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ORIGINAL PAPER

Expeditious reaction of ninhydrin with active methylene compounds on montmorillonite K10 clay

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Abstract Ninhydrin reacted expeditiously with thirteen active methylene compounds on montmorillonite K10 clay at room temperature to furnish, in 5 min, a Knoevenagel condensate in one case, aldols in six cases, aldol-derived cyclic hemiketals in three cases, and interesting products in the remaining three cases. Almost identical results were obtained, but faster, when the reactions were carried out in water on steam-bath. The structures of two novel products were also confirmed by single-crystal X-ray diffraction analysis.

Keywords Ninhydrin · Active methylene compounds · Montmorillonite K10 clay · Water · Aldolization

Introduction

The Knoevenagel reaction is an important C–C bond-forming reaction [1, 2], carried out classically in solutions heated under reflux in the presence of acids or bases as catalysts [3, 4]. In view of the harsh conditions and long periods of these reactions, which involve tedious work-ups to furnish the Knoevenagel condensates in wide-ranging yields, milder catalysts and conditions continue to be developed for this reaction [5–11]. The so-called "solvent-free" synthesis on solid supports [12, 13], often promoted by infrared [14] and microwave irradiation [15–17], catalyst-free reactions in water alone [18–20], and, most importantly, catalyst-free and solvent-free stoichiometric conversion of reactants to products using "reactive milling" (recently by use of commercial ball mills) known as "mechanochemistry" [21] or "tribochemistry" [22], and also as "melt reactions" [23, 24] have been successfully applied to Knoevenagel reactions in recent years [13, 25].

Our ongoing interest in carrying out useful reactions either in the so-called solvent-free manner on environment-friendly solids as catalysts or in water with or without the use of microwave irradiation (MWI) [26–28], drew our attention to the fact that most of the Knoevenagel reactions reported so far were studied with benzaldehydes. We were interested in the Knoevenagel reaction of ninhydrin (**1**), which bears a masked carbonyl group at C-2, because of the synthetic potential of the corresponding Knoevenagel condensates, e.g. as "ene" components in Diels–Alder reactions [29, 30] and as synthons for complex molecules [31–34]. Surprisingly, **1** has been reported to undergo successful Knoevenagel reaction with only one active methylene compound, viz. malononitrile (**2a**) under three different conditions [30, 35, 36]. The Knoevenagel condensates of **1** with several other active methylene compounds were prepared by the base (trifluoroacetic anhydride, pyridine)-catalysed or acid (concentrated sulfuric acid)-catalysed dehydration of the corresponding preformed aldols [37, 38]. The aldols had, in turn, been prepared from **1** and the various active methylene compounds by heating in dilute sulfuric acid [39] and at room temperature or beyond in dimethoxyethane (DME) (with

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molecular sieve, MS 3 Å) [35, 40], ethanol [41], water [42], or acetic acid [43, 44] or by using a ball mill [45]. All but the last named grinding method suffered from disadvantages, for example use of acid or solvents, long reaction periods (e.g. up to 22 h), tedious work-ups for isolation of the pure products, and often low yields of the aldols (e.g. 46%, 51/58%, etc). Only the ball mill method furnished the aldol from **1** and dimedone in quantitative yield.

But because the ball mill method has been applied to the reaction of **1** with dimedone only and because ball mills are undeniably expensive equipments, we wondered if the initial condensation of ninhydrin with active methylene compounds and subsequent acid-catalysed dehydration of the resulting aldols to form the corresponding Knoevenagel condensates could be accomplished together in one pot by using commercially available montmorillonite K10 clay (hereinafter referred to as clay) because it is highly acidic, has a large specific area, and yet is environment-friendly [46], hence enjoying widespread use in organic synthesis [47]. Accordingly, **1** was treated with several active methylene compounds separately on clay at room temperature. The results, albeit contrary to our expectation, were quite diverse and interesting. For comparative evaluation, the reactions were also carried out in water, which furnished nearly the same results. Our experiments and their outcome are presented herein.

Results and discussion

When a mixture of equimolar amounts of **1** and each of thirteen active methylene compounds (**2a**–**2m**) was uniformly adsorbed on clay and kept at room temperature, the reactions were complete (TLC) in 5 min, except for **2g** which required 30 min when heated at 60–70 °C in an oven (Table 1). In all these examples, except for Meldrum's acid (**2m**), a single product was formed; **2m** furnished two products, which were separated by column chromatography. Throughout, the products were leached from the clay with methanolic ethyl acetate except for **2c**, for which dichloromethane was used, because the product was thermally labile. The known products were identified by comparison (melting point, IR, and/or supportive ^{1}H NMR data) and the new products by thorough spectroscopic analysis and, in two cases, also by single-crystal X-ray diffraction analysis.

The product from **1** and malononitrile (**2a**), despite having a somewhat higher (by ca 10 °C) melting point than that reported earlier for the corresponding Knoevenagel condensate (**3a**) prepared from indane-1,2,3-trione and **2a** in DME/MS 3 Å [35], was identified as **3a** from its IR, ^{1}H, and ^{13}C NMR spectroscopic data (Scheme 1).

