A One-step Synthesis of Acridines *via* Palladium(II)-catalysed Ring Formation of Allylated Enaminones

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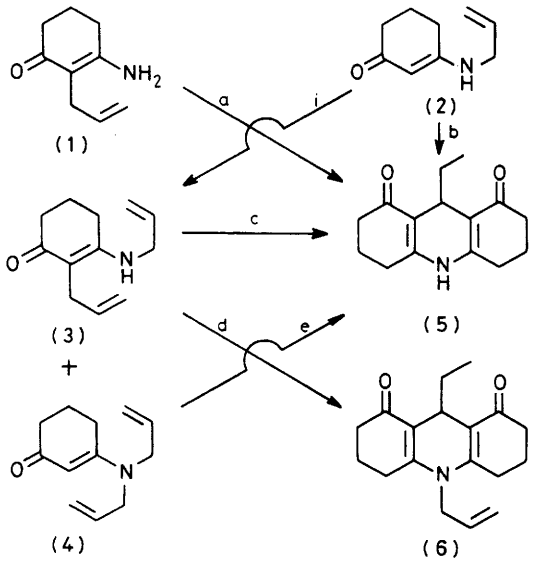
Summary 9-Ethyl-3,4,5,6,9,10-hexahydroacridine-1(2*H*),-8(7*H*)-dione (**5**) and its *N*-allyl analogue (**6**) were formed in a one-step ring-forming reaction from both the 2- and/or *N*-allyl derivatives of 3-aminocyclohex-2-enone (**1**)—(**4**) and from the bisenaminone (**7**), obtained from the *N*-allylenaminone (**2**), on treatment with $PdCl_2(MeCN)_2$.

SINCE the first report of π-allylpalladium compounds in 1957,[1] interest has increased rapidly in their use in organic synthesis.[2] In the expectation that reactions involving π-allylpalladium species would occur, we have used a highly conjugated enamine system bearing one or more allyl groups. We report here a novel one-step acridine synthesis *via* palladium-assisted ring formation from C^{α}- and/or *N*-allylated enaminones.

A mixture of the C^{α}-allylenaminone (**1**)† and 10 mol % of $PdCl_2(MeCN)_2$ [based on (**1**)] in tetrahydrofuran (THF) was refluxed for 18 h. The usual work-up followed by silica gel chromatography ($CHCl_3$) gave a fluorescent product identified as the acridine-dione (**5**)‡ (26%),§ m.p. 250—253 °C, ν_{max} ($CHCl_3$) 3400, 3260, 3180, and 1630 cm^{-1}; δ [$CDCl_3$–$(CD_3)_2SO$] 0·66 (3 H, t, *J* 7 Hz, CH_2Me), 1·18—1·46 (2 H, m, CH_2Me), 1·88—2·61 (12 H, 6 × CH_2), 3·99 (1 H, t, *J* 7 Hz, $CHCH_2Me$), and 8·88 (1 H, br s, NH).



SCHEME. *Reagents*: i, CH_2=$CHCH_2Br$, NaH, toluene.

† Prepared by treatment of 3-aminocyclohex-2-enone with allyl bromide in the presence of sodium hydride in toluene. For an alternative preparation of (**1**) [and also (**3**)], see H. Iida, Y. Yuasa, and C. Kibayashi, *Heterocycles*, **1978**, **9**, 1745.

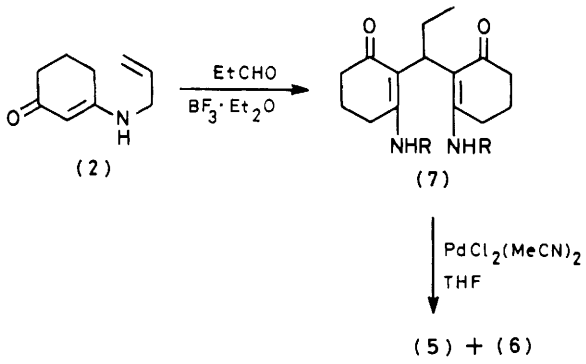
‡ Satisfactory elemental analyses and spectral data were obtained for all new compounds reported.

