Pergamon

Tetrahedron Letters, Vol. 36, No. 20, pp. 3573-3576, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)00562-5

Intramolecular *Ortho* and *Meta* Photocycloadditions of 3-Alkyl-4-phenoxybut-1-enes

Erik Van der Eycken, Denis De Keukeleire*
University of Gent, Faculty of Pharmaceutical Sciences,
Harelbekestraat 72, B-9000 Gent (Belgium)

and

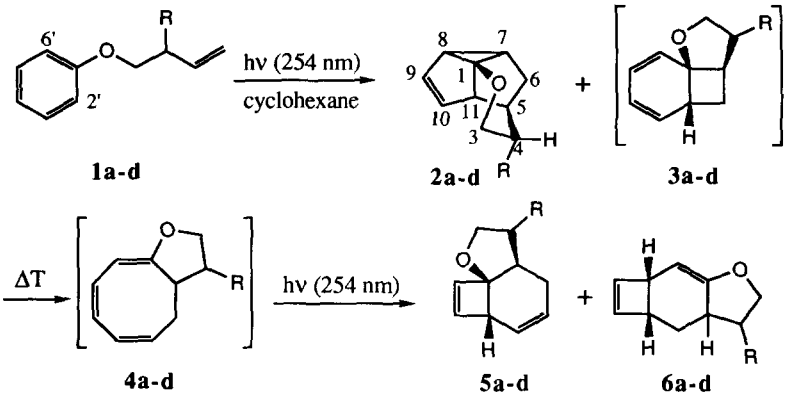
André De Bruyn
University of Gent, Department of Organic Chemistry,
Krijgslaan 281 (S.4), B-9000 Gent (Belgium)

Abstract: Upon irradiation of 3-alkyl-4-phenoxybut-1-enes **1a-d** at 254 nm in cyclohexane, *ortho* and *meta* photocycloadditions occur. The *ortho* photocycloadducts rearrange readily, while the *meta* photocycloaddition involves the 2',6'-positions of the arene as directed by the alkoxy group. In each case only a single *meta* photocycloadduct with an *endo* alkyl group is formed resulting in six contiguous stereocentres. A 3-alkyl group does not influence significantly the mode selectivity.

Previous studies on the irradiation of 4-phenoxybut-1-enes carrying substituents on the arene or alkene moieties showed that intramolecular *ortho* and *meta* photocycloadditions occurred.[1] The *meta* addition is directed by the alkoxy tether to the arene 2',6'-positions. Methyl substitution on both chromophores does not affect the regiochemistry of the reaction, but the presence of a 2'-methoxy group inhibits the *meta* process and only *ortho* addition is observed. We now wish to report on the photocycloadditions of 4-phenoxybut-1-enes substituted with an alkyl group at C-3 in the tether (methyl, *i*-propyl, *tert*-butyl).

Irradiation at 254 nm (Rayonet photochemical reactor) of 3-*tert*-butyl-4-phenoxybut-1-ene (**1d**) (0.245 mmol) in cyclohexane (42 ml) for 80 min afforded a mixture of reaction products (Scheme 1), which was separated by preparative HPLC (silicagel; hexane:ethyl acetate 98:2).[2] ^{1}H-NMR analysis revealed the structures of reaction products **2d**, **5d** and **6d**.[3] Compound **2d** (2-oxatetracyclo[5.4.0.0^{1,8}.0^{5,11}]undec-9-ene) is formed by intramolecular arene-alkene *meta* photocyloaddition at the 2',6'-positions, as a result of stabilization of the partial positive charge developing at C-1' in the singlet excited state of the benzene ring on approach of the alkene.[4] Moreover, only the *endo* epimer at C-4 was formed, while the 1,6-bridged *meta* adduct was not observed.[5]

Cyclobutene derivatives **5d** and **6d** are deduced to have arisen from initial intramolecular *ortho* photocycloaddition, disrotatory ring opening of the thermally labile bicyclo[4.2.0]octa-2,4-diene **3d** (not detectable in the ^{1}H-NMR spectra) and (2+2)-photocyclization of cyclooctatriene **4d** (only traces observed in the ^{1}H-NMR spectra). The ratio of **1d**:**2d**:**5d**:**6d**:**4d** is 0.27:0.69:0.23:1.00:0.11. Although HPLC separation proved to be feasible ^{1}H-NMR spectra of pure cyclobutenes **5d** and **6d** could not be obtained as they were readily interconverted upon standing at room temperature. Moreover, it was not possible to completely convert substrate **1d**. These observations suggest that not only the photoproducts interconvert, but also that cycloreversion of photocycloadduct **3d** regenerates the starting material. Similar observations have been made by Wagner et al. during irradiations of 5-(*p*-acylphenyl)pent-1-enes.[6]



