, 35.2, 37.3, 55.3, 57.9, 111.3, 114.2, 129.7, 134.0, 134.4, 161.5, 213.8. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.93; H, 8.34.

Ketone **11**, thick oil, yield 85%; IR (neat) 1680 cm^{-1}; ^1H NMR δ 1.49−1.78 (m, 8H), 2.10 (t, J = 6 Hz, 2H), 3.02 (t, J = 6 Hz, 2H), 7.03 (d, J = 5.1 Hz, 1H), 7.36 (d, J = 5.1 Hz, 1H); ^{13}C NMR δ 23.0, 25.6, 43.7, 36.5, 52.6, 123.1, 125.5, 136.1, 154.0, 197.6. Anal. Calcd for $C_{12}H_{14}OS$: C, 69.86; H, 6.84. Found: C, 70.10; H, 7.18.

Ketone **30**, oil (62%), IR (neat) 1700 cm^{-1}; ^1H NMR δ 1.17 (s, 3H), 1.21 (s, 3H), 1.27−2.18 (m, 2H).

Ketone **33**, yield 85%, liquid; IR (neat) 1680 cm^{-1}; ^1H NMR δ 1.42 (s, 3H), 1.63−1.73 (m, 6H), 2.30−2.34 (m, 2H), 7.40−7.47 (m, 3H), 7.85−7.88 (m, 2H).

Preparation of Dithiane Alcohols 12, 14, 16, 18, 20, 22, 24, 26, 28, 31, 34. Dithiane Alcohol 12. To a stirred solution of 1,3-dithiane (180 mg, 1.5 mmol) in dry THF (3 mL) was added n-BuLi (1 mL, 1.3 mmol, 1.3 M in hexane) dropwise at −25 °C, and stirring was continued at that temperature for 1.5 h. Then the mixture was cooled to −78 °C, and the ketone **3** (202 mg, 1 mmol) in THF (2 mL) was added dropwise. The tempeature of the reaction mixture was again increased to −25 °C and kept at this temperature for additional 2.5 h. Then the reaction mixture was slowly allowed to attain room temperature and left overnight. After quenching the reaction mixture with ice−water, the product was extracted with ether. The ether extract was washed successively by water and brine and dried over Na_2SO_4. Evaporation of the solvent and purification by silica gel column chromatography furnished the dithiane alcohol **12** (238.6 mg, 74%) as a solid (mp 124 °C); IR (KBr) 3500−3400, 1600 cm^{-1}; ^1H NMR δ 1.20 (s, 3H), 1.54−2.10 (m, 9H), 2.65−2.82 (m, 4H), 4.47 (s, 1H), 4.92 (d, J = 3.3 Hz, 1H), 6.79 (d, J = 8.1 Hz, 1H), 6.94 (t, J = 7.2 Hz, 1H), 7.23 (dt, J = 7.8, 1.8 Hz, 1H), 7.57 (dd, J = 7.8, 1.8 Hz, 1H); ^{13}C NMR δ 19.0, 19.7, 25.1, 29.4, 30.0, 33.4, 33.6, 49.6, 56.6, 75.2, 84.7, 116.1, 119.5, 123.4, 126.9, 129.4, 153.7. Anal. Calcd for $C_{17}H_{22}O_2S_2$: C, 63.32; H, 6.88. Found: C, 63.12; H, 6.84.

Dithiane alcohol **14**, yield 72%, solid, mp 106−109 °C, IR (KBr) 3500−3300, 1600 cm^{-1}; ^1H NMR (as a mixture or *cis*−*trans* isomers) δ 0.86 (s, 1.5 H), 1.30 (s, 1.5 H), 1.37−1.87 (m, 11H), 2.39−2.95 (m, 6H), 3.11 (s, 1H), 4.64 (s, 0.5 H), 4.74 (s, 0.5 H), 7.09−7.25 (m, 3H), 7.65−7.70 (m, 1H). Anal. Calcd for $C_{19}H_{26}OS_2$: C, 68.22; H, 7.83. Found: C, 68.06; H, 7.84.

