The complex photochemistry of 2,3-dibenzylidenesuccinates

Tokouré Assoumatine, Brigitte L. Yvon, and James L. Charlton

Abstract: The photochemistry of diethyl *E,E*-2,3-(3,4,5-trimethoxybenzylidene)succinate (**8**) is solvent dependent. In both protic and aprotic solvents, there is a photoequilibrium established between **8** and its *E,Z*-isomer (**9**). In chloroform at high light intensity, very little **9** is formed and the main product is 1,4-dihydronaphthalene (**10**), formed via photoinduced intramolecular [1,3]-sigmatropic hydrogen shift within an intermediate 1,8a-dihydronaphthalene (**11**). In protic solvents, irradiation of either **8** or **9** ultimately gives primarily the *cis*-1,2-dihydronaphthalene product (**13**), along with smaller amounts of the trans isomer (**14**). By using deuterated solvents, it was shown that **13** and **14** are formed by solvent protonation (or deuteration) of the 1,8a-dihydronaphthalene intermediate (**11** or **12**).

Key words: 2,3-dibenzylidenesuccinate, photocyclization, dihydronaphthalene, lignan.

Résumé : La photochimie du *E,E*-2,3-(3,4,5-triméthoxybenzylidène)succinate de diéthyle (**8**) dépend de la nature du solvant. Dans les solvants tant protique qu'aprotique, il s'établit un photoéquilibre entre le composé **8** et son isomère *E,Z* (**9**). Dans le chloroforme, à une intensité lumineuse intense, il se forme très peu de composé **9** et le produit principal est le 1,4-dihydronaphtalène (**10**) qui se forme, à partir de l'intermédiaire 1,8a-dihydronaphtalène (**11**), par un déplacement photoinduit d'hydrogène [1,3]-sigmatropique. Dans les solvants protiques, l'irradiation des composés **8** ou **9** conduit toujours à des quantités importantes du produit *cis*-1,2-dihydronaphtalène (**13**) aux côtés de plus faibles quantités de l'isomère trans (**14**). En utilisant des solvants deutérés, il a été possible de démontrer que les composés **13** et **14** se forment par protonation (ou deutération) d'un intermédiaire 1,8a-dihydronaphtalène (**11** ou **12**) par le solvant.

Mots clés : 2,3-dibenzylidènesuccinate, photocyclisation, dihydronaphtalène, lignane.

[Traduit par la Rédaction]

Introduction

There is a rich literature on the photochemistry of *E,E*-2,3-dibenzylidenesuccinate derivatives (1–23). Although the majority of the work deals with the photochemical cyclization of fulgides (the cyclic anhydrides of *E,E*-dibenzylidenesuccinic acids; **1**, X = O), there are also examples of photoreactions of fulgimides (the cyclic imides of *E,E*-dibenzylidenesuccinic acids; **1**, X = NR), dibenzylidenebutyrolactones, and acyclic derivatives. Heller and co-workers (6) have provided a general mechanistic scheme to explain the photochemistry that has been observed for various fulgides and fulgimides (Scheme 1, where R represents various aromatic substitution patterns).

Although the results of irradiation vary with substituents R and solvents, photoinduced isomerization between the *E,E*- and *E,Z*-isomers **1** and **2** is generally observed. Isomers **1** and **2** also undergo photochemical conrotatory ring closure to form the *cis*- and *trans*-1,8a-dihydronaphthalenes (1,8a-DHNs) **3** and **4,** respectively. The thermal disrotatory opening of **3** and **4** to give **2** and **1,** respectively, is assumed to be the mechanism for the photoinduced isomerization of **1** and **2**. The 1,8a-DHNs **3** and **4** are seldom isolated owing to their thermal and photochemical instability, and the final isolated products (other than **1** and **2**) are more often the 1,4-DHN **5** and (or) the 1,2-DHNs **6** and **7** (or the corresponding naphthalenes if oxygen is present). On the basis of temperature and pH effects, Heller and co-workers (6) tentatively concluded that 1,4-DHN **5** was formed photochemically from **3** and **4** (a [1,3]-intramolecular sigmatropic H-shift) and that 1,2-DHNs **6** and **7** were formed by an acid-catalysed rearrangement of **3** and **4,** respectively, rather than by a thermal intramolecular [1,5]-sigmatropic shift (Scheme 1) (6). In previous papers by Heller's group, it had been assumed that the latter rearrangement involved an intramolecular [1,5]-sigmatropic H-shift (17, 18, 20).

