

INDANE-1,2,3-TRIONE ; A HIGHLY REACTIVE ENOPHILE

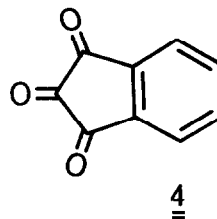
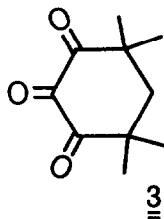
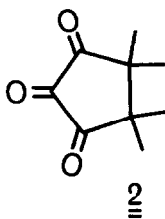
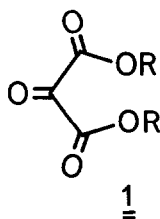
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Among the 1,2,3-tricarbonyl systems investigated, indane-1,2,3-trione has been found to be a particularly reactive enophile. Cleavage of the adducts with periodic acid affords allyl carboxylic acids. Both addition and cleavage reactions are essentially quantitative.

The ene addition to olefins of compounds possessing activated C=O groups, under thermal or Lewis acid-catalysed conditions, is now fairly well documented.¹ We have sought, by the judicious choice of X,Y substituents in molecules of the type X-(C=O)-Y, to fashion "super-enophiles". Indeed, various precedents in the literature indicate that this aim for a very low LUMO energy has been partly realised [e.g. X,Y=(CN)₂, (CF₃)₂, and (CF₂)₃].² The general chemical reactivity of 1,2,3-tricarbonyl systems,³ and the good acceptor properties of such molecules,⁴ indicated to us that compounds such as 1-4 would be worth screening as enophiles of potentially high reactivity.

An economical method for estimating the potency of a given enophile is possible by taking account of the variation in olefin reactivity^{1,5}:
1,1-dialkylethylenes > 1,1,2-trialkylethylenes > 1-alkenes > 1,2-dialkylethylenes > 1-alkynes > 3-substituted 1-alkenes > 2-X-substituted propenes (X-electron withdrawing group). Thus, β -pinene, 1-hexene, and cyclohexene form a convenient 'reactivity series', and the thermal reactions of 1-4 with these three olefins were investigated.⁶



Unfortunately, 3 is thermally unstable; a major decomposition pathway appears to be decarbonylation to give 3,3,5,5-tetramethylcyclopentan-1,2-dione. Likewise, 2 underwent slow decomposition at 80°C, precluding observation of the ene addition to the least reactive olefin, cyclohexene. Progress of the addition reactions, conducted under anhydrous conditions and with an inert atmosphere, could be monitored visually by the fading of the colour of the 1,2,3-tricarbonyl reactants, this being easier for the more deeply-coloured triketones 2-4.

Comparative results for the thermal additions of 2 and of 4 to the three olefins are shown in the Table. The relatively low solubility of indane-1,2,3-trione 4 in chloroform leads to a rate limitation on its reactions; the additions of 4 are substantially faster in the (less convenient) solvents THF or DMF in which the trione is more soluble. Preliminary kinetic measurements⁷ at 30°C of the pseudo first order rate constants (k_{obs}) obtained for reactions conducted in the presence of 11-21 fold excess of β -pinene gave the following results:

$$\text{For } \underline{4} \text{ in DMF: } k_{\text{obs}} = 3.1 \times 10^{-4} \text{ sec}^{-1}$$

$$\text{For } \underline{1} \text{ in THF: } k_{\text{obs}} = 1.3 \times 10^{-5} \text{ sec}^{-1}$$

Reactions of 1 (R=Et) with β -pinene in DMF did not give consistent results. Nevertheless, the very much higher reactivity of 4 relative to 1, approximately

