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# A Novel Ring Closure of 1-Acyl-2,2-dialkylhydrazines

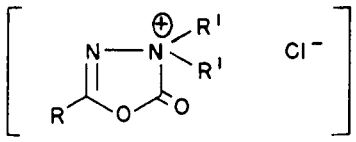
Robert F. Meyer and Betty L. Cummings

A series of 14 new 2,4-substituted-$\Delta^2$-1,3,4-oxadiazolin-5-ones was prepared by a novel ring closure of the corresponding 1-acyl-2,2-dialkylhydrazines with phosgene, whereby one alkyl group is lost as alkyl chloride. This new cyclization was carried out too with thiophosgene and with *p*-chlorothiobenzoic acid, 2,2-dimethylhydrazide to give the corresponding 2,4-disubstituted-$\Delta^2$-1,3,4-oxadiazoline-5-thione, -thiadiazolin-5-one and -thiadiazoline-5-thione, respectively.

The treatment of 1-acylhydrazines with phosgene or thiophosgene is known to give $\Delta^2$-1,3,4-oxadiazolin-5-ones (1) or $\Delta^2$-1,3,4-ozadiazolin-5-thiones (2) respectively. The phosgene ring closure was applied successfully on 2-monosubstituted 1-acylhydrazines to give 2,4-substituted $\Delta^2$-1,3,4-oxadiazolin-5-ones (3).

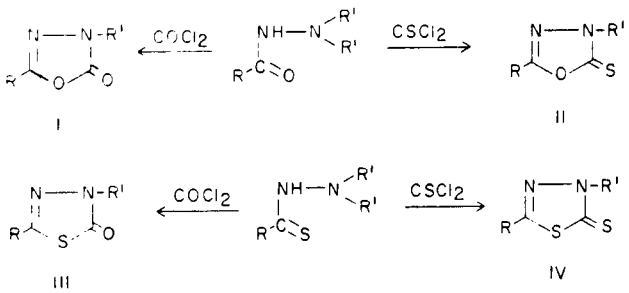
Application of the above to 1-acyl-2,2-disubstituted hydrazines is not reported in the literature although the action of phosgene on a cold solution of 2,2-dialkylformylhydrazine in the presence of trimethylamine is reported (4) briefly to lead to the formation of dialkylisocyanides. When a solution of the proper concentration of 1-acyl-2,2-dialkylhydrazine in dioxane was treated at room temperature with an excess of phosgene, a precipitate of the hydrochloride of the 1-acyl-2,2-dialkylhydrazine was obtained in about 50% yield. The filtrate quenched in ice water gave about a 40% yield of 4-alkyl-$\Delta^2$-1,3,4-oxadiazolin-5-one. When this reaction was carried out at gentle reflux, the initial precipitate of the above hydrochloride dissolved and a good yield of the $\Delta^2$-1,3,4-oxadiazolin-5-one (I) was obtained. Its structure was established by methylation of 2-phenyl-$\Delta^2$-1,3,4-oxadiazolin-5-one using the known procedure of N-alkylation of oxadiazolones (5).

The mechanism of this novel phosgene ring closure may be explained by postulating as key intermediate the transitory quaternary ammonium ion:



which then decomposes with the elimination of a molecular equivalent of alkyl chloride. A somewhat similar intermediate was postulated in the formation of 2-pyrrolidones from $\gamma$-dialkylaminobutyryl chlorides (6). By analogy, *p*-chlorothiobenzoic acid, 2,2-dimethylhydrazide was converted in high yield to 2-(*p*-chlorophenyl)-4-methyl-$\Delta^2$-1,3,4-thiadiazolin-5-one (III).

Substitution of thiophosgene for phosgene gave the corresponding thiones II and IV in good yield:



Compounds of the type I were characterized by the strong carbonyl absorption in the infrared at 5.6 $\mu$. The carbonyl peak in III was shifted to 5.95 $\mu$, whereas the infrared spectra of II and IV lacked the absorption in the carbonyl region.

The acyl derivatives of N-aminopyrrolidine and N-aminohomopiperidine, the two cases of cyclic hydrazides investigated, behaved as expected on phosgene treatment. The 5- and 7-membered ring was cleaved giving the corresponding $\omega$-chloroalkyl $\Delta^2$-1,3,4-oxadiazolin-5-one:

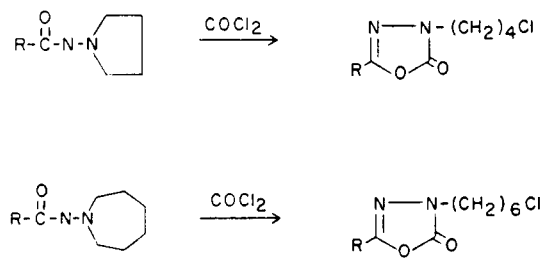


TABLE I

R-C(=O)-NH-Subst.