While there have been many published studies of the photochemistry of cyclic derivatives of dibenzylidenesuccinates, such as the fulgides and fulgimides discussed above, there have been fewer published examples of the study of the photochemistry of the corresponding acyclic succinate derivatives. In an earlier paper (23), we reported the first example of the photolysis of a dibenzylidenesuccinate diester. In that preliminary study, we reported that the photolysis of *E,E*-2,3-(3,4,5-trimethoxybenzylidene)succinate (**8**) in ethanol acidified with trifluoroacetic acid (TFA), followed by column chromatography of the photolysis product, gave the dihydronaphthalene esters **13** (34% yield) and **14** (2% yield) (Scheme 2) (23). We have now conducted a more detailed study of the photochemical behaviour of **8** in various solvents and observed that the products depend quite strongly

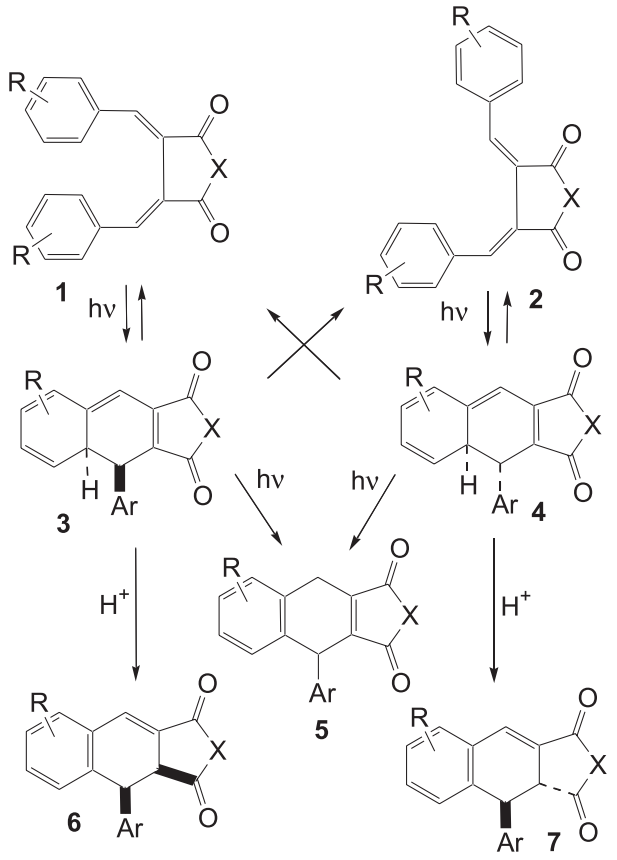
Received 31 January 2004. Published on the NRC Research Press Web site at http://canjchem.nrc.ca on 12 January 2005.

T. Assoumatine, B.L. Yvon, and J.L. Charlton.[1]
Department of Chemistry, University of Manitoba, Winnipeg, MB R3T 2N2, Canada.

[1]Corresponding author (e-mail: charltn@cc.umanitoba.ca).

 doi: 10.1139/V04-143

Scheme 1. Photoreactions of fulgides (X = O) and fulgimides (X = NH, NR, or NAr).



on the solvent and reaction conditions. By using deuterated solvents, we have established the mechanisms of the various prototropic rearrangements.

