Pergamon

Tetrahedron, Vol. 53, No. 40, pp. 13867-13872, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00875-2

Synthesis of 3,4-Disubstituted Furans via Unsaturated Cyclic Peroxides Arising by Photooxygenation of 2,3-Bis (bromomethyl)-1,3-butadiene and Derived Exocyclic Dienes

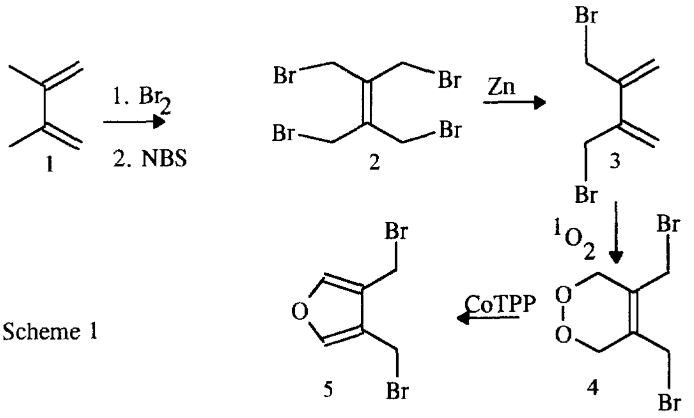
Basri Atasoy* and Recep Özen

Gazi University, Education Faculty of Gazi, Department
of Chemistry Education, Beşevler-Ankara/TURKEY

Abstract: The reaction of 2,3-bis (bromomethyl)-1,3-butadiene (**3**) with singlet oxygen resulted in the formation of a peroxide (**4**) which rearanged with CoTPP to bis(bromomethyl)furan. Zinc-induced debromination of cycloadducts which were obtained from the [2+4] Diels-Alder reactions of **3** with DMAD and benzyne gave exocyclic dienes **7** and **11** from which fused ring furans were prepared by photooxygenation followed by rearrangement. 4,5-Dimethylene-1,2-dioxane (**14**) was synthesized by zinc-induced debromination of **4**. The cycloaddition reactions of **14** with MTAD, singlet oxygen and DMAD were studied. © 1997 Elsevier Science Ltd.

In previous report[1], we demonstrated that 4,5-dimethylene-1,2-dioxane (**14**), readily avaliable from the reaction of **4** with zinc-copper couple, is a useful intermediate for the synthesis of furans. In connection with this we now report a convenient route to prepare 3,4-fused ring furans starting from 2,3-bis (bromomethyl)-1,3-butadiene (**3**).

