# Synthesis of *N,N*-Disubstituted 4-Amino-3,4-dihydro-6-phenyl-1,2-oxathiin 2,2-Dioxides and of 4-Methylphenylamino-3,4-dihydro-5,6-polymethylen-1,2-oxathiin 2,2-Dioxides

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The title compounds were obtained by cycloaddition of sulfene to *N,N*-disubstituted 3-amino-1-phenyl-2-propen-1-ones and to 2-methylphenylaminomethylenecycloalkanones, respectively. Steric and electronic aspects of these reactions, as well as the failure of cycloaddition in the case of *N,N*-disubstituted 4-amino-3-buten-2-ones, are also discussed.

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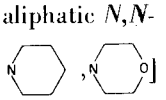
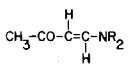
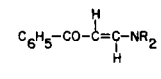
As part of our continuing study of sulfene cycloaddition to *N,N*-disubstituted α-aminomethyleneketones (1), we have undertaken a systematic research concerning open-chain α-aminomethyleneketones. We now wish to report results obtained with *N,N*-disubstituted 4-amino-3-buten-2-ones I and 3-amino-1-phenyl-2-propen-1-ones II. Enaminoketones I and II are mostly known, excepting the morpholino derivatives (I and II, $NR_2$ =  ) (Table I), which were prepared by Benary's method (2) and by a previously described procedure (3), respectively.

Reaction of enaminoketones II bearing aliphatic *N,N*-disubstituents [$NR_2 = N(CH_3)_2, N(C_2H_5)_2$,  ] with methanesulfonyl chloride and triethylamine (sulfene prepared *in situ*) gave in good to fair yields the expected 4-dialkylamino-3,4-dihydro-6-phenyl-1,2-oxathiin 2,2-dioxides (IIIa-d) (Table II), whereas the corresponding compounds I did not react and were recovered unchanged from the reaction mixture. When in I, $NR_2$ = $N(CH_3)C_6H_5$, the sole product isolated in low yield was *N*-methyl-*N*-phenylmethanesulfonamide as a result of direct attack of sulfene on the nitrogen atom.

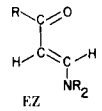
The structures of IIIa-d were supported by ir and nmr spectral data (Table III). To account for these apparently anomalous results, it should be considered that open-chain β-aminoenones I and II may exist only in two geometrical isomers Ia, IIa (EZ) and Ib, IIb (EE). Actually, the other two possible isomers ZZ and ZE are excluded by nmr data [J for the vinyl protons about 12.5 Hz; compare (4-6) and Table I]. On the other hand, ir spectra of enaminoketones I show, in comparison with those of II, an additional band in the double bond stretching region, which was attributed to rotational isomerism (5), namely to the presence of the isomer Ib (see Table I). In conclusion, if rotamer Ib predominates in solution, clearly the cycloaddition of sulfene is prevented; the reaction can occur with enaminoketones II because they exist exclusively as rotamers IIa.



I

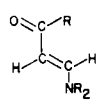


II



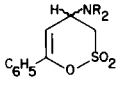
EZ

Ia: R = $CH_3$
IIa: R = $C_6H_5$

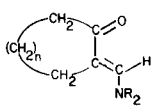


EE

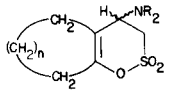
Ib: R = $CH_3$
IIb: R = $C_6H_5$



IIIa-d



IV: n = 1-4



V

Va: $NR_2 = N(CH_3)C_6H_5$; n = 2
Vb: $NR_2 = N(CH_3)C_6H_5$; n = 3
Vc: $NR_2 = N(CH_3)C_6H_5$; n = 4

Another point we have taken into account is the electron availability of nitrogen in the $NR_2$ group of enaminoketones. To study the influence of $NR_2$ on the cycloaddition, we have considered the reaction of sulfene with the most suitable (from a steric viewpoint) enaminoketones, namely, a series of cyclic compounds IV. Actually, we had already found (7) that these enaminoketones, rigid both in the configurational and conformational aspect (8,9), gave in high yields a facile cycloaddition with sulfene when $NR_2$ was a dialkylamino group. In these cases, the most suitable isomerism (E) resulted both from the above considerations and from nmr data, namely, a shielding effect of 0.3-0.5 ppm caused by the diphenylamino group in compounds IV [$NR_2 = N(C_6H_5)_2$] on the methylene protons adjacent

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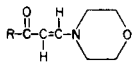
Table I

