

Tandem Norrish Type I Reaction and Intramolecular Arene–Alkene *meta*-Photocycloaddition: Novel Photoisomerization of Aryl-substituted Norbornan-2-ones to Triquinanes

Denis De Keukeleire* and Shu-Lin He

Laboratory of Organic Chemistry, University of Gent, Krijgslaan 281 (S.4), B-9000 Gent, Belgium

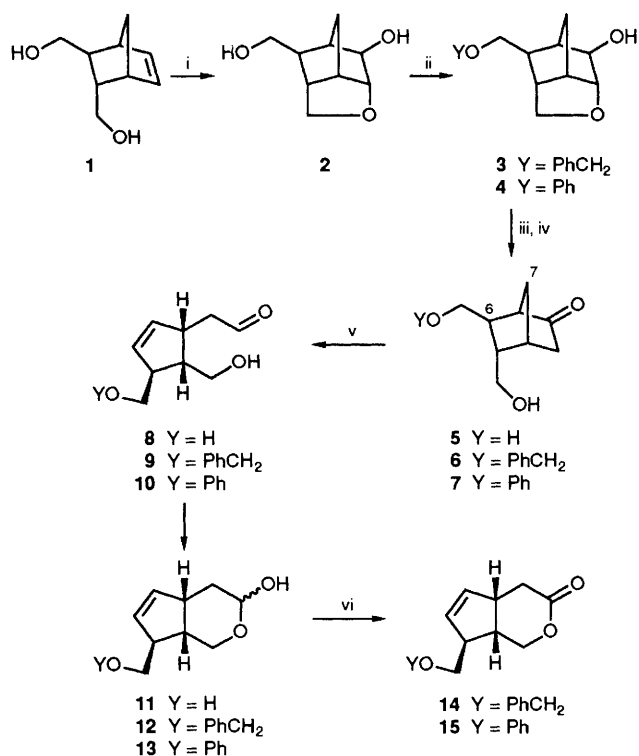
Irradiation of the aryl-substituted norbornan-2-ones **6** and **7** at 254 nm furnishes the triquinanes **16** and **17** (from **6**) and **18** (from **7**) *via* tandem Norrish Type I reaction and intramolecular arene–alkene *meta*-photocycloaddition of the intermediate unsaturated lactols **12** and **13**, respectively.

Synthetic applications of the Norrish Type I reaction of cyclic ketones rely on the regioselectivity of the α -cleavage. Thus the group of Roberts has reported on the synthesis of various prostaglandins based on the Norrish Type I reaction of cyclobutanones.¹ Regioselective cleavage of the C(1)–C(2) bond in norbornan-2-ones, such as **5** (Scheme 1), provides an efficient entry into functionalized cyclopentenones. Transfer of the C(7) hydrogen atom in the intermediate acyl–alkyl diradical leads to the γ,δ -enal **8**, which is isolated as the corresponding lactol **11**.² Depending on the substitution pattern at C(6) high quantum (0.2–0.7) and chemical (>60%) yields are noted. This photoreaction has been applied as the key step in a versatile strategy for the synthesis of iridoids.³ In these instances, the cyclopentene double bond is hydrogenated or oxidized on subsequent elaboration.

We have found that upon irradiation at 254 nm the cyclopentene double bond can take part in intramolecular cycloaddition if a phenyl group is present. The enormous value of such arene–alkene *meta*-photocycloadditions in complex molecule synthesis has been elegantly demonstrated by Wender.⁴ In our systems the intramolecular *meta*-photocycloaddition may be carried out after isolation of the cyclopentene derivatives as the corresponding lactones **14** and **15**. Intriguingly, both photoreactions can be performed in a tandem fashion, whereby simple norbornan-2-ones, such as **6** and **7**, are converted directly to intricate triquinanes. Herein we report on this novel photoisomerization.