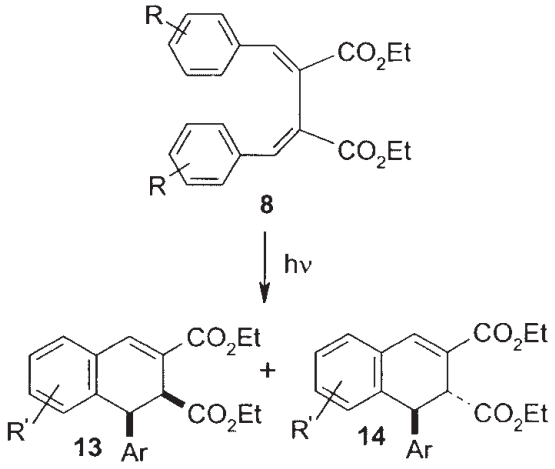
It is hoped that a better understanding of the photochemistry of 2,3-dibenzylidenesuccinates will make their photochemical reactions more useful for the synthesis of lignans, particularly the aryltetralin and aryldihydronaphthalene types. This goal has been partially achieved with the recent publication of an asymmetric synthesis of (+)-lyoniresinol dimethyl ether from a derivative of compound **8** (24).

Results and discussion

Diethyl *E,E*-2,3-(3,4,5-trimethoxybenzylidene)succinate (**8**) was prepared as previously described (23). Although **8** is shown in Scheme 2 in an *s*-cis conformation, it should be noted that this molecule does not have a planar butadiene system. Molecular mechanics calculations show that it exists as an equilibrating mixture of twisted *s*-cis and *s*-trans conformers. A fuller discussion of its conformation can be found in our previous publication (24). In the synthesis (23), **8** is formed in an *E,E* configuration as the sole product. This product is easily distinguished from the corresponding *E,Z* and *Z,Z* isomers by NMR (17).

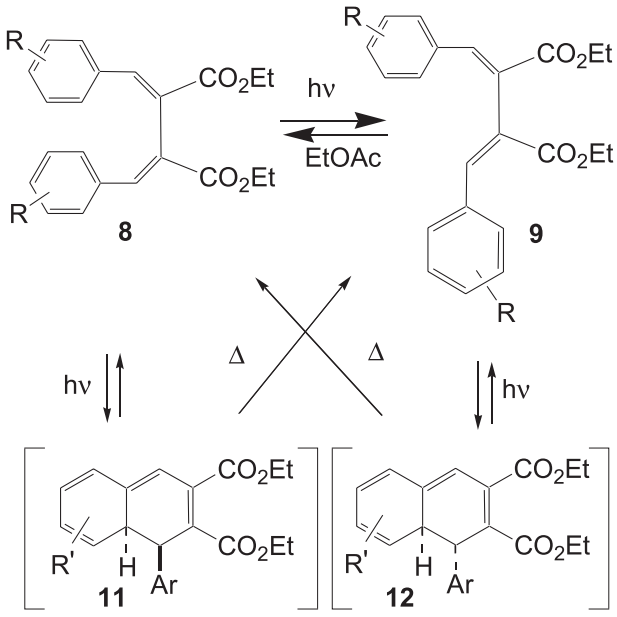
Irradiation of **8** in ethyl acetate with a medium-pressure mercury lamp through Pyrex glass gave only a slow and incomplete conversion of **8** to the corresponding *E,Z*-isomer **9** (Scheme 3). Further irradiation of the mixture resulted in the formation of several products (including **10**; see below). It

Scheme 2. Previous study of photolysis of *E,E*-2,3-(3,4,5-trimethoxybenzylidene)succinate (**8**).



R = 3,4,5-trimethoxy R' = 6,7,8-trimethoxy
Ar = 3,4,5-trimethoxyphenyl

Scheme 3. Irradiation of **8** in ethyl acetate.