Enaminoketones



1 2 3 4

| Compound No. | R | Yield % | B.p./mm Hg or M.p. °C | Molecular Formula | Analyses % Calcd./Found C | H | N |
|---|---|---|---|---|---|---|---|
| I | $CH_3$ | 58 | 96/0.1 | $C_8H_{13}NO_2$ | 61.91<br>61.66 | 8.44<br>8.49 | 9.03<br>9.26 |
| II | $C_6H_5$ | 60 | 93 (a) | $C_{13}H_{15}NO_2$ | 71.87<br>71.66 | 6.96<br>6.98 | 6.45<br>6.73 |

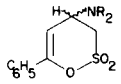
Uv, Ir and Nmr Spectral Data

| | Uv λ Max Nmr (Log ε) | Ir $cm^{-1}$ (tetrachloromethane) C=O | C=C | Nmr δ |
|---|---|---|---|---|
| I | 301 (4.39) | 1657 | 1610<br>1560 | 1.98 (s, $CH_3CO$), 3.34 (m, $2NCH_2$), 3.58 (m, $2CH_2O$), 5.08 (d, J = 12.7, CH-3), 7.30 (d, J = 12.7, CH-4) (b) |
| II | 246.5 (4.06)<br>343 (4.38) | 1650 | 1560 | 3.36 (m, $2NCH_2$), 3.55 (m, $2CH_2O$), 5.81 (d, J = 12.6, CH-3), 7.2-8.0 (m, $C_6H_5$), 7.59 (d, J = 12.6, CH-4) (c) |

(a) From diethyl ether. (b) In deuteriochloroform. (c) In tetrachloromethane.

Table II

*N,N*-Disubstituted 4-Amino-3,4-dihydro-6-phenyl-1,2-oxathiin 2,2-Dioxides (IIIa-d)



| Compound No. | $NR_2$ | Yield % | M.p., °C | Molecular Formula | Analyses % Calcd./Found C | H | N |
|---|---|---|---|---|---|---|---|
| IIIa | $N(CH_3)_2$ | 45 | 77 (a) | $C_{12}H_{15}NO_3S$ | 56.90<br>57.11 | 5.97<br>6.11 | 5.53<br>5.66 |
| IIIb | $N(C_2H_5)_2$ | 54 | 79 (a) | $C_{14}H_{19}NO_3S$ | 59.76<br>59.96 | 6.81<br>6.85 | 4.98<br>4.92 |
| IIIc |  | 66 | 125 (b) | $C_{15}H_{19}NO_3S$ | 61.41<br>61.72 | 6.53<br>6.63 | 4.77<br>4.82 |
| IIId |  | 77 | 153 (b) | $C_{14}H_{17}NO_4S$ | 56.93<br>56.76 | 5.80<br>6.02 | 4.74<br>4.47 |

(a) From anhydrous diethyl ether. (b) From anhydrous diethyl ether/acetone.

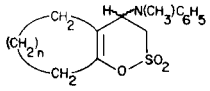
Table III

Ir and Nmr Spectral Data of Compounds IIIa-d

| | Ir $Cm^{-1}$ C=C | (Chloroform) O=S=O | | Nmr δ (Deuteriochloroform) |
|---|---|---|---|---|
| IIIa | 1655 | 1375 | 1170 | 2.34 (s, $2NCH_3$), 3.44 (m, $J_{AB}$ = 9.4, $CH_2$-3), 4.12 (dq, $J_{AB}$ = 9.4, $J_{AX}$ = 0.35, CH-4), 5.87 (d, J = 0.35, CH-5), 7.40 (m, $C_6H_5$) |
| IIIb | 1658 | 1375 | 1170 | 1.11 (t, J = 6.7, $2CH_3$), 2.54 and 2.65 (2q, J = 6.7, $2NCH_2$), 3.46 (m, $J_{AB}$ = 10.2, $CH_2$-3), 4.31 (m, $J_{AB}$ = 10.2, $J_{AX}$ = 0.25, CH-4), 5.78 (d, J = 0.25, CH-5), 7.46 (m, $C_6H_5$) |
| IIIc | 1662 | 1382 | 1180 | 1.54 (m, $3CH_2$), 2.56 (m, $2NCH_2$), 3.53 (m, $J_{AB}$ = 9.6, $CH_2$-3), 4.12 (dq, $J_{AB}$ = 9.6, $J_{AX}$ = 0.25, CH-4), 5.83 (d, J = 0.25, CH-5), 7.42 (m, $C_6H_5$) |
| IIId | 1655 | 1378 | 1182 | 2.62 (m, $2NCH_2$), 3.46 (m, $J_{AB}$ = 9.6, $CH_2$-3), 3.72 (m, $2CH_2O$), 4.12 (dq, $J_{AB}$ = 9.6, $J_{AX}$ = 0.25, CH-4), 5.78 (d, J = 0.25, CH-5), 7.40 (m, $C_6H_5$) |