Each of the products from ethyl cyanoacetate (**2b**), diethyl malonate (**2c**), cyclohexane-1,3-dione (**2d**),

Table 1 Reaction of **1** with **2** on clay at rt and in H_2O on a steam-bath

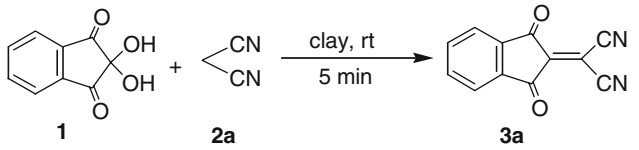
Entry	Educt	Clay			H_2O		
		Time (min)	Yield (%)[a]	Product	Time (min)	Yield (%)[a]	Product
1	**2a**	5	85	**3a** [35]	1	91	**3a**
2	**2b**	5	94	**3b** [35]	1	97	**3b**
3	**2c**	5	82	**3c** [35]	–	–	–
4	**2d**	5	80	**3d** [42]	1	83	**3d**
5	**2e**	5	83	**3e** [42]	1	90	**3e**
6	**2f**	5	91	**3f**[c]	1	98	**3f**
7	**2g**	30[b]	97	**3g**[c]	1	98	**3g**
8	**2h**	5	68	**3h** [44]	1	98	**3h′** [35]
9	**2i**	5	86	**3i** [35]	1	96	**3i**
10	**2j**	5	90	**3j** [42]	1	93	**3j**
11	**2k**	5	89	**3k**[c]	1	98	**3k**
12	**2l**	5	92	**3l**[c]	1	92	**3l**
13	**2m**	5	40	**3m**[c]	5	93	**3l**
14	**2n**	–	–	–	1[d]	–	–
15	**2o**	–	–	–	–	–	–
16	**2p**	–	–	–	1[d]	–	–

[a] Refers to isolated yield

[b] Reactants on clay were heated at 60–70 °C in an oven

[c] New compounds

[d] Products underwent decomposition



Scheme 1

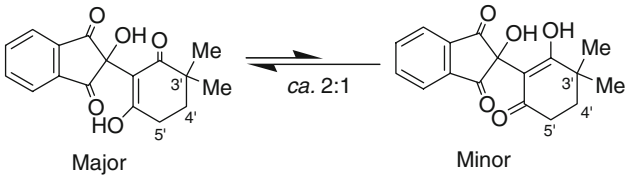


Fig. 1 Equilibrium of **3f** in DMSO-d_6

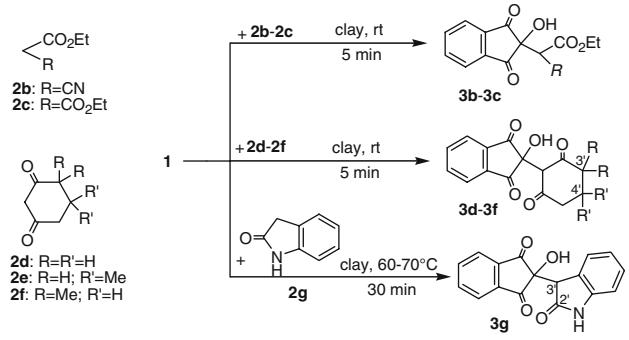
dimedone (**2e**), 4,4-dimethylcyclohexane-1,3-dione (**2f**), and oxindole (**2g**) displayed significantly, inter alia, IR absorption bands for the hydroxyl and an uncoupled, deshielded ($\delta = 4.06$–5.74 ppm) proton signal in their ^{1}H NMR spectra. They thus appeared to be the corresponding aldols (**3b**–**3g**) (Scheme 2), which received full support from their ^{13}C NMR data. But some snags we encountered while trying to identify them, and some of their additional structural characteristics are as follows.

The product **3b** had a higher melting point (by ca 15 °C) than had earlier been reported for the corresponding aldol (**3b**) prepared from indane-1,2,3-trione and **2b** in DME/MS 3 Å [35]. The product **3c** could not be crystallized by us even from petroleum ether bp 60–70 °C which had previously been reported as the solvent used for crystallization of this compound [35]. The product **3e**, which had earlier been prepared from **1** and **2e** under four different conditions [39, 42, 43, 45], contained a trace of the corresponding enol ($\delta = 11.18$ ppm, <1H) in $CDCl_3$-*DMSO*-d_6. The product **3f**, a new chemical entity, displayed in its ^{1}H NMR spectrum (*DMSO*-d_6) two sets of signals for the methylene and methyl groups (vide Experimental), suggesting that this product exists in DMSO as a ca 2:1 mixture of the two tautomers (Fig. 1). The products from **2b**–**2g** are shown in Scheme 2.

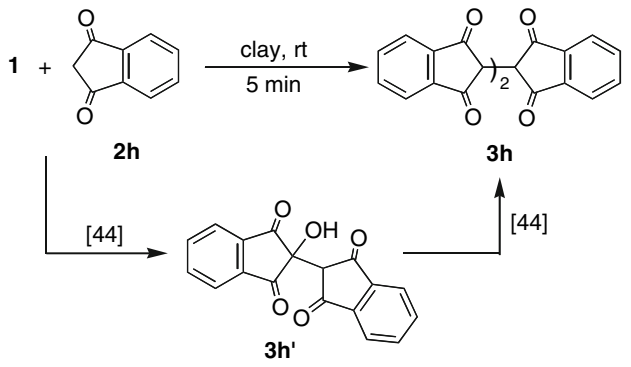
The product from **1** and indane-1,3-dione (**2h**) appeared *not* to be the corresponding aldol (**3h′**) from its much higher melting point than previously reported for **3h′** [35] and from its IR and ^{1}H NMR spectra. Indeed, the latter contained a two-proton singlet at $\delta = 5.02$ ppm, which, with its mass spectrometrically derived molecular formula, $C_{27}H_{14}O_6$, suggested it to be "trisindanedione" (**3h**), the product of tandem Knoevenagel–Michael addition reactions. This reportedly bioactive compound [48] had been prepared earlier from **2h** and **3h′** in acetic acid–sulfuric acid [44] and also by electrolysis of 2,2-dibromoindane-1,3-dione using a graphite cathode [48]. The lack of melting point of **3h** in the two previous reports precluded direct comparison. We, therefore, prepared **3h′** from **1** and **2h** in acetic acid, converted it to **3h** [44] and compared it with the product obtained from **1** and **2h** on clay. Our product was unambiguously characterized as **3h** (Scheme 3).

