# Acid catalysed condensation of 2-hydroxy-2,2′-biindan-1,1′,3,3′-tetrone with enols

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Various enolic compounds such as acetyl acetone, ethyl- and methyl-acetoacetate condense with 2-hydroxy-2,2′-biindan-1,1′,3,3′-tetrone **1** in acid medium to produce adducts, which preferentially remain in the hemi-ketal form as confirmed by X-ray diffraction studies. **1** is also found to undergo acid catalysed dimerisation to furnish a cage like adduct fabricated by ketal and hemi-ketal linkages.

**Keywords:** 2-hydroxy-2,2'-biindan-1,1',3,3'-tetrone, enols, condensation, hemi-ketals

The facile acid-catalysed condensations of ninhydrin with various phenols, enols and aromatic substrates are well known.[1] It is generally observed that the C-2 position of ninhydrin is reactive to various nitrogen-, sulfur-, oxygen-, and carbon-based nucleophiles.[2] Although 2-hydroxy-2,2'-biindan-1,1',3,3'-tetrone[3] **1** is structurally similar to ninhydrin (Scheme 1), the electrophilic chemistry of **1** was mostly unexplored until our recent report where we have shown that **1** can also condense with various carbon-based nucleophiles in an acid medium.[4] Since some of the derivatives of **1** and structurally related compounds are found to be biologically active[5] (as an anticoagulent,[5c] in ganglion-blocking,[5b] have hypotensive activity[5b] *etc*.) we have carried our studies further. In this paper we wish to report the facile acid-catalysed condensation of **1** with various enols and the structural studies of adducts so formed.

In the present study it has been observed that various enolic compounds such as acetyl acetone, ethyl- and methyl-acetoacetate condense with **1** in acetic acid medium simply by stirring at room temperature. A proposed mechanism of the reactions is presented in Scheme 1. The protonation of the hydroxy group of **1** is followed by elemination of water to produce the electron-deficient olefin **2a** which then undergoes nucleophilic attack from various species (Scheme 1).[4]

$^1$H NMR spectra of the adducts **4a–c** indicate the formation of unsymmetrical structures which are attributed to preferential hemi-ketal formation from the initial adducts **3a–c** (Scheme 1). X-ray studies of the adducts **4a** and **4b** derived by the condensation of **1** with acetyl acetone and ethyl acetoacetate respectively, confirm the hemi-ketal structures with the *cis* geometry of the *vicinal* –OH and the 1,3-indanedionyl moiety at the bridgehead of the bicyclo[3.3.0]octano system (Figs 1 and 2)[6].

Surprisingly, **1** is also found to undergo an acid-catalysed dimerisation to furnish a cage-like adduct fabricated by

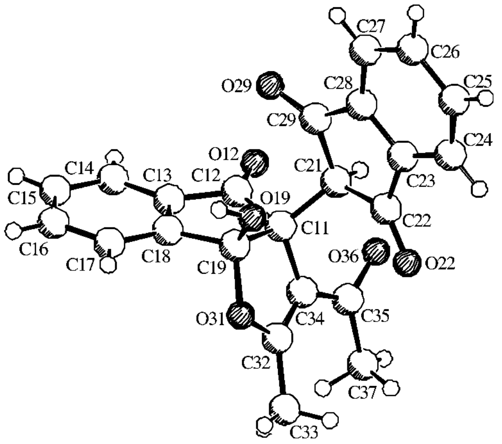
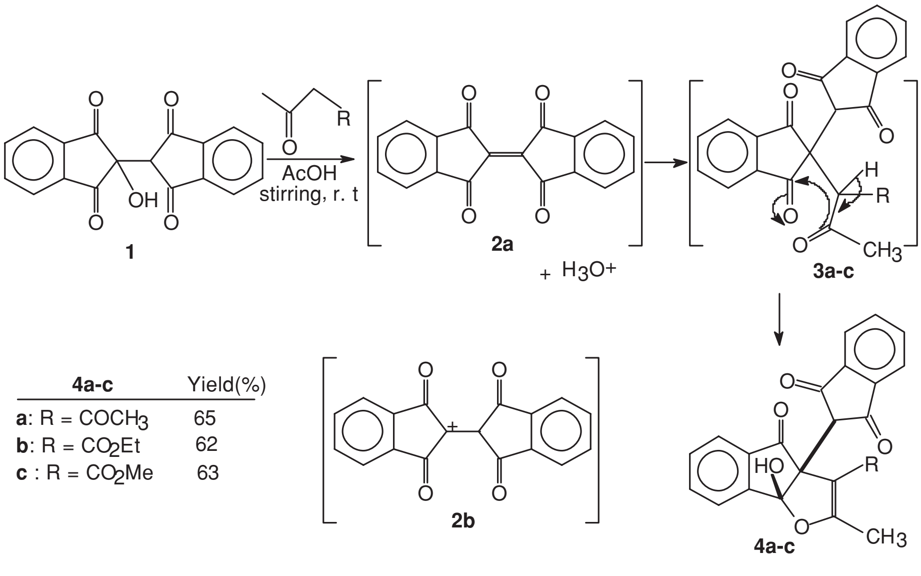