Compounds **6** and **7** were synthesized from suitable precursors **1–4** as outlined in Scheme 1. Irradiation of **6** at 300 nm (Rayonet, ethanol, 20 mg, 2 h), followed by oxidation of the crude reaction mixture with pyridinium dichromate, gave the bicyclic lactone **14**[†] in 63% yield. The Norrish Type I reaction could be conducted in polar as well as in apolar solvents.⁵ Further irradiation of compound **14** at 254 nm (Rayonet, 100 mg, 4 h) led to two main products (42% combined yield). After HPLC separation [silica gel 10 μ m, 25 \times 1 cm, 5 ml min⁻¹, ethyl acetate–cyclohexane–acetone (7:3:0.5)] the compounds were identified as the vinylcyclopropane isomers **16**[†] and **17**[†] (ratio:3:2) resulting from arene–alkene *meta*-photocycloaddition at positions 1' and 3'. The inevitable *exo*-arrangement of the triquinane skeleton has previously been noted.⁶ The photoreaction proceeded most efficiently in cyclohexane–ethyl acetate (5:1), while in more polar solvents the formation of complex mixtures was observed. In comparable simple systems in which the reacting units are linked by a chain of more than three atoms very poor and often diverse photoreactivity has been noted,⁷ indicating that the incorporation of an oxygen atom in the connecting chain has a marked effect.

[†] Satisfactory analytical (combustion and/or high resolution mass) and spectral (¹H NMR, ¹³C NMR, IR, UV, MS) data were obtained for all new compounds.

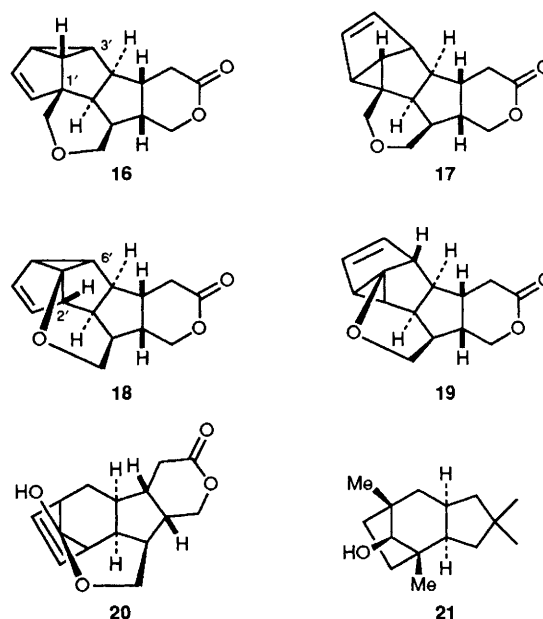


Scheme 1 Reagents and conditions: i, 3-CPBA (1.5 equiv.), CH₂Cl₂, 0°C (2 h) to room temp. (10 h), 90%; ii, *p*-TosCl (1.2 equiv.), pyridine, 0°C, 10 h, then KOH (4 equiv.), DMSO, PhCH₂OH (2 equiv.) (69%) or PhOH (2 equiv.) (70%), 12 h; iii, (COCl)₂ (3.5 equiv.), DMSO, NEt₃ (12 equiv.), CH₂Cl₂, 1 h, 85%; iv, Al-Hg, THF-EtOH (3:1), 3 h, 82%; v, *hν* (300 nm), EtOH, 2 h; vi, PDC, CH₂Cl₂, 3 h, 63% **14**. 3-CPBA = 3-chloroperbenzoic acid; Tos = tosyl; PDC = pyridinium dichromate; DMSO = dimethyl sulfoxide; THF = tetrahydrofuran.

Irradiation of **6** at 254 nm in cyclohexane-ethyl acetate (5:1) (Rayonet, 100 mg, 4 h), followed by oxidation *in situ* (pyridinium dichromate), gave the same reaction mixture as observed upon irradiation of **14** (25% isolated yield of **16** + **17**, not optimized). Thus, generation of the unsaturated lactol **12** was followed by a *meta*-photocycloaddition of the alkene to the phenyl group as evidenced by TLC monitoring. It was not possible to convert lactol **12** completely as the photoproducts **16** and **17** decomposed gradually upon prolonged exposure to light. Consequently the lactone **14** was isolated after work-up (21%).