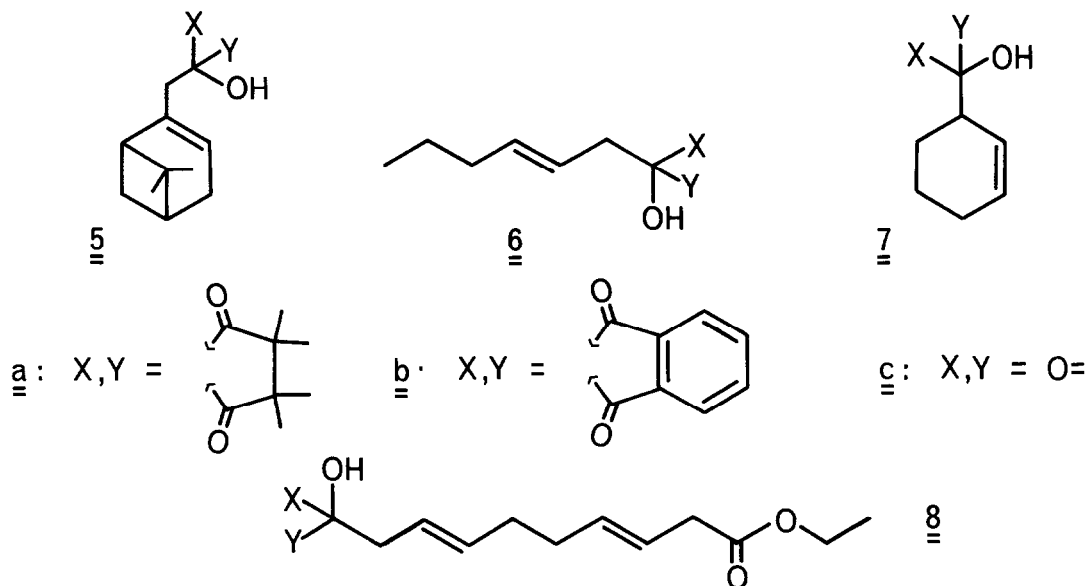
TABLE Thermal ene reactions of 2 and 4 in chloroform

Olefin	Enophile	T°C	Time (h)	Adduct	Yield (%) ^a
β -pinene	<u>2</u>	25	24	<u>5a</u>	89
	<u>4</u>	80	0.3	<u>5b</u>	100
1-hexene	<u>2</u>	80	5	<u>6a</u>	60
	<u>4</u>	80	4	<u>6b</u>	100
cyclohexene	<u>2</u>	80	10	<u>7a</u>	- ^b
	<u>4</u>	80	58	<u>7b</u>	100

^a Yields are of isolated products. Structures are in accord with spectroscopic and analytical data

^b Colour-fading of 2 occurred, but the ene adduct 7a was not detected among the decomposition products

20-25 fold, is clear. To emphasize the reactivity of 4, we have found that addition to 1-hexyne also proceeds quantitatively to afford 2-hydroxy-2-(1-hexa-1,2-dienyl)indane-1,3-dione.⁸ Successful ene additions to 1-alkynes are rarely observed, excepting with highly reactive enophiles.⁵



Preliminary results indicate that the ene additions of $\underline{\underline{4}}$ are strongly catalysed by Lewis acids, but thus far, however, these reactions have proceeded less cleanly than the thermal additions. In any event, the thermal reactions occur under convenient conditions, and the absence of a Lewis acid means that problems of tolerance to remote functional groups in the olefin do not arise. The high reactivity of indane-1,2,3-trione to nucleophiles obviously precludes the presence of OH and NH groups in the olefin, but such groups are easily deactivated by protection. Thus, $\underline{\underline{4}}$ reacted readily with ethyl nona-3,8-dienoate to afford the ene adduct $\underline{\underline{8b}}$ resulting from addition to the terminal double bond of the olefin.

Indane-1,2,3-trione is a convenient ene-equivalent of carbon dioxide. The adducts $\underline{\underline{5b-7b}}$ were smoothly cleaved by periodic acid in dry ether (25°C, 2 h). Conventional work-up, involving the removal of phthalic acid through its insolubility in 40-60° light petroleum, afforded the allyl carboxylic acids $\underline{\underline{5c-7c}}$, respectively, in essentially quantitative yield.

The 2-substituted-2-hydroxyindane-1,2-diones promise to be versatile intermediates for other transformations, making indanetrione a potentially valuable synthon. The chemistry of these systems is being actively studied, as are the extensions of the ene reaction to even more deactivated olefins. There are some fairly obvious modifications in the enophile structure possible that should lead to systems of even greater reactivity and synthetic potential; these developments are in hand.

References

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6. During the early phases of our work on diethyl mesoxalate 1 (R=Et) a detailed account of its chemistry as an enophile appeared: M.F. Salomon, S.N. Pardo and R.G. Salomon, J. Amer. Chem. Soc., 1980, 102, 2473. Few details are therefore given here.
7. Measurements were made spectrophotometrically; samples were sealed under argon in a silica cuvette, and optical densities monitored at 366 nm for 1 and 553 nm for 4.
8. This experiment was performed by Dr. A.R. Shelar.

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