Diheteroaromatic dianionic oxy-Cope rearrangement route to the synthesis of novel heterocyclic compounds

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This is a first instance where the π bonds of the two thiophene rings act as a 1,5-hexadiene system necessary for the oxy-Cope rearrangement. This new reaction termed by us as diheteroaromatic dianionic oxy-Cope rearrangement is used for the synthesis of novel heterocyclic compounds 4,5-diphenyl-3,6-dithia-4,5-dihydro-as-indacene-4,5-diol (2), 25. 26-dioxo-16. 23-dithiaheptacyclo [12.10. 2. 01,14.01,17.01,20.02,24.] hexacosa-2(7), 3, 5, 8(13), 9, 11, 15(19), 17, 20(24), 21 decaene (4) and 4.11-dithiapentacyclo [12.7.1. 03,7. 08,12. 018,22.] docosa-1(21), 3(7), 5, 8(12), 9, 14(22), 15, 17, 19-nonaene-2,13-dione (6), from simple starting materials.

Keywords: 2-Thiophenylmagnesium bromide, diheteroaromatic dianionic oxy-Cope rearrangement, tandem reaction, heterocyclic compounds, 1,2-diols

Oxy-Cope rearrangement is a [3,3]-sigmatropic rearrangement where the two π bonds of the 1,5 hexadiene system undergoes a [3,3]-sigmatropic shift. We have reported 1 oxy-Cope rearrangement where the two π bonds of the two aromatic rings undergoes [3, 3] sigmatropic shift. The involvement of π bond of one heteroaromatic ring is reported 2. But there is no report on the involvement of the two π bonds of two heteroaromatic rings in oxy-Cope rearrangement. Hence we report a first instance where the two π bonds of two heteroaromatic rings act as a 1,5 hexadiene system necessary for oxy-Cope rearrangement.

Results and Discussion

The diols, 1,2-diphenyl-1,2-di (thiophen-2-yl)-ethane-1,2-diol (1), 9,10-dihydro-9,10-di(thiophen-2-yl)phenanthrene-9,10-diol (3) and 1,2-dihydro-1,2-di(thiophen-2-yl)acenaphthylene-1,2-diol (5) were synthesized by the addition of 2-thiophenyl magnesium bromide to benzil, phenanthrene-9,10-dione and acenaphthene-1,2-dione respectively.

1,2-Diphenyl-1,2-di (thiophen-2-yl)ethane-1,2-diol (1) on treatment with 10 equivalents of NaH in THF at 25°C for 2 hr gave a waxy solid 2 in 79% yield (Scheme I). The TLC of the waxy solid showed a new single spot. The IR spectrum of 2 showed broad peak at 3399 cm⁻¹ for OH stretching and 1H NMR of 2 showed D₂O exchangeable signal at δ 1.7 (br, s, 2H), δ 7.15-7.21 (m, 4H) proton of thiophene rings and δ 7.49-7.91 (m, 10H) protons of the benzene ring. The 13C NMR spectrum of 2 showed signal at δ 77.29 due to >C-OH carbon. The mass spectrum showed m/z (M⁺ + 2) at 378.8216.

The mechanism of formation of 2 can be rationalized as the dianion of 1 undergoes tandem diheteroaromatic dianionic oxy-Cope rearrangement / [2+2] cycloaddition / cleavage as shown in Figure 1.

9,10-Dihydro-9,10-di(thiophen-2-yl)phenanthrene-9,10-diol (3) on treatment with 10 equivalents of NaH in THF at 25°C for 2 hr gave a waxy solid in 75% yield (Scheme II). The TLC of the waxy solid 4 showed a new single spot. The IR spectrum of 4 showed the absence of OH stretching and presence of >C-H stretching at 2957, 2922, 2853 cm⁻¹, >C=C< stretching at 1627 cm⁻¹ and >C-O stretching at 1260 cm⁻¹. The 1H NMR spectrum of 4 showed signals at δ 6.58 to 6.72 (m, 2H) due to α protons of thiophene ring, δ 6.82-6.89 (m, 2H) β-protons of thiophene ring and δ 7.0-7.77 (m, 8H), aromatic protons of the benzene ring. 13C NMR spectrum of 4 showed >C-O-carbon at δ 80.57 and the mass spectrum showed m/z (M⁺) at 372.5167.

The mechanism of formation of 4 can be rationalized as the dianion of 3 undergoes tandem diheteroaromatic dianionic oxy-Cope rearrangement / [2+2] cycloaddition / cleavage as shown in Figure 2. Similar mechanism has been reported by. Alder et al. 3
for tandem (3,3) sigmatropic rearrangement / criss-cross (2π+2π) cycloaddition.

1,2-Dihydro-1,2-di(thiophen-2-yl)acenaphthylene-1,2-diol 5 on treatment with 10 equivalents of NaH in THF at RT for 2 hr gave a waxy solid 6 in 70 % yield (Scheme III). The TLC of the product showed a single spot. The IR spectrum of 6 showed the absence of =O stretching and presence of >C=O stretching at 1712 cm$^{-1}$. The $^1$H NMR spectrum of 6 showed the presence of protons of thiophene ring at δ 7.10 (t, 2H) and δ 7.69 (d, 2H), the naphthalene ring protons gave signals at δ 7.51 (t, 2H), δ 7.84 (t, 2H) and δ 8.1 (d, 2H). $^{13}$C NMR spectrum of 6 showed the presence of carbonyl carbon at δ 189. The mass spectrum showed $m/z$ (M$^+$ + 2) at 348.4871.