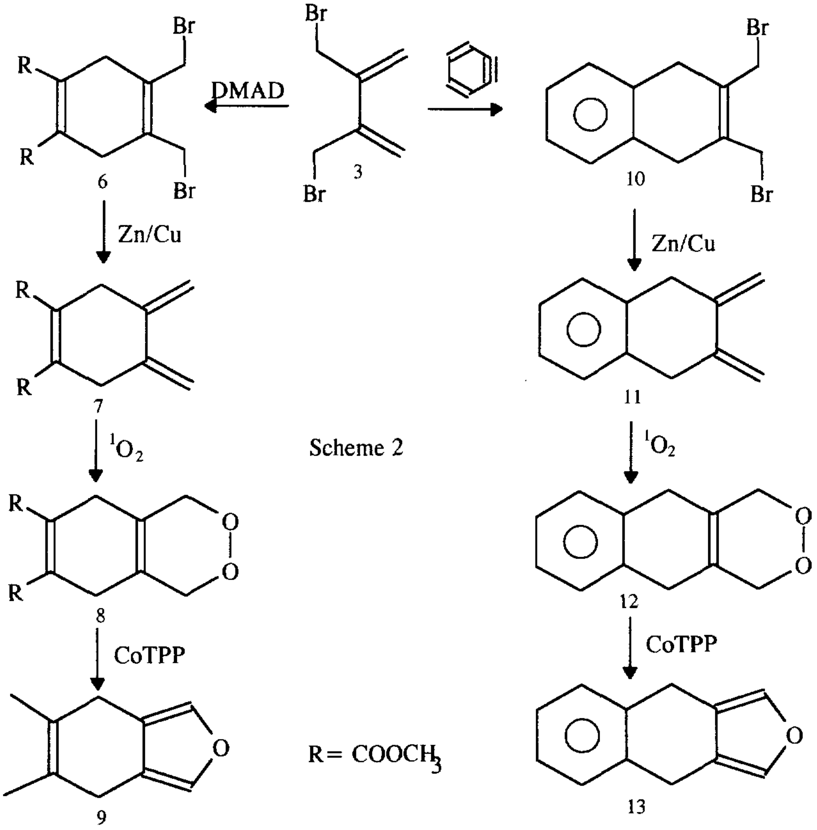
The synthesis of furans is of importance since the furan ring is present in numerous natural products which exhibit interesting biological activities.[2,3] 3,4-Disubstituted furans are building blocks of heterocyclic compounds and therefore they play an important role in organic synthesis.[4-9] A variety of approaches leading to the synthesis of this class of molecules in the literature have been reported.[10-15] However, most of these methods were not suitable for the preparation of 3,4-fused ring furans. New synthetic methods leading to the ring system are therefore of considerable importance. In our synthesis, the first stage was cycloaddition reaction of **3** with dienophiles. Then, zinc-induced debromination of cycloadducts gave exocyclic dienes from which fused ring furans were prepared by photooxygenation followed by rearrangement.



Scheme 1

Singlet oxygen undergoes 1,4-cycloaddition to the conjugated dienes to give cyclic peroxides and addition to mono olefins to form 1,2-dioxetans and hydroperoxides.[16] Cobalt(II)tetraphenylporphyrin (CoTPP) catalyzes the rearrangement of unsaturated bicyclic endoperoxides to bisepoxides and of monocyclic endoperoxides to furans.[17]

The synthesis of 2,3-bis(bromomethyl)furan began with the bromination of 2,3-dimethylbutadiene.[18] followed by twofold NBS bromination and reduction of tetrakis (bromomethyl) ethylene with zinc-copper couple to afford 2,3-bis(bromomethyl)-1,3-butadiene.[19] The photooxygenation reaction of 2,3-bis (bromomethyl)-1,3-butadiene (3) using tetraphenylporphyrin (TPP) as sensitizer in chloroform at room temperature gave a 40 % yield of 4,5-bis(bromomethyl)-1,2-dioxacyclohexa-4-en (4); the material balance consisting of polymer. CoTPP catalyzed rearrangement of monocyclic endoperoxide (4) resulted in the formation of the expected furan 5 (Scheme 1) 90 % yield. Both of these compounds were characterized by means of spectral data. As can be seen from the structure, furan 5 can be converted to 3,4-disubstituted furans by treatment with nucleophiles.



Scheme 2

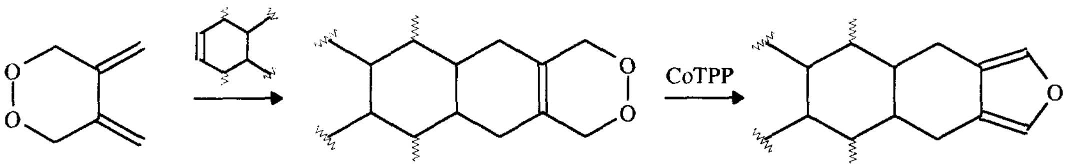
For synthesizing 3,4-fused ring furans, Diels-Alder reactions of 2,3-bis(bromomethyl)-1,3-butadiene (3) with dimethylacetylenedicarboxylate (DMAD) and benzyne were carried out. Cycloaddition of DMAD to 3 in refluxing toluene gave dimethyl-4,5-bis(bromomethyl)cyclohexa-1,4-diene-1,2-dicarboxylate (6). Heating 6 in ether with zinc-copper couple[21] afforded dimethyl-4,5-