The products stemming from **1** and, separately, acetylacetone (**2i**) and ethyl acetoacetate (**2j**) were identified as the dihydroxydihydrofuroindanones **3i** and **3j**, respectively (i.e. the cyclic hemiketals formed from the enols of the initially formed, unisolable aldols), prepared earlier from the same reactants from reactions in warm water; their depicted stereostructures were established by NOE studies and single-crystal X-ray crystallographic analyses [42] and separately in acetic acid [43]. The reaction of **1** with methyl acetoacetate (**2k**), not studied earlier, resulted in a similar formation of the third cyclic hemiketal **3k**, which was unequivocally identified from its similar spectroscopic data (Scheme 4).

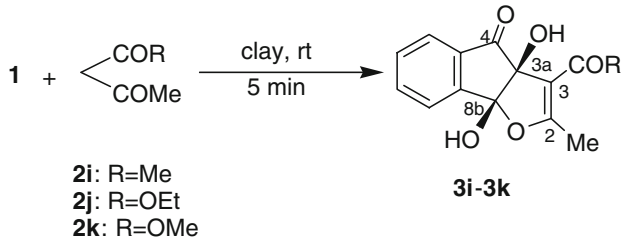
The reaction of **1** with malonic acid (**2l**) on clay furnished, in high yield, the hydroxyacid (**3l**), the product of decarboxylation of the initially formed, unisolated hydroxydicarboxylic acid, i.e. the aldol (**3l′**) (Scheme 5). Decarboxylation during the attempted Knoevenagel reaction, although documented previously for reactions carried out under reflux in solution [49], is hitherto unreported for



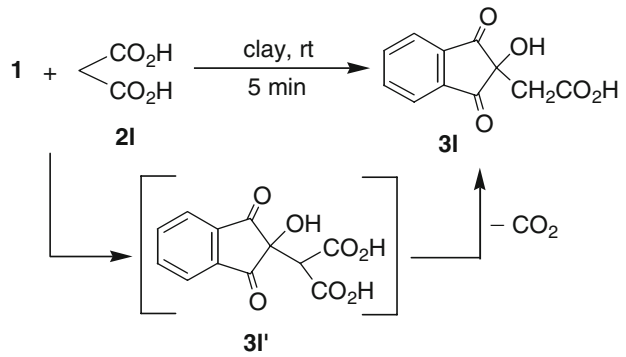
Scheme 2



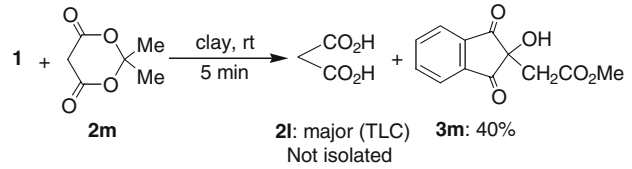
Scheme 3



Scheme 4



Scheme 5



Scheme 6

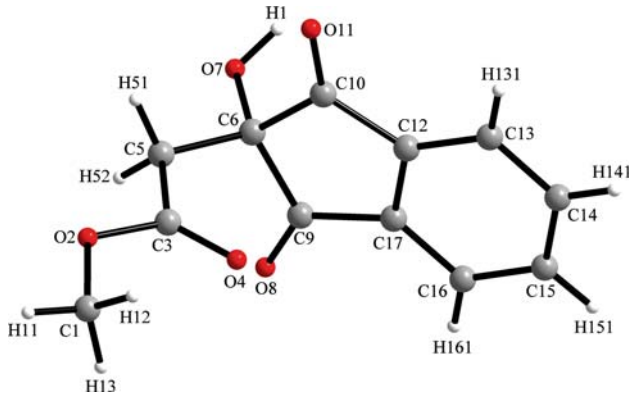


Fig. 3 X-ray crystal structure of **3m**

reactions carried out at room temperature. The structure of **3l** was, therefore, additionally supported by single-crystal X-ray diffraction analysis (Fig. 2).

Reaction of Meldrum's acid (**2m**) on clay indicated (TLC) the formation of malonic acid (**2l**) and the hydroxyacid **3l** as the major and the minor components. When, however, the clay containing the products was leached with 10% methanolic ethyl acetate, the extract showed (TLC) the presence of **2l** (not isolated by us) and, instead of **3l**, another less polar product identified spectroscopically as the new compound **3m**, i.e. the methyl ester of **3l** (Scheme 6). Because formation of **3m** was unexpected, its structure was also consolidated by single-crystal X-ray crystallography (Fig. 3).