Table IV

4-Methylphenylamino-3,4-dihydro-5,6-polymethylen-1,2-oxathiin 2,2-Dioxides (Va-c)




| Compound No. | n | Yield % | M.p., °C | Molecular Formula | Analyses % Calcd./Found C | H | N |
|---|---|---|---|---|---|---|---|
| Va | 2 | 95 | 113 (a) | $C_{15}H_{19}NO_3S$ | 61.30<br>61.30 | 6.52<br>6.54 | 4.76<br>4.57 |
| Vb | 3 | 50 | 97 (b) | $C_{16}H_{21}NO_3S$ | 62.52<br>62.43 | 6.89<br>6.96 | 4.56<br>4.62 |
| Vc | 4 | 30 | 91 (b) | $C_{17}H_{23}NO_3S$ | 63.52<br>63.30 | 7.21<br>7.34 | 4.36<br>4.30 |

Ir and Nmr Spectral Data

| | Ir $Cm^{-1}$ C=C | (Chloroform) O=S=O | | Nmr δ (Deuteriochloroform) |
|---|---|---|---|---|
| Va | 1690 | 1375 | 1182 | 1.35-2.70 (m, $4CH_2$), 2.76 (s, $NCH_3$), 3.33 and 3.46 (dq, $J_{AB}$ = 13.8, $CH_2$-3), 4.95 (m, $J_{AX}$ = 11.4, $J_{BX}$ = 6.6, CH-4), 6.6-7.5 (m, $C_6H_5$) |
| Vb | 1678 | 1375 | 1178 | 1.35-2.65 (m, $5CH_2$), 2.78 (s, $NCH_3$), 3.24 and 3.44 (dq, $J_{AB}$ = 13.8, $CH_2$-3), 4.91 (m, $J_{AX}$ = 11, $J_{BX}$ = 6.4, CH-4), 6.6-7.5 (m, $C_6H_5$) |
| Vc | 1682 | 1375 | 1180 | 1.2-2.6 (m, $6CH_2$), 2.73 (s, $NCH_3$), 3.27 and 3.44 (dq, $J_{AB}$ = 13.8, $CH_2$-3), 4.93 (m, $J_{AX}$ = 11, $J_{BX}$ = 7, CH-4), 6.7-7.5 (m, $C_6H_5$) |

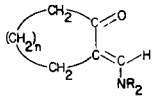
(a) From anhydrous diethyl ether/acetone. (b) From anhydrous diethyl etherpetroleum ether.

to the double bond, in comparison with other enaminoketones IV [compare (9) and Table V].

Reaction of sulfene with enaminoketones IV in which nitrogen bears electron-withdrawing substituents was attempted for $NR_2$ = $N(CH_3)C_6H_5$ and $N(C_6H_5)_2$. In the former case, the cycloaddition occurred to give in good to fair yields, 4-methylphenylamino-3,4-dihydro-5,6-polymethylene-1,2-oxathiin 2,2-dioxides (Va-c) (Table IV);

Table V

Nmr Spectral Data of some *N,N*-Disubstituted 2-Aminomethylenecycloalkanones (IV)



| n | $NR_2$ | Nmr δ (Deuteriochloroform) |
|---|---|---|
| 2 | $N(CH_3)C_6H_5$ | 1.71 (m, $2CH_2$), 2.15 (m, $CH_2C{=}C$), 2.42 (m, $CH_2CO$), 3.40 (s, $NCH_3$), 6.9-7.6 (m, $NC_6H_5$), 7.63 (near s, =CHN) |
| 2 | $N(C_6H_5)_2$ | 1.66 (m, $2CH_2$ + $CH_2C{=}C$), 2.41 (m, $CH_2CO$), 6.85-7.50 (m, $2NC_6H_5$), 7.64 (near s, =CHN) |
| 3 | $N(CH_3)C_6H_5$ | 1.67 (m, $3CH_2$), 2.22 (m, $CH_2C{=}C$), 2.58 (m, $CH_2CO$), 3.41 (s, $NCH_3$), 6.9-7.6 (m, $NC_6H_5$), 7.71 (s, =CHN) |
| 3 | $N(C_6H_5)_2$ | 1.60 (m, $3CH_2$), 1.85 (m, $CH_2C{=}C$), 2.56 (m, $CH_2CO$), 6.9-7.6 (m, $2NC_6H_5$), 7.72 (s, =CHN) |
| 4 | $N(CH_3)C_6H_5$ | 1.51 (m, $4CH_2$), 2.55 (m, $CH_2CO$ + $CH_2C{=}C$), 3.45 (s, $NCH_3$), 6.9-7.6 (m, $NC_6H_5$), 7.67 (s, =CHN) |
| 4 | $N(C_6H_5)_2$ | 0.8-1.9 (m, $4CH_2$), 2.10 (m, $CH_2C{=}C$), 2.62 (m, $CH_2CO$), 6.85-7.60 (m, $2NC_6H_5$), 7.67 (s, =CHN) |