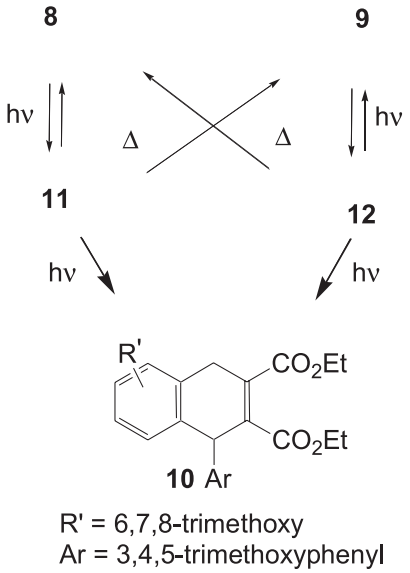


R = 3,4,5-trimethoxy R' = 6,7,8-trimethoxy
Ar = 3,4,5-trimethoxyphenyl

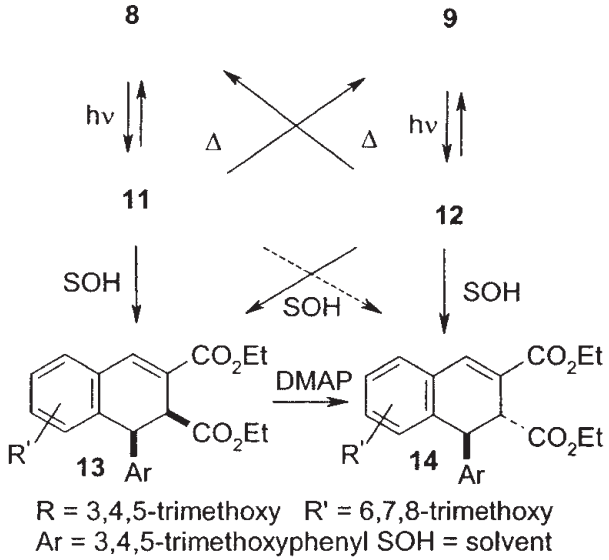
was possible to separate **9** from **8** by HPLC and to characterize **9** by ^{1}H and ^{13}C NMR. A possible mechanism for the conversion of **8** to **9** is photochemical cyclization to the 1,8a-DHN **11** followed by thermal disrotatory opening to **9**. It is also possible that there is a direct photoisomerization of the double bond. The irradiation of isolated **9** in ethyl acetate gave the same mixture of **8** and **9**, and the conversion of **9** to **8** may pass through intermediate **12**.

Surprisingly, irradiation of **8** in chloroform gave the 1,4-DHN **10** almost exclusively (Scheme 4). The reaction was most efficient if low concentrations of **8** were irradiated in tubes placed very close to the lamp (higher light intensity).

Scheme 4. Irradiation of **8** in chloroform.



Scheme 5. Irradiation of **8** in alcoholic solvents.



On moving the sample further from the lamp (30 cm), it was possible to detect the concurrent formation of the *E,Z*-isomer **9,** which, although it appeared early in the reaction, also slowly disappeared to form the 1,4-DHN **10**. When **8** was irradiated in deuterochloroform (that had been washed with D_2O to prevent any possibility that traces of water would protonate an intermediate), there was no incorporation of deuterium into the 1,4-DHN **10**. The lack of any deuterium incorporation when the reaction was run in D_2O-washed deuterochloroform confirmed that the proposed conversion of **11** to **10** was an intramolecular 1,3-sigmatropic hydrogen shift, an allowed photochemical pericyclic reaction. It thus appears that **11** (or **12**) is photochemically converted to **10** and that this allowed photochemical sigmatropic reaction competes very well with thermal opening of **11** (or **12**) to **9** (or **8**). The intermediate formation of *E,Z*-isomer **9** during irradiation in chloroform at lower light intensities, and its ultimate conversion to **10**, suggests that this is also a two-step photochemical conversion via the 1,8a-DHN **12**.

Irradiation of **8** in alcoholic solvents (methanol, ethanol, or 2-propanol), until the disappearance of **8**, gave primarily the *cis*-1,2-DHN **13** accompanied by the *trans*-1,2-DHN **14** in a 4:1 ratio (Scheme 5). Similar results were reported in a preliminary publication (23). However, irradiation for shorter periods of time showed that the *E,Z*-isomer **9** was initially formed along with the two DHN derivatives **13** and **14**. When **9** reached about 80% of the concentration of **8,** it ceased to increase and both **8** and **9** subsequently diminished as **13** and **14** formed. It therefore appears that a photoequilibrium between **8** and **9** also takes place in alcoholic solvents. A similar irradiation of **9** in methanol produced **8** and thereafter a slow conversion to a mixture of **13** and **14** in a 4:1 ratio.

