

# A novel azulene synthesis from the Ramirez ylide involving two different modes of its reaction with activated alkynes†

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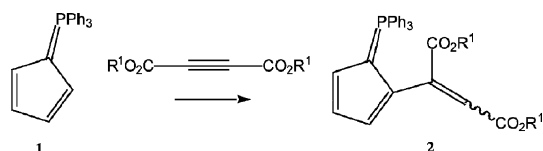
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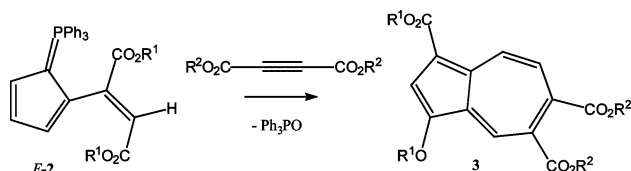
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The Ramirez ylide undergoes electrophilic substitution with acetylenedicarboxylates to form *Z* and *E* adducts. The latter can react by cycloaddition with another equivalent of the alkyne to provide a new route to novel tetra-substituted azules, which show interesting bond localisation and crystal packing effects.

The ylide cyclopentadien-1-ylidenetriphenylphosphorane **1**, originally reported by Ramirez and Levy,<sup>1</sup> is notable for being probably the least reactive phosphorus ylide, failing to undergo the Wittig reaction and unaffected by boiling alkali.<sup>1,2</sup> This inertness is attributed to the aromatic nature of the cyclopentadienyl moiety.



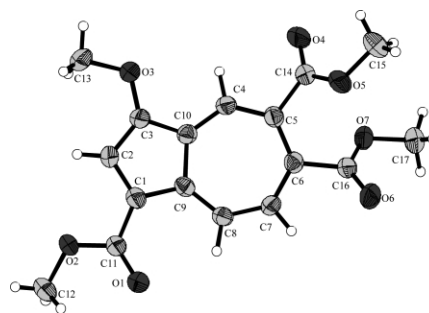
Consistent with this, Yoshida and co-workers<sup>3</sup> noted that **1** reacts with electrophiles to undergo substitution at the 2 position of the five-membered ring. In one reaction they used an activated alkyne (diethyl acetylenedicarboxylate) to give a putative vinyl adduct **2** but its structure was not established securely. We recently re-investigated their work and found<sup>4</sup> that a photochemically sensitive *Z/E* mixture is produced. More significantly we also found that the *E* adducts can react with a further molecule of activated alkyne to give moderate yields (20–30%) of the novel tetra-substituted azules **3** ( $R^1/R^2 = \text{Me, Et, } ^t\text{Bu}$ ). Their striking blue-green colour and high  $R_f$  values enabled them to be isolated relatively easily by chromatography from the reaction mixtures, which also contained a number of other products. The structures of the azules **3** could not be established unambiguously by spectroscopy and we had to rely on a single crystal X-ray structure determination for the methyl ester case ( $R^1/R^2 = \text{Me}$ , Figs. 1 and 2).†



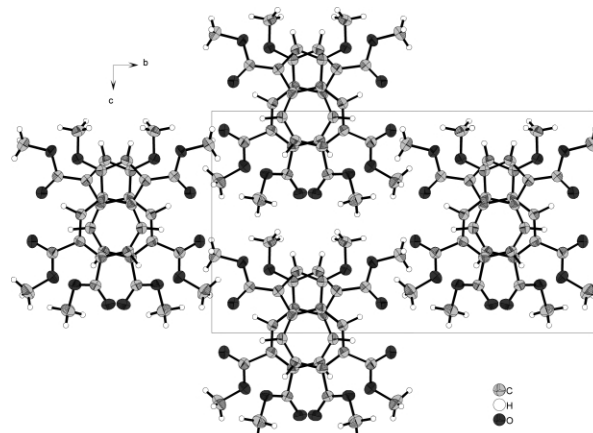
Azules are important compounds used in applications as varied as pharmaceuticals,<sup>5a,b</sup> cosmetics,<sup>5c</sup> infrared absorbers,<sup>5d</sup> liquid crystals<sup>5e</sup> and optical films.<sup>5f</sup> However their preparation is not facile in many cases: low yields are not uncommon and many substitution motifs remain difficult to synthesise.<sup>6</sup> The very short and unusual<sup>7</sup> new synthesis reported here is significant, providing a convenient route to this rare 1,3,5,6-substitution pattern<sup>8</sup> in what is a respectable yield for an azulene synthesis.

† Electronic supplementary information (ESI) available: full experimental procedures and characterisation for **1–3**. See <http://www.rsc.org/suppdata/cc/b3/b316759c/>

Another aspect to azulene **3** ( $R^1/R^2 = \text{Me}$ ) relates to its bond lengths. There is currently interest in the solid-state structures of azules<sup>9,10</sup> in relation to the propensity of substituents to cause alternation of C–C bonding distances. In azulene itself<sup>11</sup> the peripheral bond lengths are almost equivalent (1.38–1.40 Å, ~0.02 Å difference) but alternation is evident in the 5,6-furanyl adduct of azulene<sup>10</sup> with an average difference in lengths of adjacent bonds of 0.06 Å (1.36 Å for the short bonds, 1.42 Å for the long ones). For **3**, the shortest peripheral bond is 1.366(3) (C8–C9) and the longest 1.413(3) (C5–C6), a maximum difference of 0.047 Å showing that the substitution pattern of **3** causes a moderate alternation effect. The five-membered ring of **3** demonstrates bond angle distortions from 120° with  $C_1$  and  $C_3$  values of 109.59(17)° and 109.25(18)° respectively, similar to those found for azulene-1,3-dipropionic acid.<sup>12</sup> The crystal packing diagram of **3** (Fig. 2) is also unusual in that the seven-membered rings are stacked above each other in the *bc* plane, as are the five-membered rings with a planar separation between the azulene molecules of the order 3.5–3.8 Å. This is a