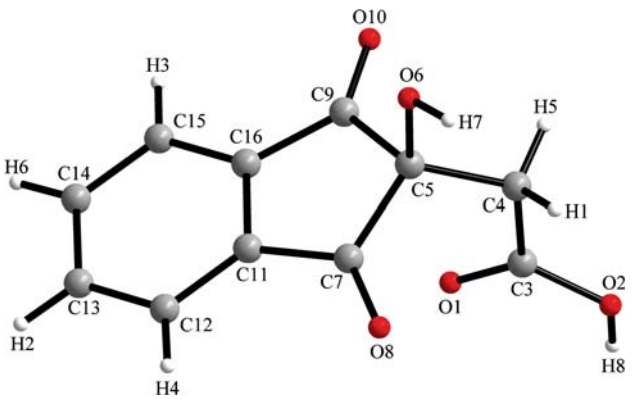
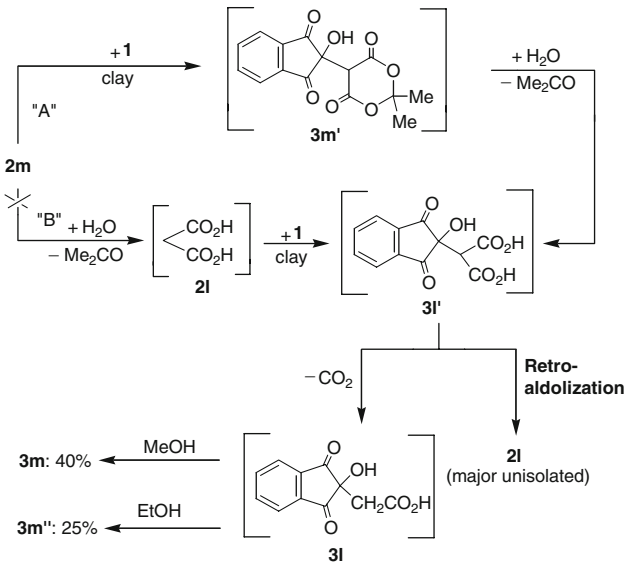


Fig. 2 X-ray crystal structure of **3l**

Conceivably, **3m** originated from the clay-catalysed esterification of **3l** (methanol used for extraction being the source of the alcohol part of **3m**), which, in turn, must have originated from **3l′**. The latter may have been formed in either of two possible ways. Reaction of **1** with **2m** may lead to the aldol **3m′**, which may undergo hydrolytic cleavage to **3l′** with concomitant loss of acetone (route "A"). Alternately, **2m** itself may undergo a similar cleavage on clay to furnish acetone and malonic acid (**2l**), and the latter may then undergo aldol condensation with **1** to form **3l′** (route "B") (Scheme 7). When, in a separate experiment, only **2m** was uniformly adsorbed on clay and kept at room temperature for 30 min, it remained unchanged (TLC), which ruled out route "B". The other end product, i.e. malonic acid (**2l**) is likely to have been formed by a competitive retro-aldolization of **3l′**—a process presumably faster than the decarboxylative methylation of **3l′** to **3m**, because **2l** was the major product (Scheme 7).

In order to confirm the source of the alcohol part of **3m**, an equimolar mixture of **1** and **2m** was dissolved in a minimum volume of ethanol (and not methanol), adsorbed uniformly on clay and kept at room temperature until (5 min) the reactants were fully consumed (TLC). The resulting products were leached from the clay with 10% ethanolic (and not methanolic) ethyl acetate, and the extract showed (TLC) the presence of **2l** and a product which was more polar than **3m**. This second product was separated and identified spectroscopically as **3m″**, i.e. the



Scheme 7

ethyl ester of **3l**, thereby consolidating the origin of the alcohol part of **3m** and also of **3m**″ (Scheme 7).

Interestingly, although methanolic ethyl acetate was used for leaching the product(s)-on-clay in the reaction of **1** with both malonic acid (**2l**) and Meldrum's acid (**2m**), separately, **3m**, i.e. the methyl ester of **3l**, was obtained only in the latter case. This strongly suggested that both **2m** (itself a strong acid) and clay have a role to play in the esterification process. In order to verify this possibility, an equimolar mixture of the acid **3l** and **2m** in methanol was uniformly adsorbed on clay, kept at room temperature for 30 min, and leached with methanolic ethyl acetate, when the extract was found to contain **3m** (not detailed in the Experimental section). Our assumption thus turned out to be true.

Ninhydrin (**1**) was also allowed to react with cyanoacetamide (**2n**), hydantoin (**2o**), and thiazolidine-2,4-dione (**2p**) in a similar manner on clay. All three failed to react at room temperature or at elevated temperature (60–70 °C). In order to check the recyclability of clay, the reaction of **1** with each of **2b**, **2d**, and **2i**, separately, was carried out twice more using clay recovered and reactivated after the first and the second set of experiments. Clay recovered from the first cycle was found to furnish **3b**, **3d**, and **3i** in the same time (5 min) and in slightly lower yields (84, 72, and 78%) than in the first cycle. However, clay recovered from these experiments, when used in the second recycle, led to the starting materials remaining largely unconsumed (not detailed in the Experimental section). Clay is thus recyclable at best up to the second cycle.

Pertinently, the reaction of **1** with **2a** and the four 1,3-dicarbonyl compounds **2d**, **2e**, **2i**, and **2j** had earlier been carried out in water [36, 42]. Of these, only **2a** furnished the corresponding Knoevenagel condensate **3a** in boiling water (5 min; 70% yield) [36]. The reactions of **2d**, **2e**, **2i**, and **2j** in water at room temperature had reportedly furnished the aldols **3d** and **3e** and the aldol-derived cyclic hemiketals **3i** and **3j** in 82–86% yields but required 15–22 h for completion [42]. We, therefore, investigated the catalyst-free reactions of **1** with **2a**–**2p** in water but on a steam-bath. All the reactions were complete in 1 min, except for **2m** (5 min) and **2c** (which did not react) (Table 1). The substrates, except for **2h** and **2m**, furnished the corresponding products that were obtained from the clay-mediated reactions but in better yields, 83–98%. While **2h** resulted in the formation of the expected aldol **3h** nearly quantitatively, **2m** efficiently furnished the hydroxyacid **3l**, which was not unexpected, because its isolation did not involve any extractive work-up. Among the substrates **2n**–**2p**, only **2n** and **2p** reacted with **1** and were fully consumed in 1 min, but the products underwent decomposition during isolation.