Cis-1,2-DHN **13** could be quantitatively converted to *trans*-1,2-DHN **14** by warming with a trace of *N,N*-dimethyl-4-aminopyridine (DMAP) in ethanol, confirming that the trans ester **14** is thermodynamically more stable than **13**. When the irradiation of **8** was conducted in perdeuteromethanol (CD_3OD), a mass spectrum revealed that the 1,2-DHN product **13** was monodeuterated. This shows that rearrangement of **8** to **13** involves protonation by solvent. It seems likely that the 1,8a-DHN **11** (or **12**) is thermally protonated at the 2-position followed by the loss of a proton at carbon 8a. This mechanism is consistent with that proposed by Heller and co-workers for the acid-catalysed reactions of 1,8a-DHN formed from fulgides (6).

It was not possible to conclusively determine whether dihydronaphthalenes **13** and **14** were being formed via solvent protonation of both **11** and **12**, although it seems likely. In any event, an earlier suggestion by Heller and co-workers that the *trans*-DHN **14** is coming exclusively from irradiation of the *E,Z*-isomer seems incorrect for this series of compounds (6).

In summary, we have provided the first detailed study of the photochemistry of an *E,E*-2,3-dibenzylidenesuccinate diester and proposed a mechanism for the products formed in various solvents. In aprotic solvents, there is an equilibrium between **8** and **9**, in competition with the two-step photochemical conversion to the 1,4-DHN **10**. It is proposed that the isomerization between the *E,E*-isomer and the *E,Z*-isomer occurs by disrotatory closure to 1,8a-DNH **11** (or **12**) followed by conrotatory thermal opening to **9** (or **8**). In protic solvents, there is also an equilibrium between **8** and **9,** but solvent protonation of **11** (and (or) **12**) produces primarily (but not exclusively) the *cis*-1,2-DHN **13**. The possibility that **13** is formed via an intramolecular thermal [1,5]-sigmatropic hydrogen shift was ruled out by the fact that deuterium is incorporated from deuterated solvents.

Experimental

General methods

Proton and ^{13}C-NMR spectra were recorded on a Bruker AM-300 FT instrument using residual $CHCl_3$ in the $CDCl_3$ as internal standard, unless otherwise specified. Silica gel (40–63 μm) (Silicycle, Quebec City, Que.) was used for all chromatography. High-resolution mass spectra (HRMS) were obtained on a VG Analytical 7070E-HF instrument. Irradiations were conducted with a 450-W medium-pressure mercury lamp housed in a Pyrex water-cooled jacket or with

a circular set of low-pressure mercury lamps (254 nm, 100 W). In all cases, the temperature of the solutions being irradiated was 25 ± 5 °C. HPLC was conducted on a reverse-phase C_{18} column using methanol (50–80%) in water as eluent. Literature references for known compounds are: **8** (23)**, 13** (23), and **14** (25).

Diethyl *E,Z*-2,3-(3,4,5-trimethoxybenzylidene)succinate (9)

A solution of diethyl *E,E*-2,3-(3,4,5-trimethoxybenzylidene)succinate (**8**) (0.020 g, 0.040 mmol) in EtOAc (4 mL) in a Pyrex test tube was purged with N_2 for 5 min. The test tube was sealed, fixed at 24 cm from the medium-pressure mercury lamp, and irradiated for 6 h. The solvent was evaporated to leave a mixture of the *E,E*- and *E,Z*-isomers, **8** and **9** (approximately 57:43 as determined by ^{1}H NMR). The *E,Z*-isomer **9** was separated from the mixture by HPLC. ^{1}H NMR ($CDCl_3$) δ 1.17 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 3.78 (s, 6H), 3.81 (s, 6H), 3.84 (s, 3H), 3.85 (s, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 6.63 (s, 2H), 6.73 (s, 1H), 6.91 (s, 2H), 7.75 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 14.0, 14.3, 56.0 (2C), 56.1 (2C), 60.9, 60.9 (2C), 61.3, 106.5 (2C), 107.8 (2C), 127.8, 129.9, 130.3, 130.7, 140.8, 141.9, 152.8 (3C), 153.0 (3C), 166.9, 167.5.