All compounds were already described (8).

however, the reaction failed in the latter case for all compounds tried (n = 1-4). Also, enaminoketone [II, $NR_2$ = $N(CH_3)C_6H_5$] did not react with sulfene and was quantitatively recovered from the reaction mixture. A convenient electron availability on the nitrogen atom of the enaminoketone seems therefore essential in order to allow the reaction even in those cases where the stereoisomerism is favourable.

Finally, a proper divarication of the conjugated C=O and $C{=}CNR_2$ groups seems also necessary, because we have found that the reaction did not occur even in the case of (IV, n = 1, $NR_2$ = $N(CH_3)C_6H_5$). This difficulty of enaminoketones derived from cyclopentanone to react with sulfene has already been observed by us (10).

## EXPERIMENTAL

Uv spectra were measured in 95% ethanol with a Hitachi-Perkin-Elmer Model EPS-3T spectrophotometer. Ir spectra were taken on a Perkin-Elmer Model 257 spectrometer; nmr spectra were recorded on a Perkin-Elmer Model R-12 instrument (60 MHz; TMS as internal standard; J in Hz). Melting points were determined with a Fisher-Johns apparatus.

Compounds I and II (Table I) were prepared according to (2) and (3), respectively.

General Procedure for Compounds IIIa-d and Va-c.

Compounds IIIa-d (Table II) and Va-c (Table IV) were prepared according to (3), starting from the appropriate enaminoketone (30 mmoles), methanesulfonyl chloride (33 mmoles) and triethylamine (60 mmoles) in anhydrous benzene (50 ml.). All compounds were purified before recrystallisation by chromatography on Florisil®, using petroleum ether (b.p. 40-70°)-diethyl ether 10:1 as eluant.

In the case of 4-methylphenylamino-3-buten-1-one, *N*-methyl-*N*-phenylmethanesulfonamide (0.89 g., 16%) was obtained; m.p. 76° from diethyl ether [lit. (11), m.p. 76.5°]; ir (chloroform): ν max 1347, 1148 $cm^{-1}$; nmr (deuteriochloroform): δ 2.84 (s, $NCH_3$), 3.33 (s, $SCH_3$), 7.40 (m, $NC_6H_5$).

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## REFERENCES AND NOTES

(1) Part V. L. Mosti, P. Schenone and G. Menozzi, *J. Heterocyclic Chem.*, in press.

(2) E. Benary, *Ber.*, **63**, 1573 (1930).

(3) P. Schenone, G. Bignardi and S. Morasso, *J. Heterocyclic Chem.*, **9**, 1341 (1972).

(4) A. Bargagna, F. Evangelisti and P. Schenone, *ibid.*, in print.

(5) J. Dabrowski and K. Kamieńska-Trela, *Spectrochim. Acta*, **22**, 211 (1966); see also *J. Am. Chem. Soc.*, **98**, 2826 (1976).

(6) C. Kashima, H. Aoyama, Y. Yamamoto, T. Nishio and K. Yamada, *J. Chem. Soc., Perkin Trans. II*, 665 (1975).

(7) G. Minardi, P. Schenone and G. Bignardi, *Ann. Chim. (Rome)*, **58**, 1320 (1968).

(8) G. Bignardi, P. Schenone and F. Evangelisti, *ibid.*, **61**, 326 (1971).

(9) G. Bignardi, F. Evangelisti, P. Schenone and A. Bargagna, *J. Heterocyclic Chem.*, **9**, 1071 (1972).

(10) L. Mosti, G. Bignardi, F. Evangelisti and P. Schenone, *ibid.*, **13**, 1201 (1976).

(11) C. S. Marvel, M. D. Helfrick and J. P. Belsley, *J. Am. Chem. Soc.*, **51**, 1272 (1929).