dimethylenecyclohexene-1,2-dicarboxylate (**7**) in 95 % yield.[19] Dimethyl-1,2,3.4,5,8-hexahydro-2,3-dioxanaphthalene-6,7-dicarboxylate (**8**) was prepared from the reaction of **7** with singlet oxygen under usual conditions in chloroform at room temperature in a 58 % yield. CoTPP catalyzed rearrangement of **8** gave dimethyl-4,7-dihydro benzofuran-5,6-dicarboxylate (**9**) in 65 % yield (Scheme 2). The structures of **8** and **9** were established on the basis of their ^{1}H-and ^{13}C-NMR spectra.

Benzyne is among the most reactive acetylenic dienophiles known, and we expected that its use might allow the isolation of cycloadduct. The reaction of **3** with excess benzenediazonium carboxylate hydrochloride[20] refluxing dichloroethane for 2h resulted in a 26 % yield of 2,3-bis (bromomethyl)-1,4-dihydronaphthalene (**10**). Its debromination with zinc-copper couple[21] in ether gave 2,3-dimethylene-1,2,3,4-tetrahydronaphthalene (**11**) in 80 % yield and in a purity of 90 % (Scheme 2), which was satisfactory for subsequent use. Its ^{1}H-NMR data and mp are identical with those reported previously.[22]

1,2,3,4,9,10-Hexahydro-2,3-dioxaantracene (**12**) was obtained from the reaction of **11** with singlet oxygen. Treatment of **12** with 5-10 mol % CoTPP in chloroform at room temperature gave 4,9-dihydronaphtho[2,3-c]furan (**13**) in 70 % yield. Their spectral properties were identical with those previously reported.[23] Exocyclic diene **11** and furan **13** has been prepared previously by the pyrolysis of 1,4-dihydronaphtho[b]cyclobutene[22] (20 % yield) and treatment of 1-phenyl-4-oxahepta-1,6-diyne[23] with KO-t-Bu (20 % yield) respectively. As can be seen, yields are low and required special substances and conditions. Our synthesis does not necessitate the use of anhydrous solvents and strong bases and does not require low reaction temperature and the yields are high.

On the strength of these results, our next target was the synthesis of the unknown 4,5-dimethylene-1,2-dioxane (**14**). As can be seen from its structure, it is a versatile reactive synthetic intermediate. The versatility of **14** derives from its having both exocyclic diene and peroxide moieties. The diene moiety can react with different dienophiles to form cycloadducts which can be rearranged to 3,4-disubstituted furans. Such a sequence is of use in the synthesis of various multicyclic molecules (Scheme 3).