Fig. 1 SCHAKAL-plot with atomic numbering scheme of **4a**.



| 4a-c | Yield(%) |
|---|---|
| **a**: R = $COCH_3$ | 65 |
| **b**: R = $CO_2Et$ | 62 |
| **c** : R = $CO_2Me$ | 63 |

Scheme 1

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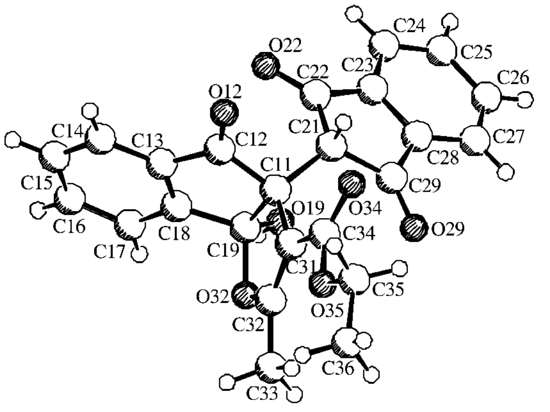


**Fig. 2** SCHAKAL-plot with atomic numbering scheme of **4b**.

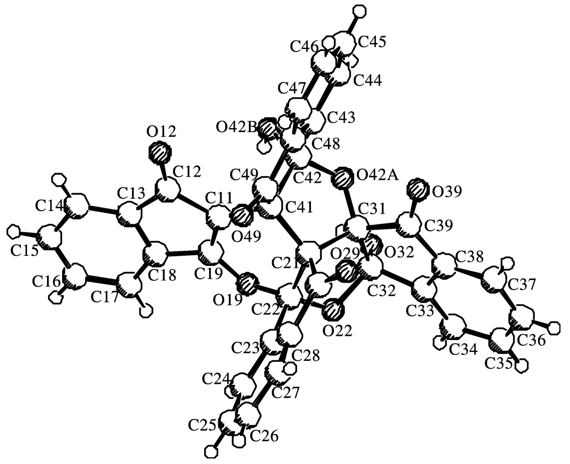


**Fig. 3** SCHAKAL-plot and atomic numbering scheme of **6**.

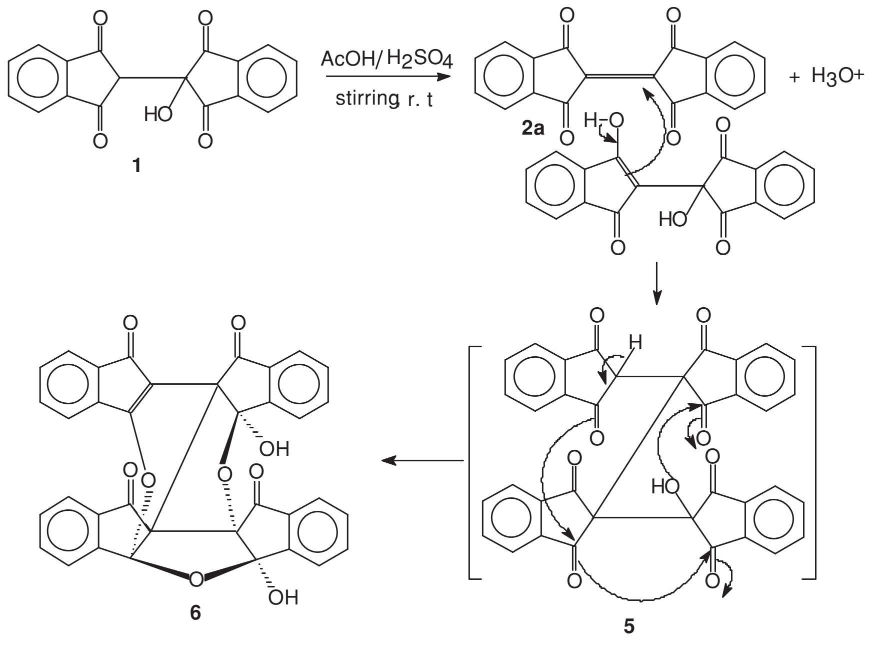
ketal and hemi-ketal linkages. Compound **1,** in its enolic form, condenses with olefin **2a** generated from itself in the acid medium to produce the dimeric adduct **5** (Scheme 2). Then **5** undergoes an intramolecular ketal and two hemi-ketal formations to fabricate a cage-like structure **6**. The two hemi-ketal linkages are consecutive. Interestingly, in compound **6** six stereogenic centres are set up in a single step with complete diastereocontrol over all six centres. Such an event is rarely found in the chemical literature. More excitingly all six are quaternary centres. Due to steric crowding, the dimerisation process of **1** needs a few drops of conc. $H_2SO_4$ as catalyst along with acetic acid and also a prolonged reaction time for the dimer formation. The X-ray crystal structure of **6** is presented in Fig. 3.[6]