To conclude, montmorillonite K10 clay was unable to bring about the desired Knoevenagel condensation of ninhydrin (**1**) with the active methylene compounds **2b**–**2p**. But it was proved to be quite efficient and expeditious in their aldolization and formation of some novel compounds with interesting mechanisms of formation. Water was found to be somewhat better suited, which furnished somewhat different results but much faster and more efficiently. Because montmorillonite K10 clay is commercially available, inexpensive, and harmless to the environment, and because the reactions were carried out in a manner involving use of substantially lesser amounts of solvents, the present method should be considered as a viable alternative to the best method(s) available for the purpose.

Experimental

Montmorillonite K10 clay was procured from Fluka. Melting points were determined on a Toshniwal apparatus. FTIR spectra were recorded on a Nicolet Impact 410 spectrophotometer, ^{1}H (500/300 MHz) and ^{13}C (125/75 MHz) NMR spectra, including DEPT 135, on Bruker DRX 500/300 NMR spectrometers, LR EIMS on a Jeol JMS-AX505HA, and HR EI/FAB and ESI-MS on Jeol JMS-700 MStation and Waters Qtof Micro YA263 mass spectrometers, respectively. In FABMS spectra, *m*-nitrobenzyl alcohol was used as the liquid matrix. The six new compounds (**3f**, **3g**, **3k**, **3l**, **3m**, and **3m**″) were subjected to elemental analyses on a Perkin Elmer 2400 Series II C, H, N Analyzer and the results were found to be in good agreement with the calculated values. Thin-layer chromatography (TLC) was carried out on silica gel G plates (Merck, India) and column chromatography (CC) was carried out on silica gel (60–120 mesh; Qualigens, India).

For known compounds, only data not reported elsewhere have been furnished here. PE refers to petroleum ether, bp 60–80 °C. The yields of the products have been rounded to the nearest integers.

General procedure for reaction on montmorillonite K10 clay

A mixture of 1 mmol **1** and 1 mmol **2** was dissolved in 0.5–1.0 cm^3 MeOH, adsorbed uniformly on 1.0 g clay, and kept inside a hood at rt. The reactants were consumed (TLC) in 5 min (except for **2g**). The clay was then leached with 3 × 15 cm^3 5–10% MeOH–EtOAc, solvent was removed from the pooled extracts by distillation, and the resulting residue was purified either by CC (for **3m**) or directly by crystallization (for the rest) to furnish **3a**–**3f**, **3h**–**3m**. The purity of these products was checked by TLC and ^{1}H NMR spectroscopy.

In the reaction with **2g**, the reactants remained largely unconsumed (TLC) even after 4 h. A fresh batch of the reactants-on-clay was, therefore, prepared in a similar manner and heated in an oven at 60–70 °C when the starting materials were consumed in 30 min. The clay was then cooled to rt, leached with 5% MeOH–EtOAc and the product, obtained after a similar work-up, was purified by crystallization to furnish pure **3g**.

General procedure for reaction in water

A suspension of a mixture of 1 mmol **1** and 1 mmol **2** in 2 cm^3 water was heated on steam-bath until the reactants were consumed (TLC). For each of **3a**, **3b**, **3e**, **3f**, **3h′**, **3i**, **3j**, and **3l**, the precipitated solid was isolated by filtration, washed with water, dried, and purified by crystallization. For **3d**, **3g**, and **3k** the resulting gummy material was extracted with 3 × 15 cm^3 EtOAc, the solvent was removed from the pooled extracts by distillation, and the resulting residue was purified by crystallization. The purity of the final products was checked by TLC and ^{1}H NMR spectroscopy.

*Alternative preparation of **3h′** and **3h***

Following a reported procedure [44], **3h′** was prepared from **1** and **2h** on a 2-mmol scale in 86% yield (0.52 g) as light yellow crystals, mp 238–240 °C (dec) ([35] 238–240 °C).

Following the same reference, **3h** was prepared from **3h′** and **2h** on a 1-mmol scale in 65% yield (0.28 g) as pale yellow crystals, mp 282–284 °C (dec) ([44]; mp not reported). The identity of this compound and the product **3h** obtained from clay was verified by direct comparison (mp, mixed mp, TLC, co-TLC).

*2-Dicyanomethyleneindane-1,3-dione (**3a**)*

Golden yellow crystals; mp 267–268 °C (dec) (EtOAc) ([35] 258–260 °C); yield 0.18 g, 85% (clay)/0.19 g, 91% (water); $R_f = 0.28$ (EtOAc–MeOH, 19:1); ^{13}C NMR (125 MHz, *DMSO*-d_6): $\delta = 125.1$, 138.5 (both Ar–CH), 87.0, 111.7 (×2), 142.1, 154.5, 183.6 (×2) (all C) ppm.