Dithiane alcohol **16**, yield 75%, viscous oil, IR (neat) 3600−3200, 1610, 1210 cm^{-1}; ^1H NMR (as mixture of stereoisomers) δ 0.85 (s, 1.5 H), 1.19 (s, 1.5 H), 1.34−1.93 (m, 10H), 2.26−2.30 (m, 1H), 2.63−2.86 (m, 6H), 3.81 (s, 3H), 4.62 (s, 0.5 H), 4.70 (s, 0.5 H), 6.76−7.01 (m, 2H), 7.20−7.25 (m, 1H). Anal. Calcd for $C_{20}H_{28}O_2S_2$: C, 65.89; H, 7.74. Found: C, 65.49; H, 7.40.

Dithiane alcohol **18**, yield 70%, viscous oil; IR (neat) 3600−3300, 1600, 1040 cm^{-1}; ^1H NMR δ 1.43 (s, 3H), 1.64−2.16 (m, 10H), 2.53−2.97 (m, 5H), 3.37 (s, 1H), 4.51 (s, 1H), 7.08−7.53 (m, 4H); ^{13}C NMR δ 16.8, 21.0, 22.1, 22.9, 25.6, 30.4, 30.7, 30.84, 46.1, 51.0, 57.5, 86.0, 121.9, 125.0, 126.1, 128.5, 128.6, 144.3. Anal. Calcd for $C_{18}H_{24}OS_2$: C, 67.45; H, 7.55. Found: C, 67.90; H, 7.95.

Dithiane alcohol **20**, yield 80%, solid, mp 100−102 °C; IR (KBr) 3600−3400, 1600, 1210 cm^{-1}; ^1H NMR δ 0.95 (s, 3H), 1.30 (s, 3H), 1.65−1.87 (m, 2H), 2.40−3.16 (m, 7H), 4.38 (s, 1H), 7.08−7.18 (m, 3H), 7.40 (d, J = 2.1 Hz, 1H); ^{13}C NMR δ 22.0, 25.6, 26.8, 30.3, 31.0, 46.2, 48.0, 58.1, 86.1, 124.9, 125.6, 126.3, 128.7, 141.9, 143.8. Anal. Calcd for $C_{15}H_{20}OS_2$: C, 64.24; H, 7.19. Found: C, 64.41; H, 7.32.

Dithiane alcohol **22**, yield 75%, solid, mp 102 °C; IR (KBr) 3500−3300, 1600, 1215 cm^{-1}; ^1H NMR δ 1.58−2.00 (m, 10H), 2.67−2.94 (m, 4H), 3.13 (s, 2H), 4.47 (s, 1H), 7.17−7.25 (m, 3H), 7.51 (m, 1H); ^{13}C NMR δ 22.4, 23.8, 25.5, 30.0, 30.6, 31.8, 34.4, 43.3, 58.2, 60.1, 85.1, 124.3, 124.9, 126.1, 128.6, 141.9, 144.3. Anal. Calcd for $C_{17}H_{22}OS_2$: C, 66.62; H, 7.24. Found: C, 66.80; H, 7.32.

Dithiane alcohol **24**, yield 82%, solid, mp 57−59 °C; IR (KBr) 3600−3300, 1600, 1210 cm^{-1}; ^1H NMR δ 1.19−2.94 (m, 19H), 4.51 (s, 1H), 7.02−7.07 (m, 1H), 7.15−7.22 (m, 2H), 7.66−7.70 (m, 1H); ^{13}C NMR δ 25.3, 25.5, 25.8, 26.0, 30.8, 31.4, 31.5, 33.4, 34.5, 51.3, 59.6, 77.9, 125.0, 126.5, 127.3, 128.0, 137.1, 139.8. Anal. Calcd for $C_{18}H_{24}OS_2$: C, 67.45; H, 7.55. Found: C, 67.55; H, 7.74.