The mechanism of formation of 6 is shown in Figure 3. The mechanism involves a diheteroaromatic dianionic oxy-Cope rearrangement followed by air oxidation. A similar air oxidation is reported $^4$.

**Materials and Methods**

All m.ps. are uncorrected. The purity of the compounds was checked by Thin Layer Chromatography (TLC) on silica gel. $^1$H NMR spectra were recorded in deuteriochloroform (CDCl$_3$) using tetramethyl silane (TMS) as an internal standard on a
Bruker 300 spectrometer at 400 mega Hertz (MHz). $^{13}$C NMR spectra were recorded on a Bruker 300 spectrometer at 100 MHz and mass spectra on Jeol DX-303 spectrometer. Tetrahydrofuran was freshly distilled from sodium benzophenone ketyl before use. The reactions were carried out in a Schlenk type glass apparatus under nitrogen atmosphere.

**Experimental Section**

General procedure for the synthesis of compounds 2, 4 and 6

A solution of the diol (0.189 g, 0.0005 mol) in dry THF (10 mL) was added to a suspension of sodium hydride (NaH) (0.240 g, 0.005 mol) 50% dispersion in mineral oil washed with petroleum ether 60-80°C (3 × 10 mL) in dry THF (10 mL). The mixture was stirred under nitrogen atmosphere for 3 hr at RT. Then cooled and quenched with a saturated solution of ammonium chloride (10 mL). The product was extracted with diethyl ether (3 × 10 mL) and the combined organic phases were washed with brine, water then dried over anhydrous sodium sulphate.
(Na$_2$SO$_4$). On removal of the solvent a residue was obtained. TLC of which showed a single spot. Purification of the residue by column chromatography on silica gel, with [hexane-ethyl acetate (9:1)] as eluent, afforded the corresponding product 2, 4 and 6.

**4,5-Diphenyl-3,6-dithia-4,5-dihydro-asindacene-4,5-diol**, 2. A waxy solid. Yield 79%, IR (KBr): 3399 (-OH str.), 2948, 2842, (>C-H str.), 1651 cm$^{-1}$ (>C=C< str.); $^1$H NMR (400 MHz, CDCl$_3$/TMS): $\delta$ 1.7 (br, s, 2H, D$_2$O exchangeable-OH proton), 7.15-7.21 (m, 4H, protons of the thiophene ring), 7.49-7.91 (m, 10H, protons of the benzene ring); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 77.29 (2C), 127.95 (2C), 128.12 (4C), 128.42 (2C), 129.18 (2C), 130.06 (4C), 132.27 (2C), 138.17 (2C), 143.65 (2C). Mass spectrum: $m/z$ (M$^+$) 378.8216. Anal. Found: C, 70.19; H, 4.23; S, 17.01. Calcd. for C$_{22}$H$_{16}$O$_2$S$_2$: C, 70.21; H, 4.25; S, 17.02%.

**25. 26–Dioxa-16. 23–dithiaheptacyclo [12.10. 0$^{1,14,17,0^{13,15,19,0^{30,24}}}$] hexacosa–2(7), 3, 5, 8(13), 9, 11, 15(19), 17, 20(24), 21 decaene**, 4. A waxy solid. Yield 75%, IR (KBr): 2957, 2924, 2853 (>C-H str.), 1627 cm$^{-1}$ (>C=C< str); $^1$H NMR (400 MHz CDCl$_3$/TMS): $\delta$ 6.58-6.72 (m, 2H, $\alpha$-protons of the thiophene ring), 6.82-6.89 (m, 2H, $\beta$-protons of the thiophene ring), 7.0-7.77 (m, 8H, protons of the benzene ring); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 80.57 (2C), 126.7 (2C), 126.98 (2C), 128.03 (2C), 128.85 (4C), 128.93 (2C), 131.49 (2C), 136.29 (2C), 140 (2C), 145 (2C); Mass spectrum: $m/z$ (M$^+$) 372.5167. Anal. Found: C, 70.92; H, 3.20; S, 17.19. Calcd. for C$_{22}$H$_{12}$O$_2$S$_2$: C, 70.96; H, 3.22; S, 17.20%.

**4.11-Dithiapentacyclo [12.7.1. 0$^{3,7,0^{12,18,22}}$] docosa-1(21), 3(7), 5, 8(12), 9, 14(22), 15, 17, 19-nonaene-2,13–dione**, 6. A waxy solid. Yield 70%, IR (KBr): 3005, 2925, 2855 (>C-H str.), 1712 cm$^{-1}$ (>C=O str.); $^1$H NMR (400 MHz, CDCl$_3$/TMS): $\delta$ 7.1 (quartet, $J$ = 4 Hz, 2H, $\alpha$-protons of the thiophene ring), 7.51 (t, $J$ = 7.5 Hz, 2 H, protons of the naphthalene ring), 7.69 (dd, $J$ = 19 Hz, 8 Hz, 2 H, $\beta$-protons of the thiophene ring), 7.84 (dd, $J$ = 15.5 Hz, 7 Hz, 2 H, protons of the naphthalene ring), 8.1 (d, $J$ = 7.5 Hz, 2 H, peri protons of the naphthalene ring); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 125 (2C), 127 (2C), 132, 140 (2C), 145 (2C), 149 (2C), 159 (2C), 169 (2C), 170 (2C), 171 (2C), 172 (2C).

![Scheme III](image-url)
Conclusion

In conclusion, our work is the first instance where the two π bonds of two heteroaromatic rings act as a 1, 5 hexadiene system necessary for oxy-Cope rearrangement, which leads to the synthesis of novel heterocyclic compounds from simple starting materials.

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References