The formation of adducts **4a–c** and **6** can be compared to the condensations of ninhydrin with enols. This is probably not a very good comparison, because when an OH group is lost from ninhydrin (by protonation and elimination of water) in an acid medium, the carbonium ion which remains is stabilised by the remaining OH group. The corresponding reaction with **1** leaves a destabilised carbonium ion **2b** (Scheme 1). Therefore, a more likely mechanism may involve the formation of electron-deficient olefin **2a** (Scheme 1), which may be generated under the dehydrating conditions. The formation of Michael acceptors like **2a** is well precedented in 1,3-indanedione chemistry.[7] Compound **2a** may condense with enols by acid-catalysed Michael-type reaction or by single electron transfer (SET) mechanism.[8] However the isolation of the intermediate **2a** was not possible during the formation of adducts **4a–c** and **6**. Neither was isolation of **2b**.

## Experimental

Melting points were determined in open capillary tubes. IR spectra were examined in KBr disc on a Perkin Elmer-782 spectrophotometer. Proton magnetic resonance spectra ($^1$H NMR) and carbon magnetic resonance spectra ($^{13}$C NMR) were recorded on a Bruker DRX-500 (500 MHz) spectrometer in the solvents indicated.

*General procedure for preparation of hemiketals* **4a–c**: A mixture of 2-hydroxy-2,2'-biindan-1,1',3,3'-tetrone **1** (0.43 g, 1.4 mmol) in acetic acid (8 ml) was warmed to make a clear solution. Then the appropriate enol $CH_3COCH_2R$ (4.2 mmol) was added to the mixture at room temperature and stirred for 40–48 h (40 h for acetylacetone, 48 hr for both ethyl- and methylacetoacetate). Then the reaction mixture was kept undisturbed overnight. The colourless crystals of products **4a–c** separated were filtered off and washed thoroughly with acetic acid and then with water. Single crystals for **4a** and **4b** were grown from acetic acid.



**Scheme 2**

**4a**: Colourless crystals, m.p. 258–259 °C; IR (KBr) $\nu_{max}$ 3080, 1717, 1587, 1273, 751 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$): $\delta_H$ 8.79 (1H, s), 7.89–7.87 (2H, m), 7.85–7.78 (3H, m), 7.74–7.71 (2H, m), 7.66–7.63 (1H, m), 4.89 (1H, s), 2.37 (3H, s), 2.14 (3H, s); $^{13}$C NMR (DMSO-$d_6$): $\delta_C$ 198.9, 198.4, 198.0, 194.1, 166.5, 149.4, 142.7, 141.9, 136.6, 136.1, 136.0, 135.9, 131.7, 124.9, 124.3, 123.23, 123.19, 112.2, 111.8, 67.2, 52.9, 31.5, 16.8; Anal. Calcd for $C_{23}H_{16}O_6$: C 71.1; H 4.15. Found: C 71.2; H 4.2 %.

4**b**: Colourless crystals, m.p. 246–247°C; IR (KBr) $\nu_{max}$ 3426, 3088, 1711, 1591, 1270, 760 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$): $\delta_H$ 8.78 (1H, s), 7.93–7.87 (2H, m), 7.84–7.78 (3H, m), 7.73–7.70 (2H, m), 7.65–7.63 (1H, m), 4.97 (1H, s), 4.13 (2H, q, $J$ = 7.1Hz), 2.11 (3H, s), 1.23 (3H, t, $J$ = 7.1Hz); Anal. Calcd for $C_{24}H_{18}O_7$: C 68.9; H 4.3. Found: C 68.95; H 4.4 %.

4**c**: Colourless crystals, m.p. 252–253°C; IR (KBr) $\nu_{max}$ 3210, 1700, 1592, 1271, 757 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$): $\delta_H$ 8.80 (1H, s), 7.89–7.84 (2H, m), 7.83–7.78 (3H, m), 7.73–7.70 (2H, m), 7.66–7.63 (1H, m), 4.72 (1H, s), 3.66 (3H, s), 2.11 (3H, s); Anal. Calcd for $C_{23}H_{16}O_7$: C 68.3; H 4.0. Found: C 68.4; H 4.1 %.