| R | Subst. | M.p. | Empirical formula | Calcd. % C | Calcd. % H | Found % C | Found % H | Yield (9) % |
|---|---|---|---|---|---|---|---|---|
| $C_6H_5$- | $N(CH_3)_2$ | 105-106 | $C_9H_{12}N_2O$ (8) | | | | | 55 |
| $C_6H_5$- |  | 164-165 | $C_{11}H_{14}N_2O$ | 69.45 | 7.42 | 69.47 | 7.53 | 62 |
| $o$-$CH_3$-$C_6H_4$- | $N(CH_3)_2$ | 103-104 | $C_{11}H_{14}N_2O$ | 67.39 | 7.92 | 67.53 | 8.00 | 87 |
| $p$-Cl-$C_6H_4$- | $N(CH_3)_2$ | 136-137 | $C_9H_{11}ClN_2O$ | 54.40 | 5.59 | 54.55 | 5.68 | 68 |
| $p$-Cl-$C_6H_4$- |  | 178-179 | $C_{12}H_{13}ClN_2O$ | 61.78 | 6.78 | 61.88 | 6.73 | 70 |
| $o$-$NO_2$-$C_6H_4$- | $N(CH_3)_2$ | 140-141 | $C_9H_{11}N_3O_3$ | 51.67 | 5.30 | 51.74 | 5.33 | 76 |
| 3,5-$OCH_3$-$C_6H_3$- | $N(CH_3)_2$ | 143-144 | $C_{11}H_{16}N_2O_3$ | 58.91 | 7.19 | 59.17 | 7.31 | 80 |
| $p$-$NO_2$-$C_6H_4$-$CH_2$- | $N(CH_3)_2$ | 165-166 | $C_{10}H_{13}N_3O_3$ | 53.81 | 5.87 | 53.78 | 5.90 | 66 |
| $p$-Cl-$C_6H_4$-O-$CH_2$- | $N(CH_3)_2$ | 116-118 | $C_{10}H_{13}ClN_2O_2$ | 52.51 | 5.73 | 52.69 | 5.51 | 68 |
| 5-$NO_2$-2-furyl- | $N(CH_3)_2$ | 158-159 | $C_7H_9N_3O_4$ | 42.21 | 4.56 | 42.47 | 4.35 | 67 |
| $C_6H_5$-CH=CH- | $N(CH_3)_2$ | 111-112 | $C_{11}H_{14}N_2O$ | 69.44 | 7.42 | 69.70 | 7.33 | 45 |
| $(C_6H_5)_2CH$- | $N(CH_3)_2$ | 172-173 | $C_{16}H_{18}N_2O$ | 75.56 | 7.13 | 75.51 | 7.25 | 61 |
| $(C_6H_5)_2C(OH)$- | $N(CH_3)_2$ | 192-193 | $C_{16}H_{18}N_2O_2$ | 71.09 | 6.71 | 71.19 | 6.83 | 52 |
| $C_6H_5$-CH($OCOCH_3$) | $N(CH_3)_2$ | 91-92 | $C_{12}H_{16}N_2O_3$ | 60.99 | 6.83 | 61.01 | 6.89 | 56 |

(8) R. L. Hinman, *J. Am. Chem. Soc.*, 78, 1645 (1956). (9) The yield is based on recrystallized product.

TABLE II

| R | R' | M.p. | Empirical formula | % Calcd. C | % Calcd. H | % Calcd. N | % Found C | % Found H | % Found N | Yield % |
|---|---|---|---|---|---|---|---|---|---|---|
| $C_6H_5$- | $-CH_3$ | 100-101 | $C_9H_8N_2O_2$ | 61.35 | 4.57 | 15.91 | 61.46 | 4.76 | 16.17 | 73 |
| $C_6H_5$- | $-(CH_2)_6$-Cl | 65-66 | $C_{12}H_{13}ClN_2O_2$ | 57.03 | 5.19 | 11.09 | 57.18 | 5.21 | 10.99 | 53 |
| $o$-$CH_3$-$C_6H_4$- | $-CH_3$ | 84-85 | $C_{10}H_{10}N_2O_2$ | 63.14 | 5.30 | 14.73 | 63.18 | 5.38 | 14.91 | 89 |
| $p$-Cl-$C_6H_4$- | $-CH_3$ | 151-152 | $C_9H_7ClN_2O_2$ | 51.30 | 3.35 | 13.30 | 51.40 | 3.62 | 13.30 | 89 |
| $p$-Cl-$C_6H_4$- | $-(CH_2)_6$-Cl | 44-45 | $C_{14}H_{16}Cl_2N_2O_2$ | 53.34 | 5.12 | 8.89 | 53.30 | 5.20 | 8.64 | 91 |
| $o$-$NO_2$-$C_6H_4$ | $-CH_3$ | 131-132 | $C_9H_7N_3O_4$ | 48.87 | 3.19 | 19.00 | 48.97 | 3.46 | 19.10 | 92 |
| 3,5-$OCH_3$-$C_6H_3$- | $-CH_3$ | 184-185 | $C_{11}H_{12}N_2O_4$ | 55.92 | 5.12 | 11.86 | 56.00 | 5.33 | 11.88 | 87 |
| $p$-$NO_2$-$C_6H_4$-$CH_2$- | $-CH_3$ | 113-114 | $C_{10}H_9N_3O_4$ | 51.07 | 3.86 | 17.87 | 51.15 | 3.90 | 18.04 | 48 |
| $p$-Cl-$C_6H_4$O-$CH_2$- | $-CH_3$ | 91-92 | $C_{10}H_9ClN_2O_3$ | 49.90 | 3.76 | 11.64 | 49.75 | 3.77 | 11.52 | 42 |
| 5-$NO_2$-2-furyl | $CH_3$ | 195-196 | $C_7H_5N_3O_5$ | 39.82 | 2.39 | 19.90 | 39.90 | 2.52 | 20.08 | 61 |
| $C_6H_5$-CH=CH- | $-CH_3$ | 129-130 | $C_{11}H_{10}N_2O_2$ | 65.30 | 4.98 | 13.85 | 65.37 | 5.15 | 13.89 | 55 |
| $(C_6H_5)_2CH$- | $-CH_3$ | 83-84 | $C_{16}H_{14}N_2O_2$ | 72.16 | 5.30 | 10.52 | 72.38 | 5.27 | 10.63 | 79 |
| $(C_6H_5)_2C(OH)$- | $-CH_3$ | 183-184 | $C_{16}H_{14}N_2O_3$ | 68.07 | 5.00 | 9.92 | 68.07 | 4.95 | 10.04 | 82 |
| $C_6H_5$-CH($OCOCH_3$) | $-CH_3$ | 71-72 | $C_{12}H_{12}N_2O_4$ | 58.05 | 4.87 | 11.28 | 57.94 | 4.93 | 11.33 | 84 |