Dithiane alcohol **26**, yield 80%, solid, mp 144−146 °C; IR (KBr) 3600−3500, 1605, 1260 cm^{-1}; ^1H NMR δ 1.25−2.93 (m, 21H), 3.78 (s, 3H), 5.41 (s, 1H), 6.63 (s, 1H), 6.70 (d, J = 8.70 Hz, 1H), 7.62 (d, J = 8.7 Hz, 1H); ^{13}C NMR δ 23.1, 23.9, 25.0, 25.3, 30.3, 31.6, 33.0, 35.8, 37.1, 37.7, 53.2, 54.9, 55.0, 82.2, 109.3, 116.9, 128.2, 136.2, 139.6, 158.3. Anal. Calcd for $C_{20}H_{28}O_2S_2$: C, 65.89; H, 7.74. Found: C, 65.92; H, 7.85.

Dithiane alcohol **28**, yield 81%, solid, mp 110 °C; IR (KBr) 3600−3300, 1080 cm^{-1}; ^1H NMR δ 1.29−1.93 (m, 12H), 2.47−2.89 (m, 7H), 4.55 (s, 1H), 7.07 (d, J = 6 Hz, 1H), 7.16 (d, J = 6 Hz, 1H); ^{13}C NMR δ 21.7, 25.4, 25.5, 26.0, 31.56, 31.7, 32.0, 32.9, 33.6, 51.7, 59.7, 77.3, 122.0, 126.3, 138.6, 139.1. Anal. Calcd for $C_{16}H_{22}OS_3$: C, 58.85; H, 6.79. Found: C, 58.92; H, 7.12.

Dithiane alcohol **31**, thick oil, yield 55%, IR (neat) 3600−3400 cm^{-1}; ^1H NMR δ 1.01 (s, >3H), 1.27 (s, >3H), 1.32−1.74 (m, 23H), 2.58 (s, 1H), 2.85−3.00 (m, 4H), 4.36 (s, >1H), 4.42 (s, >1H).

Dithiane alcohol **34**, thick oil, yield 80%, IR (neat) 3500−3300, 1603 cm^{-1}; ^1H NMR δ 1.18 (s, 3H), 1.38−2.08 (m, 10H), 2.81−2.98 (m, 5H), 4.80 (s, 1H), 7.26−7.32 (m, 3H), 7.65−7.68 (m, 2H).

Rearrangement of Dithiane Alcohols to the Corresponding 1,2-Diketones 13, 15, 17, 19, 21, 23, 25, 27, 29. Diketone 13. To a stirred mixture of dithiane alcohol **12** (100 mg, 0.31 mmol) in CH_2Cl_2 (4.5 mL) and water (0.5 mL) was added *N*-chlorosuccinimide (145 mg, 1.08 mmol) under nitrogen. During the addition of *N*-chlorosuccinimide, a transient red color appeared for a few seconds. Stirring was continued for 2 h till completion of the reaction (TLC). The reaction mixture was then extracted with ether. The ether extract was washed successively with water and brine and dried over Na_2SO_4. Evaporation of solvent and purification by silica gel column chromatography afforded the corresponding 1,2-diketone **13** (63.52 mg, 89%) as a light yellow liquid; IR (neat) 1720, 1670, 1600 cm^{-1}; ^1H NMR δ 1.25 (s, 3H), 1.52−2.20 (m, 5H), 2.63−2.72 (m, 1H), 4.35 (t, J = 3.6 Hz, 1H), 7.08 (d, J = 66.9 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.55 (dt, J = 7.5, 1.8 Hz, 1H), 7.97 (dd, J = 7.8, 1.5 Hz, 1H); ^{13}C NMR δ 21.8, 22.9, 31.3, 33.2, 59.5, 93.5, 121.9, 124.0, 124.7, 129.3, 136.5, 163.2, 194.5, 204.9. Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.09; H, 6.21.

Diketone **15**, yield 90%, solid, was separated by fractional crystallization (ether−petroleum ether mixture) to give pure *cis*-**15a** and *trans*-**15b** isomers.

15a (*cis*), mp 108 °C; IR (KBr) 1700, 1665, 1595 cm^{-1}; ^1H NMR δ 1.40 (s, 3H), 1.49−1.86 (m, 8H), 2.06−2.09 (m, 1H),

2.78 (d, J = 15 Hz, 1H), 3.15 (q, J = 9 Hz, 1H), 7.24−7.36 (m, 2H), 7.46 (t, J = 7.5 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 21.0, 21.1, 21.7, 27.3, 29.3, 39.0, 42.3, 47.4, 126.8, 129.0, 130.3, 133.4, 133.6, 145.7, 198.8, 212.9. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.36; H, 7.39.