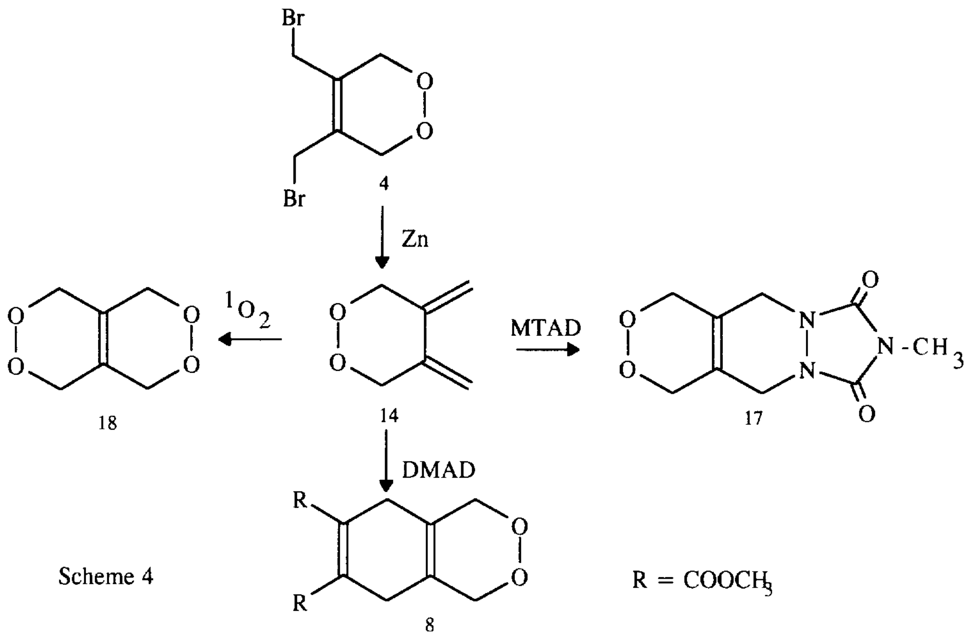


14 Scheme 3 15 16

4,5-Dimethylene-1,2-dioxane (**14**) was obtained from **4** by zinc-copper couple induced debromination in 80 % yield and its cycloaddition reactions with DMAD, singlet oxygen and MTAD were carried out (Scheme 4). Although, **14** polymerized quite rapidly in the free state it was stable in solution for at least one week, and reactions were carried out in solution with a very low extent of polymerization.

Cycloaddition reaction of **14** with DMAD was carried out firstly. It was found that the spectroscopic data of the adduct were identical with those of the singlet oxygen adduct of **7**. Thus, its structure was confirmed by chemical way.

The Diels-Alder reaction of **14** with N-methyl-1,2,4-triazoline-3,5-dione (MTAD) was performed in ether and addition took place rapidly, and adduct **17** was obtained in quantitative yield. Reaction of **14** with singlet oxygen under the usual conditions in chloroform produced 3,4,8,9-tetraoxa-1 (6)-bicyclo [4.4.0] decene (**18**). Endoperoxides are of both synthetic and theoretical importance.



Scheme 4

R = COOCH$_3$

Experimental Section

Melting points are uncorrected. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column (60 mesh). TLC was done on 0.2 mm silica gel 60F$_{254}$ plates. The ^{1}H-NMR and ^{13}C-NMR spectra were measured with a Varian EM-200 spectrometer and are given in δ units downfield from Me$_4$Si as internal standard. Infrared spectra were obtained from films on NaCl plates for liquids or from solution in 0.1 mm cells or KBr pellets for solids on a Perkin-Elmer 337 infrared recording spectrophotometer.

General procedure for photooxidation.

A solution of the diene containing tetraphenyl porphyrin (TPP) as a sensitizer (3-5x10^{-4} m) in a pyrex tube with a water cooling jacket was irradiated with a projection lamp (150 watt). Oxygen was continuously bubbled through the solution during photolysis.

General procedure for Co(II)-catalyzed rearrangement.

A solution of peroxide in methylene chloride was cooled to 0 °C. While cooling and stirring, a solution of cobalt(II)tetraphenyl porphyrin (CoTPP) in 5 ml of methylene chloride (5-10 mol %) was added within 10-15 min. Then, cooler was removed and the reaction mixture was stirred at room temperature until TLC showed complete consumption of starting material.

4,5-Bis (bromomethyl)-1,2-dioxacylohexa-4-en (4)

A solution, (4g, 17 mmol) of 2,3-bis(bromomethyl)-1,3-butadiene (prepared following the literature procedure[19]) and TPP in 25 ml chloroform was photooxidized until all the diene had reacted (100 h). The solvent was evaporated, and the residue was purified by chromatography on silica gel (eluting with chloroform/petroleum ether, 1:10) to afford **4** as a white solid (1,2 g 40 % yield); mp 95-96 °C; IR (KBr, cm^{-1}) 2860, 1460, 1190, 1030, 580; ^{1}H-NMR (CDCl$_3$) 4.02 (4H, br.s.), 4.66 (4H, br.s.) ppm; ^{13}C-NMR 131.4, 70.8, 25 ppm.Anal. calcd for $C_6H_8O_2Br_2$: C, 26.43; H, 3.21. found: C, 26.32; H, 3.18.

