I wish to thank Dr. I. Lindqvist for suggesting the problem and for his stimulating interest during the work and also Prof. G. Hägg for all the facilities placed at my disposal.

1. Lindqvist, O. and Fjellström, B. *Acta Chem. Scand.* **14** (1960) 2055.
2. Lindqvist, I. and Zackrisson, M. *Acta Chem. Scand.* **14** (1960) 453.
3. Zackrisson, M. and Lindqvist, I. *J. Inorg. Nuclear Chem.* **17** (1961) 69.
4. Gerrard, W., Lappert, M. F., Pyszora, H. and Wallis, J. W. *J. Chem.* Soc. **1960** 2144.
5. Archambault, J. and Rivest, R. *Can. J. Chem.* **36** (1958) 1461.

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A Comparison between Oxygen and Sulphur as Donor Atoms

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In an earlier paper [1] it was reported that ethyl sulphide has better donor properties than ethyl ether in reactions with $SbCl_5$ and $SnCl_4$. It is of interest, therefore, to know whether, in comparable compounds, sulphur is always a better donor atom than oxygen in reactions with these acceptor molecules. To obtain the relevant information a few acceptor-donor reactions have been studied by qualitative thermochemical measurements. In these reactions, $SbCl_5$ and $SnCl_4$ were used as acceptor molecules, while comparable compounds of sulphur and oxygen comprised the donor molecules. The various donor molecules studied include different ways of bonding the donor atoms.

Experimental. NN-dimethyl-thioacetamide was prepared according to Kindler [2]. M.p. 73–74°. Other chemicals used were commercial products which were further purified by distillation.

Table 1.

Acceptor: $SbCl_5$
$C_4H_8S > C_4H_8O$
$POCl_3 >> PSCl_3$

Acceptor: $SnCl_4$
$C_4H_8S > C_4H_8O$
$CH_3CON(CH_3)_2 = CH_3CSN(CH_3)_2$
$POCl_3 > PSCl_3$

The thermochemical experiments were made in ethylene chloride solutions as described earlier [1], but with different concentrations.

Results and discussion. The relative donor strengths are given in Table 1. As might be expected, tetrahydrothiophene and tetrahydrofuran show the same relative donor strengths as the ether and sulphide investigated earlier [1].

In both the amide and the thioamide studied here, the molecules contain two possible donor atoms since the nitrogen atom may also have donor properties. The infrared spectra of the addition compounds show, however, that the C=O bond frequency of the amide (1660 cm^{-1}) decreases upon adduct formation, as does the C=S bond frequency of the thioamide (1280 cm^{-1}) (unpublished results). Negative shifts in the carbonyl bond frequency were earlier assumed to indicate that the carbonyl oxygen functioned as the donor [3]. Accordingly it appears that the oxygen atom of the amide and the sulphur atom of the thioamide are the donor atoms. The addition compound formed between NN-dimethyl-thioacetamide and $SbCl_5$ is so slightly soluble in ethylene chloride that no measurements could be made. The adduct formed with $SnCl_4$ also precipitates when the molar ratio, acceptor:donor, is 1:2. However, at the molar ratio 1:1, measurements could be made. The table shows that no difference in the donor strengths could be detected.

$POCl_3$ is a better donor molecule than $PSCl_3$ and the difference is most marked when $SbCl_5$ is used as acceptor.

From the above considerations it is impossible to state that one type of atom, oxygen or sulphur, is a better donor than the other in reactions with the acceptor molecules studied. As far as these few experiments can show, the type of bonding to the donor atom is of importance to the relative donor strengths of sulphur and oxygen. At present, however, it is not possible to explain why in molecules of the ether type sulphur is a better donor atom than oxygen, why in molecules where the donor atoms are of the carbonyl type the donor strengths of oxygen and sulphur are approximately equal, and why in phosphoryl type molecules the phosphoryl oxygen is a better donor atom than sulphur in the same position.

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1. Lindqvist, I. and Zackrisson, M. *Acta Chem. Scand.* **14** (1960) 453.
2. Kindler, K. *Ann.* **431** (1923) 209.
3. Zackrisson, M. and Lindqvist, I. *J. Inorg. Nuclear Chem.* **17** (1961) 69.