15b (*trans*), mp 92 °C; IR (KBr) 1700, 1665, 1595 cm^{-1}; ^{1}H NMR δ 1.25 (s, 3H), 1.33−1.83 (m, 8H), 2.13−2.16 (m, 1H), 2.70 (d, J = 18 Hz, 1H), 3.13 (q, J = 9 Hz, 1H), 7.24 (t, J = 6 Hz, 1H), 7.31 (t, J = 6 Hz, 1H), 7.44 (t, J = 6 Hz, 1H), 7.73 (d, J = 9 Hz, 1H); ^{13}C NMR δ 12.0, 20.0, 25.9, 28.6, 34.3, 38.6, 43.3, 49.3, 126.8, 129.0, 130.3, 133.0, 133.9, 143.5, 200.8, 213.0. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.38; H, 7.52.

Diketone **17**, yield 92%, solid, *trans*-isomer was obtained pure, mp 102 °C; IR (KBr) 1700, 1670, 1600 cm^{-1}; ^{1}H NMR δ 1.21 (s, 3H), 1.45−1.80 (m, 8H), 2.06−2.12 (m, 1H), 2.61 (d, J = 18 Hz, 1H), 3.03 (q, J = 12 Hz, 1H), 3.79 (s, 3H), 6.96−7.17 (m, 3H); ^{13}C NMR δ 12.0, 20.0, 25.9, 28.6, 34.3, 42.7, 43.6, 49.3, 55.6, 111.4, 120.8, 131.7, 134.5, 134.9, 158.2, 200.7, 212.7. Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.69; H, 7.38.

Diketone **19**, yield 80%, yellow viscous oil, IR (neat) 1720, 1670, 1600 cm^{-1}; ^{1}H NMR δ 1.15 (s, 3H), 1.23−2.05 (m, 8H), 2.50 (d, J = 12 Hz, 1H), 7.35−7.44 (m, 2H), 7.64 (t, J = 9 Hz, 1H), 8.09 (d, J = 9 Hz, 1H); ^{13}C NMR δ 22.5, 25.9, 26.2, 33.9, 39.0, 51.1, 51.2, 127.4, 129.1, 129.3, 131.1, 135.4, 148.7, 181.3, 199.5. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found :C, 78.98; H, 7.14.

Diketone **21**, yield 65%, yellow liquid; IR (neat) 1720, 1680, 1600 cm^{-1}; ^{1}H NMR δ 1.31 (s, 6H), 3.18 (s, 2H), 7.33 (d, J = 7.8 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.5 Hz, 1H), 8.08 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 21.7, 21.8, 43.0, 47.5, 126.6, 129.4, 129.5, 133.4, 135.8, 142.1, 183.0, 200.3. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.70; H, 6.75.

Diketone **23**, yield 75%; yellow liquid; IR (neat) 1710, 1680, 1600 cm^{-1}; ^{1}H NMR δ 1.30−1.63 (m, 6H), 2.24−2.32 (m, 2H), 3.29 (s, 2H), 7.39 (d, J = 6.5 Hz, 1H), 7.49 (t, J = 6.5 Hz, 1H), 7.64 (t, J = 6.5 Hz, 1H), 8.13 (d, J = 6.5 Hz, 1H); ^{13}C NMR δ 25.6, 36.9, 41.7, 58.5, 127.6, 129.1, 129.3, 135.1, 142.9, 183.6, 198.9. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.50; H, 6.80.

Diketone **25**, yield 70%, solid, mp 52−54 °C; IR (KBr) 1700, 1660, 1600 cm^{-1}; ^{1}H NMR δ 1.41−1.50 (m, 2H), 1.64−1.69 (m, 4H), 2.07−2.11 (m, 2H), 2.28−2.32 (m, 2H), 2.94−2.98 (m, 2H), 7.20−7.48 (m, 3H), 7.88 (dd, J = 7.8, 1.2 Hz, 1H); ^{13}C NMR δ 25.6, 32.6, 35.3, 38.3, 57.3, 127.3, 129.5, 130.8, 133.3, 134.2, 145.5, 199.3, 210.5. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.25; H, 7.20.