The similar photoisomerization of the norbornan-2-one **7** could be performed both in a two-step process involving the isolated lactone **15** (35% overall) and in the tandem fashion *via* the lactol **13** (34%). Only the photocycloadduct **18**[†] was observed, since, as previously noted, the formation of the vinylcyclopropane isomer **19** is prohibited.^{7c} As expected the addition occurred at the positions 2' and 6'.⁸ A simple model compound, in which the double bond is constrained to the (*Z*)-form, has not been studied. (*E*)-5-Phenoxy-2-ene gave the 2',6'-adduct (33%),¹⁰ while the homologue 4-phenoxybut-1-ene was reported to undergo 2',4'-addition with extensive polymer deposition.^{7a}

In contrast to compounds **16** and **17**, photoadduct **18** proved to be unstable. Treatment with dilute hydrochloric acid provoked quantitative cleavage of the non-allylic bond in the three-membered ring to the lactol **20**.[†] Calculations¹⁰



showed that lactol **20** is more stable than the alternative structures resulting from cleavage of either allylic cyclopropane bond. Such a conversion gives direct access to the recently discovered bullerane skeleton.¹¹ Studies towards the synthesis of naturally occurring bulleranes, such as (+)-cerapicol **21**, are in progress.

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References

- R. F. Newton, in *Photochemistry in Organic Synthesis*, ed. J. D. Coyle, The Royal Society of Chemistry, London, Special Publication No. 57, 1986, ch. 3, p. 39, and references contained therein.
- P. Yates and R. V. Loutfy, *Acc. Chem. Res.*, 1975, **8**, 209.
- See, e.g., P. Storme, P. Callant and M. Vandewalle, *Tetrahedron Lett.*, 1983, 5797; P. Storme, L. Quaghebeur and M. Vandewalle, *Bull. Soc. Chim. Belges*, 1984, **93**, 999; E. Van der Eycken, P. Callant and M. Vandewalle, *Tetrahedron Lett.*, 1985, **26**, 367; D. De Keukeleire, Y. Ruyschaert and M. Vandewalle, *Adv. Photochem.*, 1989, 229.
- For a review, see: P. Wender, L. Siggel and J. M. Nuss, *Organic Photochemistry*, ed. A. Padwa, Marcel Dekker, New York, 1989, vol. 10, ch. 4, p. 416.
- J. C. Netto-Ferreira, V. Wintgens and J. C. Scaiano, *J. Photochem. Photobiol. A: Chem.*, 1991, **57**, 153.
- D. Bryce-Smith, M. G. B. Drew, G. A. Fenton, A. Gilbert and A. D. Proctor, *J. Chem. Soc., Perkin Trans. 2*, 1991, 779.
- (a) A. Gilbert, *Pure Appl. Chem.*, 1980, **52**, 2669; (b) P. A. Wender and J. J. Howbert, *J. Am. Chem. Soc.*, 1981, **107**, 688; (c) G. C. R. Ellis-Davies, A. Gilbert, P. Heath, J. C. Heath, J. C. Lane, J. C. Warrington and D. L. Westover, *J. Chem., Soc., Perkin Trans. 2*, 1984, 1833.
- J. A. van der Hart, J. J. C. Mulder and J. Cornelisse, *J. Mol. Struct. (Theochem)*, 1987, **151**, 1.
- H. A. Neijenesch, E. J. Ridderikhoff, C. A. Ramsteijn and J. Cornelisse, *J. Photochem. Photobiol. A: Chem.*, 1989, **48**, 317.
- The calculations were performed using a combination of SCA and MacroModel, see: J. Hoflack and P. J. De Clercq, *Tetrahedron*, 1988, **44**, 6667.
- H.-P. Hanssen and W.-R. Abraham, *Tetrahedron*, 1988, **44**, 2175.