*Procedure for preparation of* **6:** 2-Hydroxy-2,2'-biindan-1,1',3,3'-tetrone **1** (0.43 g, 1.4 mmol) in acetic acid (5 ml) was warmed to make a clear solution. Then a few drops of conc. $H_2SO_4$ were added to the reaction mixture, which was stirred for 2–2.5 days at room temperature. Then the reaction mixture was kept undisturbed overnight. The yellow crystals of product **6** were filtered off and washed thoroughly with acetic acid followed by water (yield ~ 45%). Single crystals of **6** were grown from acetone/pet-ether. Yellow crystals, m.p. 215–217°C; IR (KBr) $\nu_{max}$ 3417, 3204, 1736, 1706, 1648, 1599, 1285, 968, 763 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta_H$ 7.95–7.92 (2H, m), 7.89–7.86 (1H, m), 7.76–7.71 (2H, m), 7.65–7.61 (1H, m), 7.59–7.58 (2H, m), 7.53–7.50 (1H, m), 7.43–7.39 (2H, m), 7.38–7.36 (1H, m), 7.34–7.29 (4H, m); Anal. Calcd for $C_{36}H_{18}O_9$: C 72.7; H 3.05. Found: C 72.85; H 3.1 %.

## Crystal data

**4a**: Formula $C_{23}H_{16}O_6$, $M$ = 388.36, colourless crystal 0.20 × 0.10 × 0.10 mm, $a$ = 14.644(1), $b$ = 15.245(1), $c$ = 16.884(1) Å, $V$ = 3769.3(4) Å$^3$, $\rho_{calc}$ = 1.369 g cm$^{-3}$, $\mu$= 8.28 cm$^{-1}$, empirical absorption correction ($0.852 \le T \le 0.922$), $Z$ = 8, orthorhombic, space group $P$bca (No. 61), $\lambda$= 1.54178 Å, $T$ = 223 K, $\omega$ and $\varphi$ scans, 5684 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sin$\theta$)/$\lambda$] = 0.58Å$^{-1}$, 3040 independent ($R_{int}$ = 0.036) and 2412 observed reflections [$I \ge 2\ \sigma(I)$], 265 refined parameters, $R$ = 0.047, $wR^2$ = 0.120, max. residual electron density 0.23 (–0.16) e Å$^{-3}$, hydrogen atoms calculated and refined as riding atoms.

**4b**: Formula $C_{24}H_{18}O_7$, $M$ = 418.38, colourless crystal 0.30 × 0.20 × 0.15 mm, $a$ = 8.722(1), $b$ = 15.114(1), $c$ = 15.548(1) Å, $\beta$ = 101.95(1)°, $V$ = 2005.2(3) Å$^3$, $\rho_{calc}$ = 1.386 g cm$^{-3}$, $\mu$= 8.57 cm$^{-1}$, empirical absorption correction ($0.783 \le T \le 0.882$), $Z$ = 4, monoclinic, space group $P2_1$/c (No. 14), $\lambda$= 1.54178 Å, $T$ = 223 K, $\omega$ and $\varphi$ scans, 11830 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sin$\theta$)/$\lambda$] = 0.58Å$^{-1}$, 3187 independent ($R_{int}$ = 0.042) and 2976 observed reflections [$I \ge 2\ \sigma(I)$], 283 refined parameters, $R$ = 0.043, $wR^2$ = 0.105, max. residual electron density 0.24 (–0.19) e Å$^{-3}$, hydrogen atoms calculated and refined as riding atoms.

**6**: Formula $C_{36}H_{18}O_9$ * 2 $C_3H_6O$, $M$ = 710.66, yellow crystal 0.15 × 0.10 × 0.05 mm, $a$ = 10.463(1), $b$ = 12.200(1), $c$ = 14.135(1) Å, $\alpha$ = 89.76(1), $\beta$ = 71.46(1), $\gamma$ = 83.07(1)°, $V$ = 1697.1(2) Å$^3$, $\rho_{calc}$ = 1.391 g cm$^{-3}$, $\mu$= 8.41 cm$^{-1}$, empirical absorption correction ($0.884 \le T \le 0.959$), $Z$ = 2, triclinic, space group $P$1bar (No. 2), $\lambda$= 1.54178 Å, $T$ = 223 K, $\omega$ and $\varphi$ scans, 15288 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sin$\theta$)/$\lambda$] = 0.59Å$^{-1}$, 4678 independent ($R_{int}$ = 0.067) and 2741 observed reflections [$I \ge 2\ \sigma(I)$], 464 refined parameters, $R$ = 0.073, $wR^2$ = 0.203, max. residual electron density 0.76 (–0.46) e Å$^{-3}$, hydrogen atoms calculated and refined as riding atoms, due to crystal size and disorder in one of the two solvent molecules accuracy of the analysis is poor.

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