Diketone **27**, yield 93%, solid, mp 106 °C; IR (KBr) 1690, 1630, 1590 cm^{-1}; ^{1}H NMR δ 1.47−1.78 (m, 10H), 2.30 (broad, 2H), 2.78 (m, 2H), 3.85 (s, 3H), 6.65 (d, J = 2.4 Hz, 1H), 6.87 (dd, J = 9, 1.8 Hz, 1H), 8.12 (d, J = 9 Hz, 1H); ^{13}C NMR δ 25.6, 26.2, 33.4, 35.2, 55.9, 56.5, 113.2, 116.4, 127.4, 131.6, 145.2, 165.4, 196.9, 214.9. Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.15; H, 7.51.

Diketone **29**, yield 82%, solid, mp 45 °C; IR (KBr) 1690, 1675, 1550 cm^{-1}; ^{1}H NMR δ 1.45−1.71 (m, 6H), 2.15−2.32 (m, 4H), 3.05−3.09 (m, 2H), 7.07 (d, J = 6 Hz, 1H), 7.38 (d, J = 6 Hz, 1H); ^{13}C NMR δ 25.4, 27.0, 35.5, 39.2, 57.6, 124.0, 127.9, 135.9, 157.5, 191.3, 209.3. Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 60.80; H, 6.34.

Treatment of Dithiane Alcohol 31 with NCS. The alcohol **31** on similar treatment with NCS as in other rearrangement reactions produced the hydroxyaldehyde **32** as a viscous oil (90%); IR (neat) 3600−3400, 1715, 1560 cm^{-1}; ^{1}H NMR δ 0.96 (s, >3H), 1.04 (s, >3H), 1.40−2.46 (m, 21H), 3.45 (broad 1H), 10.14 (s, >1H), 10.28 (s, >1H).

Treatment of Dithiane Alcohol 34 with NCS. This alcohol also produced the hydroxyaldehyde **35** as a viscous oil (89%), IR (neat) 3600−3200, 1710, 1605 cm^{-1}; ^{1}H NMR δ 1.02 (s, 3H), 1.23−1.91 (m, 8H), 3.87 (s, 1H), 7.26−7.39 (m, 3H), 7.59 (d, J = 9 Hz, 2H).

Isolation of Intermediate 36. To a stirred solution of dithiane alcohol **24** (160 mg, 5 mmol) in dry CH_2Cl_2 (3.5 mL) was added *N*-chlorosuccinimide (80 mg, 6 mmol) under nitrogen. During the addition of *N*-chlorosuccinimide, a transient red color have developed. The mixture was stirred for 15 min, and after that CH_2Cl_2 was removed under vacuum. The residue was extracted with ether. Evaporation of ether followed by purification by silica gel column chromatography afforded the α-keto dithiane derivative **36** (119 mg, 75%) as a solid (mp 123−124 °C); IR (KBr) 1680, 1420, cm^{-1}; ^{1}H NMR δ 1.01−1.07 (m, 2H), 1.38−1.43 (m, 4H), 1.90−2.21 (m, 6H), 2.63−2.70 (m, 2H), 2.95 (t, J = 9 Hz, 2H), 3.50 (dd, J = 15, 3 Hz, 2H), 7.10−7.33 (m, 3H), 7.99 (d, J = 9 Hz, 1H); ^{13}C NMR δ 24.1, 24.5, 28.8, 31.4, 37.8, 44.1, 58.9, 59.0, 127.3, 127.4, 128.8, 129.8, 137.5, 139.5, 205.5. Anal. Calcd for $C_{18}H_{22}OS_2$: C, 67.78; H, 6.96. Found: C, 67.79; H, 6.96.

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Supporting Information Available: Tables of crystal data, structure solution and refinement, atomic coordinates, bond lengths and angles, and anisotropic thermal parameters for **15a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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