3,4-Bis (bromomethyl) furan (5)

To a solution of **4** (1g, 3.7 mmol) in methylene chloride (20 ml) the solution of CoTPP (75 mg) in 5 ml methylene chloride was added and stirred at room temperature for (24h). Solvent was evaporated, and the residue was chromatographed on silica gel eluting with ether/petroleum ether (1:10) to afford **5** as a white solid (0.9 g 90 % yield); mp 74 °C; IR (KBr, cm^{-1}) 1540, 1425, 1210, 1040, 805; ^{1}H-NMR (CDCl$_3$) 4.48

(4H, br.s.), 7.47 (2H, br.s); ^{13}C-NMR 143.17, 122.2, 22.05 ppm. Anal. Calcd for $C_6H_6Br_2O$: C, 28.38; H, 2.38. found: C, 28.25; H, 2.35.

Dimethyl-1,2,3,4,5,8-hexahydro-2,3-dioxa-6,7-dicarboxylate (8).

A solution of TPP and (0.5 g, 3.2 mmol) **7** (prepared following the literature procedure[18]) in chloroform was photooxidized until all the diene had reacted (30 h). The solvent was evaporated, and the residue was prufied by chromatography on silica gel (eluting with ether/petroleum ether 1:10) to afford **8** as a white solid (0.35 g 58 % yield); mp 170 °C; IR (KBr, cm^{-1}) 2870, 1715, 1430, 1265, 1055, 740; ^{1}H-NMR ($CDCl_3$) 2.94 (4H, s), 3.8 (6H, s), 4.42 (4H, s); ^{13}C-NMR 28.10, 52.4, 72.0, 123.0, 132.2, 168.5 ppm. Anal.Calcd for $C_{12}H_{14}O_6$: C, 56.69; H, 5.55 found: C, 56.53; H, 5.52

Dimethyl-4,7-dihydrobenzofuran-5,6-dicarboxylate (9)

To a solution of **8** (0.59g, 1.97 mmol) in methylene chloride (20 ml) a solution of 50 mg CoTPP in methylene chloride was added. After reaction was completed (TLC); solvent was evaporated, and the residue was chromatographed on silica gel (eluting with chloroform/petroleum ether (1:10) to afford **9** as colorless oil (0.36 g 65 % yield); IR (NaCl, cm^{-1}) 2950, 1720, 1640, 1430, 1270, 1060, 760; ^{1}H-NMR ($CDCl_3$) 3.54 (4H, br.s), 3.8 (6 H, s), 7.3 (2 H, br.s); ^{13}C-NMR 23.12, 52.94, 117.20, 133.52, 138.12, 169.05 ppm Anal. Calcd for $C_{12}H_{12}O_5$; C, 61.01; H, 5.12 found: C, 60.73; H, 5.15.

2,3-Bis (bromomethyl)-1,4-dihydronaphthalene (10)

A solution of **3** (4g, 2.66 mmol) in 150 ml 1,2-dichloro ethane was stirred and refluxed under nitrogen, and (5g, 3.3 mmol) benzenediazonium 2-carboxylate hydrochloride (prepared following the procedure in the literature[20]) and 10 ml. propylene oxide was added. After one hour, equal amounts of salt and propylene oxide were added and the mixture was stirred (2h). Solvent was evaporated. The dark residue was chromatographed on silica gel (eluting with chloroform/petroleum ether 1:10) to afford **10** as a white solid (1.4 g, 26 % yield); mp. 118 °C; IR (KBr, cm^{-1}) 3020, 2845, 1495, 1245, 750; ^{1}H-NMR ($CDCl_3$) 3.6 (4 H, s), 4.4 (4 H, s), 7.4 (4 H, s); ^{13}C-NMR 133.45, 132.57, 126.24, 126.92, 34.51, 31.35 ppm. Anal.Calcd for $C_{12}H_{12}Br_2$: C, 45.60; H, 3.82; found: C, 45.50; H, 3.81.