§ All yields refer to isolated and purified materials.

When the *N*-allylenaminone (**2**), b.p. 165 °C (0·11 mmHg), readily available by condensation of cyclohexane-1,3-dione with allylamine (benzene, reflux, 2 h), was used as a substrate and treated under the same conditions, the acridine (**5**) was again formed.

The C^{α},*N*- and *N*,*N*-diallyl derivatives, (**3**) and (**4**) respectively, of 3-aminocyclohex-2-enone were then prepared by treatment of (**2**) with allyl bromide (NaH, toluene, 100 °C, 1 h). Palladium-catalysed reaction of (**3**) under the same conditions given for (**1**) afforded the acridine (**5**) (33%) and its *N*-allyl analogue (**6**) (21%), m.p. 131—132 °C; ν_{max} ($CHCl_3$) 1625 cm^{-1}; δ ($CDCl_3$) 0·59 (3 H, t, *J* 7 Hz, CH_2Me), 1·11—1·27 (2 H, m, CH_2Me), 1·82—2·55 (12 H, m, 6 × CH_2), 3·72—3·79 (1 H, m, $CHCH_2Me$), 4·08—4·12 (2 H, m, $NCH_2CH{=}CH_2$), 4·95—5·26 (2 H, m, $NCH_2CH{=}CH_2$), and 5·56—5·96 (1 H, m, $NCH_2CH{=}CH_2$); λ_{max} (EtOH) 374 (log ϵ 3·15), 269 (3·48), and 248 (3·22) nm. The acridine (**5**) was also formed on similar treatment of (**4**) with the palladium complex.

For an alternative synthesis of these acridines the *N*-allylenaminone (**2**) was allowed to react with propionaldehyde in the presence of boron trifluoride–diethyl ether (benzene, room temperature, 24 h) to give the bisenaminone (**7**) (R = allyl), m.p. 37—38 °C, ν_{max} ($CHCl_3$) 3240, 3125, 1630, and 1600 cm^{-1}; δ ($CDCl_3$) 0·78 (3 H, t, *J* 7 Hz, CH_2Me), 1·74—1·99 (6 H, m, 3 × CH_2), 2·04—2·64 (8 H, m, 4 × CH_2), 3·77—3·88 (4 H, m, 2 × $NCH_2CH{=}CH_2$), 4·04 (1 H, t, *J* 7 Hz, $CHCH_2Me$), 5·01—5·06 [2 H, m, 2 × $CH_2CH{=}CH(cis)H$], 5·17 [2 H, approx. s, 2 × $CH_2CH{=}CH(trans)H$], 5·66—6·03 (2 H, m, 2 × $NCH_2CH{=}CH_2$), and 8·97 and 9·88 (each 1 H, br s, NH). Treatment of this compound with 5 mol % of $PdCl_2(MeCN)_2$ (THF, reflux, 24 h) afforded the acridines (**6**) (66%) and (**5**) (24%), which were identical in all respects with compounds obtained by the foregoing method.



(2) (7) (5) + (6)

From these results the bisenaminones (**7**) (R = H, allyl) can be postulated as intermediates for acridine formation *via* routes a, c, and d (Scheme). Other routes b and e, from (**2**) and (**4**), may involve [3,3] sigmatropic rearrangements of (**2**) to (**1**) and (**4**) to (**3**), respectively, thus being related to routes a and c, respectively. Although these reactions to give acridines imply that several reactions involving π-allylpalladium species are occurring, the detailed mechanisms are not yet clear.

(*Received*, 20*th October* 1980; *Com.* 1131).

[1] P. E. Slade, Jr. and H. B. Janassen, *J. Am. Chem. Soc.*, 1957, **79**, 1277.
[2] For a recent review, see B. M. Trost, *Tetrahedron*, 1977, **33**, 2615.