Diethyl 1-(3,4,5-trimethoxyphenyl)-6,7,8-trimethoxy-1,4-dihydronaphthalene-2,3-dicarboxylate (10)

A solution of **8** (0.138 g, 0.260 mmol) in $CHCl_3$ (26 mL) in a Pyrex test tube was purged with N_2 for 5 min. The test tube was sealed, fixed at 7 cm from the medium-pressure Hanovia mercury lamp, and irradiated for 3 h. The solvent was evaporated, and the residue mixture was purified by flash chromatography on silica gel using 50% EtOAc in hexanes to give the product (0.464 g, 33% yield). ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 3.63 (dd, *J* = 2.6 and 21.5 Hz, 1H), 3.87 (dd, *J* = 4.2 and 21.5 Hz, partly obscured by OMe signal at 3.85 Hz, 1H), 3.51 (s, 3H), 3.75 (s, 6H), 3.76 (s, 3H), 3.79 (s, 3H), 3.85 (s, 3H), 4.08–4.25 (m, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 5.21 (dd, *J* = 2.6 and 4.3 Hz, 1H), 6.37 (s, 2H), 6.52 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 14.16, 14.22, 31.9, 43.5, 56.1, 56.3 (2C), 60.5, 60.9, 61.0, 61.3, 61.5, 105.8 (2C), 106.3, 123.0, 127.7, 131.5, 137.2, 138.4, 138.6, 141.3, 151.0, 153.0, 153.2 (2C), 167.7 (*C*=O), 167.8 (*C*=O). MS *m/z* (relative intensity): 530 (M^+, 64), 484 (60), 456 (35), 411 (56), 380 (27), 362 (26), 317 (100), 289 (66), 245 (12), 181 (28), 168 (21); HRMS calcd. for $C_{28}H_{34}O_{10}$: 530.2152; found: 530.2148.

Diethyl *cis*- and *trans*-1-(3,4,5-trimethoxyphenyl)-6,7,8-trimethoxy-1,2-dihydronaphthalene-2,3-dicarboxylate (13 and 14)

The characterizations of **13** and **14** are reported elsewhere (23, 24) but are included here for completeness.

13. ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 7.2 Hz, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 3.46 (s, 3H), 3.71 (s, 3H), 3.72 (s, 6H), 3.82 (s, 3H), 3.86 (s, 3H), 4.08 (dd, *J* = 2.8, 9.1 Hz, 1H), 4.17 (m, 2H), 4.76 (d, *J* = 9.1 Hz, 1H), 6.32 (s, 2H), 6.63 (s, 1H), 7.36 (d, *J* = 2.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 13.8, 14.3, 40.5, 48.1, 56.10, 56.13 (2C), 60.4, 60.5, 60.7, 60.8 (2C), 106.4 (2C), 108.0, 123.7, 126.2, 127.1, 135.4, 136.4, 137.2, 144.2, 151.1, 152.6 (2C), 152.9, 167.3, 171.5; MS *m/z* (relative intensity): 530 (M^+, 100), 484 (44), 456 (62), 411 (65), 384 (33), 358 (69); HRMS calcd. for $C_{28}H_{34}O_{10}$: 530.2151; found: 530.2139.

14. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, *J* = 7.2 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 3.67 (s, 3H), 3.72 (s, 6H), 3.77 (s, 3H), 3.88 (s, 3H), 3.89 (s, 3H), 4.06 (d, *J* = 1.2 Hz, 1H), 4.12 (2 overlapping quartets, *J* = 7.2 Hz, 2H), 4.23 (2 overlapping quartets, *J* = 7.1 Hz, 2H), 5.00 (d, *J* = 1.2 Hz, 1H), 6.28 (s, 2H), 6.71 (s, 1H), 7.62 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 14.3, 39.4, 46.2, 56.0 (4C), 60.71, 60.77 (one quaternary carbon not observed). EIMS *m/z* = 530 [M^+], 456 (base), 411, 384, 196; HRMS calcd. for $C_{28}H_{34}O_{10}$: 530.2152; found: 530.2129.

Acknowledgements

We are grateful to the Natural Sciences and Engineering Research Council of Canada and the University of Manitoba for financial support of this project.

References

1. S.-T. Chang, S.-Y. Wang, U.C. Su, S.-L. Hunag, and Y.-H. Kuo. Hozforschung, **53**, 142 (1999).
2. A.S.R. Anjaneyulu, D. Santikumar, and U.V. Mallavadhani. Indian J. Chem., Sect. B,. **31B**, 401 (1992).
3. J.C.A. Boeyens, L. Denner, and G.W. Perold. J. Chem. Soc., Perkin Trans. 2, 1749 (1988).
4. A.S.R. Anjaneyulu, P. Raghu, and K.V.R. Rao. Indian J. Chem., Sect. B, **19B**, 511 (1980).
5. A.S.R. Anjaneyulu, P. Raghu, and K.V.R. Rao. Indian J. Chem., Sect. B, **18B**, 535 (1979).
6. O. Crescente, H.G. Heller, and S. Oliver. J. Chem. Soc., Perkin Trans. 1, 150 (1979).
7. T. Momose, T. Nakamura, and K. Kanai. Chem. Pharm. Bull. **26**, 3186 (1978).
8. T. Momose, K. Kanai, and K. Hayashi. Chem. Pharm. Bull. **26**, 3195 (1978).
9. T. Momose, K. Kanai, and T. Nakamura. Chem. Pharm. Bull. **26**, 1592 (1978).
10. T. Momose, K. Kanai, T. Nakamura, and Y. Kuni. Chem. Pharm. Bull. **25**, 2755 (1977).
11. T. Momose, T. Nakamura, and K. Kanai. Heterocycles, **6**, 277 (1977).
12. T. Momose, K. Kanai, and T. Nakamura. Heterocycles, **4**, 1481 (1976).
13. H.G. Heller and P.J. Strydom. J. Chem. Soc., Chem. Commun. 50 (1976).
14. R.J. Hart, H.G. Heller, R.M. Megit, and M. Szewczyk. J. Chem. Soc., Perkin Trans. 1, 2227 (1975).
15. J.S. Hastings, H.G. Heller, and K. Salisbury. J. Chem. Soc., Perkin Trans. 1, 1995 (1975).
16. H.G. Heller and M. Szewczyk. J. Chem. Soc., Perkin Trans. 1, 1487 (1974).
17. R.J. Hart and H.G. Heller. J. Chem. Soc., Perkin Trans. 1, 1321 (1972).
18. H.G. Heller and K. Salisbury. J. Chem. Soc. C, 873 (1970).
19. M.D. Cohen, H.W. Kaufman, D. Sinnreich, and G.M.J. Schmidt. J. Chem. Soc. B, 1035 (1970).
20. R.J. Hart, H.G. Heller, and K. Salisbury. J. Chem. Soc., Chem. Commun. 1627 (1968).
21. H.G. Heller and B. Swinney. J. Chem. Soc. C, 2452 (1967).

22. D.C. Ayres, B.G. Carpenter, and R.C. Denney. J. Chem. Soc. 3578 (1965).
23. P.K. Datta, C. Yau, T.S. Hooper, B.L. Yvon, and J.L. Charlton. J. Org. Chem. **66**, 8606 (2001).
24. T. Assoumatine, P.K. Datta, T.S. Hooper, B.L. Yvon, and J.L. Charlton. J. Org. Chem. **69**, 4140 (2004).
25. C. Cow, C. Leung, and J.L. Charlton. Can. J. Chem. **78**, 553 (2000).