## EXPERIMENTAL (7)

Preparation of 1-Acyl-2,2-dialkylhydrazines.

To a solution of 2.2 equivalents of the appropriate hydrazine in ether or tetrahydrofuran one equivalent of the acid chloride was added dropwise with stirring at room temperature. After standing for 3 hours the precipitate of unsymmetrical hydrazine hydrochloride was removed by filtration and the product isolated from the filtrate. The hydrazides are tabulated in Table I.

2-($p$-Chlorophenyl-4-methyl-$\Delta^2$-1,3,4-oxadiazolin-5-one.

Into a solution of 356 g. of 1-($p$-chlorobenzoyl)-2,2-dimethylhydrazine in 2500 ml. of dioxane was passed an excess of phosgene at gentle reflux. A white solid, which had precipitated initially, dissolved within about 2-3 hours. The resulting solution was evaporated to dryness under reduced pressure. The residue was recrystallized from 2-propanol, (see Table I) and was identical in every respect with a sample prepared by methylation (5).

2-($p$-Chlorophenyl)-4-methyl-$\Delta^2$-1,3,4-oxadiazoline-5-thione.

To a solution of 39.6 g. (0.2 mole) of 1-($p$-chlorobenzoyl)-2,2-dimethylhydrazine in 250 ml. of chloroform was added 25.3 g. (0.22 mole) of thiophosgene. The suspension was refluxed for 4 hours under nitrogen. The 1-($p$-chlorobenzoyl)-2,2-dimethylhydrazine hydrochloride was removed by filtration, the filtrate was evaporated, the residue triturated with water and recrystallized from 2-propanol. The product was obtained as a white crystalline solid, m.p. 147-148°; yield 26 g. (51%).

*Anal.* Calcd. for $C_9H_7N_2ClOS$: C, 47.68; H, 3.11; N, 12.35. Found: C, 47.85; H, 3.23; N, 12.29.

2-($p$-Chlorophenyl)-4-methyl-$\Delta^2$-1,3,4-thiadiazolin-5-one.

Into a solution of 200 g. of $p$-chlorothiobenzoic acid 2,2-dimethylhydrazide (10), m.p. 154-155°, in 1000 ml. of dioxane was passed an excess of phosgene. The white precipitate dissolved readily on short heating to reflux temperature. Evaporation of solvent gave a crude product, m.p. 97-100°. Recrystallization from 2-propanol gave a white, crystalline product, m.p. 103-104°, yield 195.5 g. (93%).

*Anal.* Calcd. for $C_9H_7ClN_2OS$: C, 47.68; H, 3.11; N, 12.36. Found: C, 47.98; H, 3.41; N, 12.23.

2-($p$-Chlorophenyl)-4-methyl-$\Delta^2$-1,3,4-thiadiazoline-5-thione.

To a solution of 25 g. (0.22 mole) of thiophosgene in 250 ml. of chloroform was added 43 g. (0.2 mole) of $p$-chlorothiobenzoic acid, 2,2-dimethylhydrazide. The initial precipitate dissolved on heating to reflux. After 2 hours at this temperature the solvent was evaporated leaving a pale yellow solid, m.p. 142-145°. One recrystallization raised the m.p. to 146-147°, yield, 34.5 g. (71%).

*Anal.* Calcd. for $C_9H_7ClN_2S_2$: C, 44.52; H, 2.90; N, 11.54. Found: C, 44.63; H, 2.89; N, 11.38.

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