*Ethyl cyano(2′-hydroxyindane-1′,3′-dione-2′-yl) acetate (**3b**)*

White crystals; mp 140–142 °C (dec) (*n*-hexane–EtOAc) ([35] 123–125 °C); yield 0.25 g, 94% (clay)/0.26 g, 97% (water); $R_f = 0.50$ (C_6H_6–MeOH, 19:1); ^{1}H NMR (500 MHz, $CDCl_3$ + *DMSO*-d_6): δ = 1.09 (t, J = 7.0 Hz, 3H), 4.05 (q, J = 7.0 Hz, 2H), 4.55 (s, 1H), 7.51 (s, 1H), 7.90–7.94 (m, 2H), 8.01–8.05 (m, 2H) ppm; ^{13}C NMR (125 MHz): $\delta = 13.8$ (CH_3), 63.7 (CH_2), 41.9, 124.3, 124.5, 136.6 (all CH), 72.4, 113.7, 140.9, 141.3, 163.7, 195.86, 195.87 (all C) ppm.

*Diethyl (2′-hydroxyindane-1′,3′-dione-2′-yl) malonate (**3c**)*

Gummy material ([35] 76–78 °C); yield 0.26 g, 82% (clay); $R_f = 0.50$ (C_6H_6–EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.2 Hz, 6H), 4.17 (s, 1H), 4.13–4.33 (m, 4H), 5.06 (s, 1H), 7.84–7.93 (m, 2H), 7.99–8.07 (m, 2H) ppm.

*2-(Cyclohexane-2′,6′-dione-1′-yl)-2-hydroxyindane-1,3-dione (**3d**)*

White crystals; mp 173–175 °C (dec) (PE–EtOAc) ([42] 174–175 °C); yield 0.22 g, 80% (clay)/0.23 g, 83% (water); $R_f = 0.37$ (EtOAc–MeOH–AcOH, 96:3:1).

*2-(4′,4′-Dimethylcyclohexane-2′,6′-dione-1′-yl)-2-hydroxyindane-1,3-dione (**3e**)*

White crystals; mp 208 °C (dec) (*n*-hexane–EtOAc) ([42] 208 °C); yield 0.25 g, 83% (clay)/0.27 g, 90% (water); $R_f = 0.40$ (EtOAc–MeOH, 9:1); ^{1}H NMR (500 MHz, $CDCl_3$ + *DMSO*-d_6): $\delta = 1.05$ (s, 6H), 2.21 (s, 4H), 5.74 (br s, 1H), 7.32 (brs, 1H), 7.58–8.06 (m, 4H), 11.18 (br s,<1H).

2-(3′,3′-Dimethylcyclohexane-2′,6′-dione-1′-yl)-2-hydroxyindane-1,3-dione (**3f**, $C_{17}H_{16}O_5$)

White crystals; mp 168–170 °C (dec) (*n*-hexane–EtOAc); yield 0.27 g, 91% (clay)/0.29 g, 98% (water); $R_f = 0.44$ (EtOAc–MeOH, 9:1); IR (nujol): $\bar{\nu}$ = 3302, 3,191, 1,741, 1,720, 1,647, 1,600, 1,342, 1,256, 1,149, 1,096, 976, 870, 764, 724 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$ + *DMSO*-d_6): δ = 1.04 (br, 6H), 1.79 (s, 2H), 2.40 (br s, 2H), 5.54 (br, 1H), 6.84 (br, 1H), 7.54–8.03 (m, 4H) ppm; ^{1}H NMR (500 MHz, *DMSO*-d_6; major:minor = *ca.* 2:1): δ = 0.84 and 0.99 (s each, 4H:2H, 2 × CH_3), 1.23 and 1.63 (s each, 1.3H:0.7H, 4′-CH_2), 1.71 and 2.20 (s each, 1.3H:0.7H, 5′-CH_2), 6.15 (s, 1H), 7.63 (br s, 1H), 7.69 (br s, 1H), 7.85 (s, 2H), 8.23 (s, 1H) ppm; ^{13}C NMR (125 MHz): $\delta = 25.0$,

25.2 (both CH_3), 34.9, 36.2 (both CH_2), 123.8, 125.5, 132.1, 136.9 (all Ar–CH), 41.5, 83.7, 135.0, 147.5, 175.4, 181.9, 192.7, 197.8 (all C) ppm; LR EI-MS: *m/z* (%) = 300 (M^+, 63), 285 (9), 284 (15), 282 (9), 272 (11), 229 (21), 216 (20), 203 (40), 167 (27), 160 (10), 140 (29), 132 (39), 112 (16), 105 (27), 104 (100), 76 (73); HR ESI-MS calcd for $C_{17}H_{16}O_5Na$, 323.0895 $(M + Na)^+$, found 323.0897.

2-Hydroxy-2-(oxindol-3′-yl)indane-1,3-dione (**3g**, $C_{17}H_{11}NO_4$)