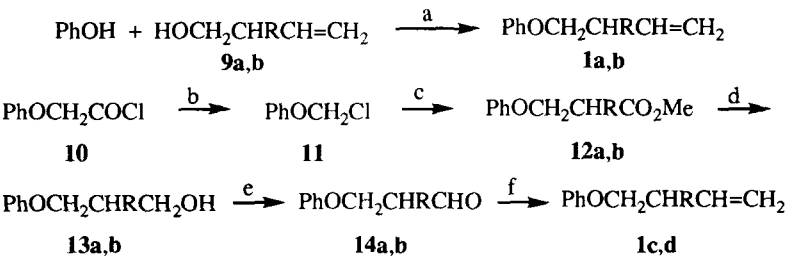
1a-d **2a-d** **3a-d** **4a-d** **5a-d** **6a-d**

a: R = H; **b**: R = Me; **c**: R = *i*-Pr; **d**: R = *tert*-Bu

SCHEME 1

An analogous TLC pattern was obtained on monitoring the irradiation of 3-alkyl-4-phenoxybut-1-enes **1a-c**. As the photoproducts of **1a** and **1b** are volatile, we were not able to isolate cyclobutenes **5a,b** and **6a,b**, and only small amounts of *meta* cycloadducts **2a** and **2b** were isolated by HPLC. Upon irradiation of **1a-c** a single *meta* photocycloadduct **2a-c** is formed in each case, as was observed for the *tert*-butyl derivative **1d**. Furthermore, **2b** and **2c** were the *endo*-epimers at C-4.

Synthesis of Bichromophores 1a-d. 4-Phenoxybut-1-ene (**1a**) and 3-methyl-4-phenoxybut-1-ene (**1b**) were prepared from phenol via a Mitsunobu-type coupling reaction with the appropiate homoallyl alcohol **9a** and **9b** respectively (Scheme 2). 3-*Tert*-butyl-4-phenoxybut-1-ene (**1d**) and 3-*i*-propyl-4-phenoxybut-1-ene (**1c**) were accessed via alkylation of esters **12a** and **12b**, respectively, with phenyl chloromethyl ether (**11**) (Scheme 2).



9a, **1a**: R = H; **9b**, **1b**: R = Me; **12a**, **13a**, **14a**, **1d**: R = *tert*-Bu; **12b**, **13b**, **14b**, **1c**: R = *i*-Pr

a: Ph_3P, DEAD, THF, r.t.; **1a**: 84%, **1b**: 75%; b: $(Ph_3P)_3RhCl$, 170°C, 1h, 81%; c: RCH_2CO_2Me, LDA, THF, DMSO, -78°C to r.t.; **12a**: 81%, **12b**: 51%; d: LAH, THF, r.t.; **13a**: 91%, **13b**: 78%; e: DMSO, $(COCl)_2$, CH_2Cl_2; Et_3N, -60°C to r.t.; **14a**: 98%, **14b**: 98%; f: $TiCl_4$, CH_2Br_2, Zn, THF, r.t.; **1d**: 45%, **1c**: 41%.

SCHEME 2

This reagent was prepared by decarbonylation of commercially available phenoxyacetyl chloride (**10**) upon treatment with Wilkinson's catalyst at 170°C.[7] Lithium aluminumhydride reduction of esters **12a** and **12b**, followed by Swern-type oxidation,[8] afforded aldehydes **14a** and **14b**, which were immediately converted to alkenes **1d** and **1c**. To avoid elimination expected to occur during a Wittig-type procedure, deoxomethylenation was effected using Lombardo's protocol.[9] Although a large excess of this reagent was necessary for complete conversion of the starting material (30 ml for 2.485 mmol aldehyde), yields are moderate due to formation of several unidentified side products and decomposition.

In summary, the presence of an alkyl group at C-3 in 4-phenoxy-but-1-enes has only a small impact on the mode selectivity of the photocycloaddition, as compared to the unsubstituted system. The exclusive formation of one *meta* photocycloadduct with an *endo* alkyl group at C-4 is remarkable, thus leading to tetracyclic compounds **2b-d** with six contiguous stereocenters in a well-defined configuration.

ACKNOWLEDGMENTS

Financial support by the Special Research Fund of the University of Gent (project number 01109394) to DDK is gratefully acknowledged.