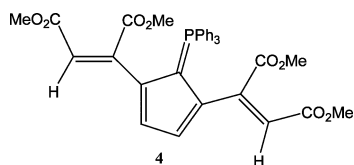
**Fig. 1** Structure of **3** ( $R^1/R^2 = \text{Me}$ ) (50% probability ellipsoids). Selected bond distances (Å) and angles (°): C(1)–C(2) 1.393(3), C(1)–C(9) 1.414(3), C(3)–C(2) 1.388(3), C(3)–C(10) 1.404(2), C(4)–C(5) 1.394(3), C(4)–C(10) 1.377(17), C(5)–C(6) 1.413(3), C(6)–C(7) 1.378(3), C(7)–C(8) 1.405(3), C(8)–C(9) 1.366(3), C(9)–C(10) 1.495(3), C(1)–C(2)–C(3) 109.28(18), C(3)–C(10)–C(4) 125.01(18), C(4)–C(5)–C(6) 126.62(18).



**Fig. 2** Packing of **3** viewed down the crystallographic *a* axis.

surprising observation because the strongly dipolar azulene moiety usually stacks five-membered rings above seven-membered.<sup>13</sup> The opposite arrangement here implies that the dipolar contribution in **3** is small. Another notable feature of Fig. 2 is that it shows the molecules of **3** within the *bc* plane to be  $> 5 \text{ \AA}$  apart.

A surprisingly large number of possible mechanisms can be advanced for the formation of an azulene from *E*-**2** and an alkyne. A number of difficulties attend each of them, the most notable being that phosphorus ylides do not readily react with esters<sup>14</sup> and cyclopentadienyl ylides do not undergo Wittig reaction at all.<sup>1,2</sup> We have performed an extensive set of mechanistic investigations<sup>15</sup> that enabled us to eliminate five of the potential mechanisms to arrive at our best proposal shown in Scheme 1. The most important observation was that we could isolate a bis-alkyne adduct **4** from the reaction mixture in low yield but this compound *did not lead* to azulene under any conditions tried, thermal or photochemical. Also relevant is that adduct *E*-**2** is thermally stable in the absence of alkyne.

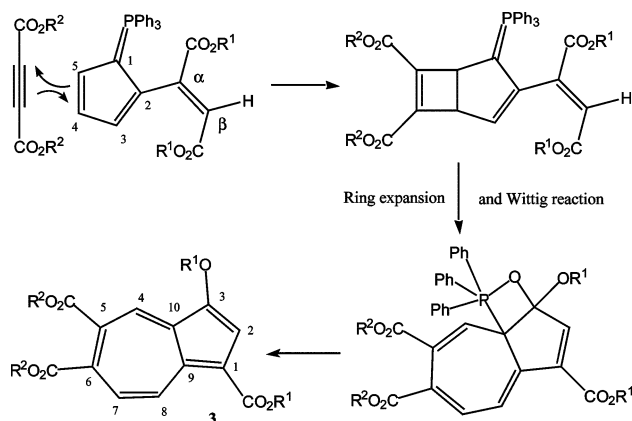


We suggest therefore that the azulene forming reaction involves a *different mode of reaction of the second alkyne molecule* and we propose: first, its cycloaddition across the C4–C5 bond of the cyclopentadiene ring, then ring expansion to a seven-membered ring and, last, Wittig reaction to form azulene.

An alternative scenario is that the Wittig step precedes the ring expansion. In both cases we reason that the Wittig reaction is now more likely as a result of both the loss of aromaticity in the five-membered ring at that stage in the reaction and additionally the resonance energy gained from formation of the azulene. One drawback to the proposed mechanism is that the [2+2] addition is disallowed thermally, although it may be tentatively suggested that the reaction proceeds in a polar stepwise manner as distinct from a concerted process.

An investigation into the scope of this reaction and a detailed mechanistic study<sup>15</sup> will be the subject of a future report.

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**Scheme 1** Proposed mechanism for the formation of **3**.

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## Notes and references

† Crystal data: **3**:  $\text{C}_{17}\text{H}_{16}\text{O}_7$ ,  $M = 332.3$ , orthorhombic, space group  $Pna2_1$ ,  $a = 7.3017(7)$ ,  $b = 19.2542(18)$ ,  $c = 11.0940(17) \text{ \AA}$ ,  $U = 1559.7(3) \text{ \AA}^3$ ,  $T = 293(2) \text{ K}$ ,  $Z = 4$ ,  $D_c = 1.415 \text{ Mg m}^{-3}$ , crystal dimensions  $0.77 \times 0.4 \times 0.5 \text{ mm}$ , Mo-K $\alpha$  radiation,  $\lambda = 0.71073 \text{ \AA}$ . Data were collected on a Bruker Smart Apex diffractometer and a total of 3019 of the 10842 reflections were unique [ $R(\text{int}) = 0.0195$ ]. Refinement on  $F^2$ ,  $wR2 = 0.0908$  (all data),  $R1 = 0.0376$  for  $[I > 2\sigma(I)]$ . CCDC 225162. See <http://www.rsc.org/suppdata/cc/b3/b316759c/> for crystallographic data in .cif or other electronic format.

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