Light brown crystals; mp 195 °C (dec) (PE–EtOAc); yield 0.285 g, 97% (clay)/0.287 g, 98% (water); $R_f = 0.30$ (C_6H_6–MeOH, 19:1); IR (nujol): $\bar{\nu} = 3432$, 3,184, 1,759, 1,719, 1,698, 1,619, 1,593, 1,272, 1,226, 1,180, 1,145, 1,081, 1,016, 963, 764, 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + *DMSO*-d_6): $\delta = 4.06$ (s, 1H), 6.63 (s, 1H), 6.70 (dt, $J_1 = 7.5$ Hz, $J_2 = 1.0$ Hz, 1H), 6.80 (d, $J = 7.5$ Hz, 1H), 6.85 (d, $J = 7.5$ Hz, 1H), 7.09 (tt, $J_1 = 7.5$ Hz, $J_2 = 1.0$ Hz, 1H), 7.81 (ddd, $J_1 = 7.5$ Hz, $J_2 = 1.5$ Hz, $J_3 = 1.0$ Hz, 1H), 7.84 (dt, $J_1 = 7.5$ Hz, $J_2 = 1.0$ Hz, 1H), 7.89 (dt, $J_1 = 7.5$ Hz, $J_2 = 1.5$ Hz, 1H), 8.05 (dt, $J_1 = 7.5$ Hz, $J_2 = 1.0$ Hz, 1H), 10.27 (s, 1H) ppm; ^{13}C NMR (125 MHz): $\delta = 47.6$, 110.9, 122.3, 124.0, 124.1, 125.2, 129.1, 136.8, 137.0 (all CH), 76.5, 123.2, 141.3, 141.5, 143.1, 177.6, 197.4, 198.6 (all C) ppm; LR EI-MS: *m/z* (%) = 293 (M^+, 49), 275 (8), 160 (13), 133 (100), 132 (35), 104 (26), 76 (13); HR EI-MS calcd for $C_{17}H_{11}NO_4$, 293.0688 $(M)^+$, found 293.0689.

2,2-Bis(indane–1′,3′-dione-2′-yl)indane-1,3-dione (***3h***)

White crystals; mp 282–283 °C (dec) (PE–$CHCl_3$) ([44], mp not reported; mp of **3h** prepared by us following [44] 282–284 °C); yield 0.29 g, 68% (clay); $R_f = 0.61$ (EtOAc–MeOH, 19:1); IR (nujol): $\bar{\nu} = 1739$, 1,707, 1,586, 1,348, 1,265, 1,238, 817, 761 cm^{-1}; HR EI-MS calcd for $C_{27}H_{14}O_6$, 434.0791 $(M)^+$, found 434.0794.

2-Hydroxy-2-(indane-1′,3′-dione-2′-yl)indane-1,3-dione (***3h′***)

Light yellow crystals; mp 238–240 °C (dec) (PE–$CHCl_3$) ([35] 238–240 °C); yield 0.3 g, 98% (water); $R_f = 0.41$ (EtOAc–MeOH, 19:1).

(3a,8b-cis)-3-Acetyl-3a,8b-dihydroxy-2-methyl-3a,8b-dihydro-4H-indeno-[1,2-b]furan-4-one (***3i***)

White crystals; mp 168 °C (dec) (PE–CH_2Cl_2) ([35] 167–169 °C); yield 0.22 g, 86% (clay)/0.25 g, 96% (water); $R_f = 0.35$ (C_6H_6–EtOAc, 1:1).

Ethyl (3a,8b-cis)-3a,8b-dihydroxy-2-methyl-4-oxo-3a,8b-dihydro-4H-indeno[1,2-b]furan-3-carboxylate (***3j***)

White crystals; mp 93–95 °C (dec) (PE–CH_2Cl_2) ([42] 93–103 °C); yield 0.26 g, 90% (clay)/0.27 g, 93% (water); $R_f = 0.36$ (C_6H_6–EtOAc, 1:1).

Methyl (3a,8b-cis)-3a,8b-dihydroxy-2-methyl-4-oxo-3a,8b-dihydro-4H-indeno[1,2-b]furan-3-carboxylate (**3k**, $C_{14}H_{12}O_6$)

White crystals; mp 107–108 °C (dec) (PE–CH_2Cl_2); yield 0.25 g, 89% (clay)/0.27 g, 98% (water); $R_f = 0.32$ (C_6H_6–EtOAc, 1:1); IR (nujol): $\bar{\nu} = 3569$, 3,476, 3,270, 1,732, 1,606, 1,255, 1,182, 1,155, 1,135, 1,102, 970, 937, 890, 777, 731 cm^{-1}; ^1H NMR (500 MHz, *DMSO*-d_6): $\delta = 2.12$ (s, 3H), 3.59 (s, 3H), 6.15 (s, 1H), 7.63 (dt, $J_1 = 8.0$ Hz, $J_2 = 3.0$ Hz, 1H), 7.71 (d, $J = 7.5$ Hz, 1H), 7.81–7.85 (m, 2H), 8.04 (br s, 1H) ppm; ^{13}C NMR (125 MHz): $\delta = 15.6$ (CH_3), 51.4 (OCH_3), 123.7, 125.6, 132.1, 136.9 (all Ar–CH), 85.0, 105.4, 110.5, 135.0, 147.7, 165.2, 170.3, 198.3 (all C) ppm; LR EI-MS: *m/z* (%) = 276 (M^+, 32), 258 (10), 244 (100), 234 (35), 226 (16), 202 (94), 201 (15), 174 (41), 173 (25), 149 (24), 146 (30), 132 (14), 104 (25), 76 (17), 43 (51); HR EI-MS calcd for $C_{14}H_{12}O_6$, 276.0634 $(M)^+$, found 276.0637.

(2′-Hydroxyindane-1′,3′-dione-2′-yl)acetic acid (**3l**, $C_{11}H_8O_5$)

Colourless crystals; mp 181–182 °C (dec) (EtOAc–MeOH); yield 0.20 g, 92% (clay)/0.20 g, 92% (water); $R_f = 0.49$ (EtOAc–MeOH, 17:1); IR (nujol): $\bar{\nu} = 3331$, 1,743, 1,709, 1,587, 1,341, 1,274, 1,182, 1,155, 1,082, 943, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + *DMSO*-d_6): $\delta = 3.16$ (s, 2H), 4.47 (br, 1H), 7.83–7.89 (m, 2H), 7.95–8.02 (m, 2H) ppm; ^{13}C NMR (125 MHz): $\delta = 38.7$ (CH_2), 124.0, 136.0 (both Ar–CH), 72.6, 141.5, 172.0, 199.6 (all C) ppm; LR EI-MS: *m/z* (%) = 220 (M^+, 6), 202 (100), 174 (43), 160 (8), 146 (28), 132 (42), 104 (84), 76 (29); HR EI-MS calcd for $C_{11}H_8O_5$, 220.0372 $(M)^+$, found 220.0374; HR FAB-MS calcd for $C_{11}H_9O_5$, 221.0450 $(M + H)^+$, found 221.0441.