REFERENCES AND NOTES

1. De Keukeleire, D.; He, S.-L.; Blakemore, D.; Gilbert, A. *J. Photochem. Photobiol. A: Chem.* **1994**, *80*, 233.
2. The progress of the photoreaction was monitored by TLC using hexane:ethyl acetate (95:5) as elutant; R_f-values: 0.60 (**1d**), 0.48, 0.32, 0.23 and 0.04, respectively. The spots are visualized with iodine (R_f 0.32 strongly absorbs iodine, R_f 0.23 is not detectable) and a spray reagent comprised of phosphomolybdic acid (2.5%), cerium(IV) sulfate (1%) and sulfuric acid (6%) in water, giving blue-coloured spots upon heating. In contrast, sulfuric acid-induced decomposition did not lead to sensitive detection of the *ortho* adducts.
3. ^{1}H-NMR: **2b** (360 MHz, $CDCl_3$): δ (ppm): 5.66 (dd, 6.2, 2.6, 1H), 5.62 (ddd, 6.2, 2.6, 1.5, 1H), 4.22 (dd, 10.8, 5.5, 1H), 3.75 (dd, 10.8, 1.2, 1H), 3.22 (dddd app. dq, 7.2, 2.0, 1H), 2.87 (ddd app. td, 2.7, 2.6, 1.1, 1H), 2.43 (broad s), 1.79 (qddd, 7.3, 5.5, 1.8, 1.2, 1H), 1.73 (ddd, 13.7, 6.6, 2.7, 1H), 1.48 (ddd app. dt, 13.7, 2.7, 2.7, 1H), 1.45 (degenerated, 2.5, 1H), 1.20 (d, 7.3, 3H).
2c (500 MHz, C_6D_6): δ (ppm): 5.53 (dd, 6.1, 2.6, 1H), 5.48 (ddd, 6.1, 2.6, 1.3, 1H), 4.00 (dd, 11.1, 4.3, 1H), 3.94 (dd, 11.1, 5.6, 1H), 3.09 (dddd app. dq, 7.4, 2.6, 2.3, 1.3, 1H), 2.86 (ddd app. td, 2.6, 2.5, 1.3, 1H), 2.46 (broad s, 1H), 1.59 (m, 8.2, .52 (ddd app. dt, 13.4, 2.9, 2.9, 1H), 1.46 (dddd, 13.4, 6.2, 2.5, 0.5, 1H), 1.30 (ddd, 7.4, 6.2, 2.9, 1H), 1.11 (dddd, 8.2, 5.6, 4.3, 2.1, 1H), 0.78 (d, 6.6, 3H), 0.76 (d, 6.8, 3H).
2d (500 MHz, C_6D_6): δ (ppm): 5.51 (dd, 6.0, 2.6, 1H), 5.45 (ddd, 6.0, 2.5, 1.4, 1H), 4.07 (dd, 10.7, 6.8, 1H), 4.02 (dd app. t, 10.7, 10.8, 1H), 3.03 (dddd, app. dq, 7.4, 2.6, 2.6, 1.4, 1H), 3.00 (dd app. q, 2.5, 2.5, 1H), 2.34 (broad s, 1H), 1.74 (ddd, 10.8, 6.8, 1.4, 1H), 1.46 (ddd app. dt, 13.0, 3.1, 2.8, 1H), 1.43 (dddd, 13.0, 5.7, 2.5, 0.5, 1H), 1.28 (ddd, 7.4, 5.7, 3.1, 1H), 0.70 (s, 9H).

5d (500 MHz, $CDCl_3$): δ (ppm): 6.28 (dd, 2.9, 0.7, 1H), 6.19 (dd, 2.9, 0.5, 1H), 5.80 (m, 2H), 4.02 (dd app. t, 8.7, 8.7, 1H), 3.76 (dd app. t, 8.7, 8.7, 1H), 3.39 (broad s, 1H), 2.41 (dddd app. dq, 15.5, 3.5, 3.5, 3.2, 1H), 1.93 (ddd app. dt, 11.7, 8.7, 8.7, 1H), 1.78 (m, 1H), 1.69 (ddd, 11.7, 11.6, 3.2, 1H).

6d (500 MHz, $CDCl_3$): δ (ppm): 6.03 (s, 2.7, 1H), 5.91 (s, 2.7, 1H), 4.88 (dd, 6.5, 2.2, 1H), 4.07 (dd app. t, 8.6, 8.5, 1H), 3.81 (dd, 10.5, 8.6, 1H), 3.37 (m, 6.5, 4.0, 1H), 3.14 (m, 4.6, 1H), 2.22 (m, 2H), 1.96 (m, 1H), 1.13 (ddd, 12.2, 10.8, 5.4, 1H).

A detailed ^{1}H-NMR study will be published in Recl. Trav. Chim. Pays-Bas, 1995.

4. Cornelisse, J. *Chem. Rev.* **1993**, *93*, 615.
5. The *endo-exo* nomenclature refers to the position of the substituent at C-4 with respect to the main bicyclic system (2-oxabicyclo[6.3.0]undec-9-ene, see Scheme 1).
6. Wagner, P.J.; Alehashem, H. *Tetrahedron Lett.* **1993**, *34*, 911.
7. Benneche, T.; Undheim, K. *Acta Chem. Scand. B36* **1982**, 409.
8. Mancuso, A.J.; Swern, D. *Synthesis* **1981**, 165.
9. Lombardo, L. *Tetrahedron Lett.* **1982**, *23*, 4293.

(*Received in UK* 28 *February* 1995; *revised* 23 *March* 1995; *accepted* 24 *March* 1995)