2,3-Dimethylene-1,2, 3,4-tetrahydronaphthalene (11)

A solution of **10** (1.2 g, 3.8 mmol) in dry ether was refluxed with vigorous stirring in the presence of 0.5 g zinc-copper couple.[21] Further portions (0.5 g) of Zn-Cu couple were added after every additional hour. When the TLC showed the reaction to be complete (5 h) the workup was carried out by filtering the reaction mixture on celite and evaporating the ether. The residue was purified by chromatography on silica gel (eluting with petroleum ether) to afford **11** as a white solid (0.5 g 80 % yield); mp 62 °C literature[22] value 64 °C.

1,2, 3,4, 9,10-Hexahydro-2,3-dioxaanthracene (12)

To a stirred solution of **11** (0.5 g, 3.2 mmol) in 10 ml chloroform 10 mg TPP was added. The mixture was photooxidized until all the diene had reacted (30 h). The solvent was evaporated, and the residue was chromatographed on silica gel (eluting with ether/petroleum ether, 1:10) to afford **12** as a white solid (0.35 g, 58 % yield); mp 200 °C; IR (KBr, cm^{-1}) 2880, 1455, 1040, 730; ^{1}H-NMR ($CDCl_3$) 3.32 (4 H, s), 4.55 (4 H, s), 7.18 (4 H, s); ^{13}C-NMR 133.40, 128.87, 126.75, 124.49, 72.65, 30.52 ppm. Anal.Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.42 found: C, 76.53; H, 6.40.

4,9-Dihydronaphtho [2,3-c] furan (13)

To a solution of **12** (300 mg, 1.6 mmol) in 10 ml methylene chloride (10 ml) the solution of CoTPP (75 mg) in methylene chloride was added. After reaction was completed (4h) the solvent was evaporated, and the residue was chromatographed on silica gel (eluting with ether/petroleum ether, 1:10) to afford **13** as a white solid (200 mg, 70 % yield); mp 78 °C (literature[23] value 79-80 °C).

4,5-Dimethylene-1,2-dioxane (14)

A solution of **4** (1g, 3.7 mmol) in dry ether was refluxed vigorous stirring in the presence of 0.5 g zinc-copper couple.[21] Further portions (0.5 g) of zinc-copper couple were added after every additional hour. After 6h TLC showed the reaction to be completed. The workup was carried out by filtering the reaction mixture on celite. The solution was concentrated. The product polymerizes when not kept in solution. ^{1}H-NMR (60 MHz), 5.4 (2 H, s), 4.9 (2 H, s), 4.7 (4 H, s); MS m/z (M$^+$) calcd 112.1280, obsd 112.1264.

Diels-Alder cycloaddition between 14 and DMAD

To a solution of **14** (112 mg, 1 mmol) in ether (10 ml) 142 mg (1 mmol) DMAD was added. The mixture was stirred at room temperature 2h. The precipitate was collected by filtration and triturated with ether to afford **8** (200 mg, 75 % yield) its spectroscopic value and mp were identical with those of the singlet oxygen adduct of **7**.

Diels-Alder cycloaddition between 14 and MTAD

To a solution of **14** (112 mg, 1 mmol) in ether (10 ml) 100 mg (1 mmol) MTAD was added. The reaction was completed immediately. The precipitate was collected and triturated with methylene chloride to leave **17** as an insoluble white solid (150 mg); mp 122 °C; IR (KBr, cm^{-1}) 2910, 1690, 1415, 780; ^{1}H-NMR (CDCl$_3$) 4.56 (4 H, s), 4.02 (4 H, s), 3.12 (3 H, s); ^{13}C-NMR 155.95, 124.38, 71.61, 44.95, 27.14. Anal.Calcd for $C_9H_{11}O_4N_3$; C, 48.00; H, 4.92; found: 47.78; H, 4.85.