Methyl (2′-hydroxyindane-1′,3′-dione-2′-yl)acetate (**3m**, $C_{12}H_{10}O_5$)

Colourless crystals; mp 95–96 °C (*n*-hexane–CH_2Cl_2); yield 0.09 g, 40% (clay); $R_f = 0.28$ (PE–C_6H_6–EtOAc, 2:2:1); IR (nujol): $\bar{\nu} = 3383$, 1,752, 1,712, 1,593, 1,215, 1,076, 1,000, 943, 751, 731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + *DMSO*-d_6): $\delta = 3.21$ (s, 2H), 3.48 (s, 3H), 6.47 (s, 1H), 7.87–7.91 (m, 2H), 7.98–8.03 (m, 2H) ppm; LR EI-MS: *m/z* (%) = 234 (M^+, 17), 202 (100), 175 (43), 174 (36), 160 (7), 146 (28), 132 (38), 104 (61), 76 (20); HR FAB-MS calcd for $C_{12}H_{11}O_5$, 235.0606 $(M + H)^+$, found 235.0614.

Preparation of ethyl (2′-hydroxyindane-1′,3′-dione-2′-yl)acetate (**3m″**, $C_{13}H_{12}O_5$)

A mixture of 1 mmol **1** and 1 mmol **2m** was dissolved in 1.0 cm^3 EtOH, adsorbed uniformly on 1.0 g clay and kept in a hood at rt. The reactants were consumed in 5 min (TLC). The clay was then leached with 3 × 15 cm^3 10%

EtOH–EtOAc, the solvent was removed from the pooled extracts by distillation and the resulting residue purified by preparative TLC in C_6H_6–EtOAc (1:1) to furnish 0.06 g (25%) pure (TLC, ^{1}H NMR) **3 m**″ as colourless crystals. Mp 107–108 °C (PE–CH_2Cl_2); $R_f = 0.37$ (PE–C_6H_6–EtOAc, 2:2:1); IR (nujol): $\bar{\nu} = 3365$, 1,753, 1,719, 1,593, 1,410, 1,340, 1,210, 1,081, 1,029, 943, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$ + *DMSO*-d_6): $\delta = 1.01$ (t, $J = 7.0$ Hz, 3H), 3.20 (s, 2H), 3.89 (q, $J = 7.0$ Hz, 2H), 6.45 (s, 1H), 7.87–7.90 (m, 2H), 7.99–8.02 (m, 2H) ppm; ^{13}C NMR (125 MHz): $\delta = 14.0$ (CH_3), 38.9 (CH_2), 61.2 (OCH_2), 124.0, 136.2 (both Ar–CH), 72.5, 141.6, 169.9, 199.6 (all C) ppm.

*X-ray diffraction data for compounds **3l** and **3m***

3l (CCDC-689405): $C_{11}H_8O_5$, $M = 220.18$ g mol^{-1}; monoclinic, $a = 6.2035(3)$, $b = 18.263(1)$, $c = 8.6388(5)$ Å, $\beta = 97.290(3)$; $V = 978.2(1)$ Å^3; $T = 293$ K; space group $P2_1/n$ (no. 14), $Z = 4$,4176 reflections measured, 2,318 unique ($R_{int} = 0.034$); R(F, $I/\sigma(I) > 1$) = 0.0576, R_w (F, $I/\sigma(I) > 1$) = 0.0485; $S = 1.16$; $\Delta\rho_{max} = 0.24$ e$^-$ Å^{-3}, $\Delta\rho_{min} = -0.23$ e$^-$ Å^{-3}; 1,404 reflections used to refine 163 parameters. Mo-K_α radiation ($\lambda = 0.71073$ Å); colourless cubes, 0.20 × 0.21 × 0.24 mm^3, density$_{calc}$ = 1.495, $\mu = 0.120$ mm^{-1}.

3m (CCDC-689404): $C_{12}H_{10}O_5$, $M = 234.21$ g mol^{-1}; monoclinic, $a = 9.9333(5)$, $b = 21.051(1)$, $c = 10.7673(6)$ Å, $\beta = 97.290(3)$; $V = 2233.3(2)$ Å^3; $T = 293$ K; space group $P2_1/a$ (no. 14), $Z = 8$,7385 reflections measured, 5,037 unique ($R_{int} = 0.025$); $R(F, I/\sigma(I) > 1) = 0.0572$, R_w (F, $I/\sigma(I) > 1$) = 0.0554; $S = 1.15$; $\Delta\rho_{max} = 0.30$ e$^-$ Å^{-3}, $\Delta\rho_{min} = -0.25$ e$^-$ Å^{-3}; 3,635 reflections used to refine 361 parameters. Mo-K_α radiation ($\lambda = 0.71073$ Å); colourless plates, 0.20 × 0.70 × 0.73 mm^3, density$_{calc}$ = 1.393, $\mu = 0.110$ mm^{-1}.

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