3,4,8,9-Tetraoxa-1(6) bicyclo [4.4.0] decene (18)

A solution of **14** (450 mg, 4 mmol) and TPP in 25 ml chloroform was photooxidized until complete consumption of the diene (30 h). Solvent was evaporated, and the residue was submitted to short silica gel column (filtering with ether) to afford **18** as a colorless oil (400 mg, 80 % yield); ^{1}H-NMR (CDCl$_3$) 4.53 (s); ^{13}C-NMR 125.15, 69.25.

Acknowledgements: The authors are indebted to the Scientific and Technical Research Council of Turkey (TÜBİTAK Grant No: TBAG-973) for the financial support of this work, to Prof.Dr. M. Balcı (Atatürk University) for providing 200 MHz-^{1}H and ^{13}C-NMR spectra.

REFERENCES

1 Atasoy, B.; Karaböcek, S. *Tetrahedron Lett.* **1992**, 33, 8127-8130.
2. Lipshutz, B.H., *Chem. Rev.* **1986**, 86, 795-819.
3. Song, Z.Z.; Ho, M.S. and Wong, H.N.C. *J.Org.Chem.* **1994**, 59, 3917-3925 (literature cited therein)
4. Froborg, J.; Magnussan, G.; Thoren, S. *J.Org.Chem.* **1975**, 40, 1595-1601.
5. Corey, E.J.; Crouse, D.N.; Anderson, J.E. *J.Org.Chem.* **1975**, 40, 2140-2141.
6. Aberbach, W.; Fritz, H.; Laber, N. *Angew.Chem. Int.Ed.Engl.* **1988**, 27, 568-569.
7. Katagiri, N. Akatsuka, H.; Haneda, T; Kaneko, C. *J.Org.Chem.* **1988,** 53-5464-5470.
8. Song, Z.Z.; Wong, H.N.C. *J.Org.Chem.* **1994**, 59, 33-41.
9. Padwa, A.; Kinder, F.R. *J.Org.Chem.* **1993**, 58, 21.
10. Katritzky, A.R. and Li, J. *J.Org.Chem.* **1995**, 60, 638.
11. Grast, M.E.; Spencer, T.A. *J.Org.Chem.* **1973**, 95, 250-252.
12. Price, M.E.; Schore, N.E. *J.Org.Chem.* **1989**, 54, 2777-2778.
13. Reich, H.J.; Olson, R.E, *J.Org.Chem.* **1987**, 52, 2315-2317.
14. Danso-Danguah, R.E.; Scott, A.I.; Becker, D. *Tetrahedron*, **1993**, 49, 8195-8210.
15. Yang, Y. Wong, H.N.C. *J.Chem.Soc.Chem.Commun.* **1992**, 656-658.
16. a) Balcı, M. *Chem.Rev.* **1981**, 81, 91.
    b) Atasoy, B.; Balcı, M. *Tetrahedron Lett.* **1984**, 25, 4033.
    c) Atasoy, B.; Balcı, M. *Tetrahedron*, **1986**, 42, 1461.
17. a) O'Shea, K.E.; Foote, C.S. *J.Org.Chem.* **1989**, 54, 3475-3477.
    b) Atasoy, B.; Bayramoğlu, F.; Hökelek, T. *Tetrahedron*, **1994**, 50, 5753-5764.
18. Cope, A.C.; Kagan, F. *J.Am.Chem.Soc.* **1959**, 80, 2499-2502.
19. Gaoni, Y.; Sadeh, S. *J.Org.Chem.* **1980**, 45, 870-881.
20. Hart, H. and Oku, A. *J.Org.Chem.* **1972**, 37, 4263-4274.
21. Lambert, J.B.; Koeng, F.R.; Hamersma, J.W. *J.Org.Chem.* **1971**, 36, 2941-2947.
22. Thummel, R.P.; Cravey, W.E and Nutakul, W. *J.Org.Chem.* **1978**, 43, 2473-2476.
23. Garratt, P.J. and Neoh, S.B. *J.Org.Chem.* **1979**, 44, 2667-2674.

(*Received in UK* 19 *June* 1997; *revised* 29 *July* 1997; *accepted* 31 *July* 1997)