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6α-Trifluoromethyl-17α-acetoxyprogesterone and some Unsaturated Analogs

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It has recently been shown [1,2], that introduction of an α-orientated fluorine, chlorine or bromine atom in the 6-position of 17α-acetoxyprogesterone causes a remarkable increase of its oral progestational activity, and that this activity is further increased by Δ^1, Δ^6 or $\Delta^{1,6}$ unsaturation of these compounds. It seemed therefore of interest to synthesize 6α-trifluoromethyl-17α-acetoxyprogesterone and some of its corresponding unsaturated analogs.

When a solution of 17α-acetoxyprogesterone-3-ethyl enol ether (I)[1] in trifluoroiodomethane [3] containing pyridine was irradiated in a quartz vessel at room temperature with ultraviolet light from a high pressure mercury lamp, 6-trifluoromethyl-17α-acetoxyprogesterone-3-ethyl enol ether (II)[m.p. 184–186°C, $[\alpha]_D^{20}$ −181° (all rot. in $CHCl_3$), λ_{max}^{EtOH} 256 mμ, ε 21 400. Found: C 66.53; H 7.66. Calc. for $C_{26}H_{35}F_3O_4$: C 66.65; H 7.53] was obtained in 60 % yield. Acid catalyzed hydrolysis of II afforded smoothly 6α-trifluoromethyl-17α-acetoxyprogesterone (III) (m.p. 206–207°C, $[\alpha]_D^{20}$ +30°, λ_{max}^{EtOH} 234 mμ, ε 15 600. Found: C 65.37; H 6.98. Calc. for $C_{24}H_{31}F_3O_4$: C 65.45; H 7.10).

The α-configuration of the trifluoromethyl group in III followed from stability toward treatment with hydrogen chloride in acetic acid [4], and from the fact, that the rotatory dispersion curve was very similar to that of 17α-acetoxyprogesterone [5].

Selenium dioxide dehydrogenation of III yielded 6α-trifluoromethyl-$\Delta^{1,4}$-pregnadiene-17α-ol-3,20-dione acetate (IV) (m.p. 213–215°C, $[\alpha]_D^{20}$ −29°, λ_{max}^{EtOH} 242 mμ, ε 17 350. Found: C 65.40; H 6.80. Calc. for $C_{24}H_{29}F_3O_4$: C 65.73; H 6.67).

6-Trifluoromethyl-$\Delta^{4,6}$-pregnadiene-17α-ol-3,20-dione acetate (V) (m.p. 233–234°C, $[\alpha]_D^{20}$ 0°, λ_{max}^{EtOH} 270 mμ, ε 20 300. Found: C 65.44; H 6.89. Calc. for $C_{24}H_{29}F_3O_4$: C 65.73; H 6.67) was synthesized from the 3-cycloethylene ketal of III [6] (m.p. 178–182°C, $[\alpha]_D^{20}$ +66°. Found: C 64.28; H 7.29. Calc. for $C_{26}H_{35}F_3O_5$: C 64.45; H 7.28) by bromination at C-7 with NBS followed by dehydrobromination in boiling collidine and hydrolysis of the ketal with methanol-sulfuric acid.

The oral progestational activities of II, III, IV, and V, determined by the Mc Phail modification of the Clauberg assay are given in Table 1.

Table 1. Oral progestational activity — Clauberg assay.

Compound	Relative activity
6α-Methyl-17α-acetoxyprogesterone	1
6α-Trifluoromethyl-17α-acetoxyprogesterone	1–2
6α-Trifluoromethyl-17α-acetoxyprogesterone-3-ethyl enol ether	0.5–1
6-Trifluoromethyl-$\Delta^{4,6}$-pregnadiene-17α-ol-3,20-dione acetate	0.5–1
6α-Trifluoromethyl-$\Delta^{1,4}$-pregnadiene-17α-ol-3,20-dione acetate	0.5–1

1. Ringold, H. J., Batres, E., Bowers, A., Edwards, J. and Zderic, J. *J. Am. Chem. Soc.* **81** (1959) 3485.
2. Bowers, A., Ibàñez, L. C. and Ringold, H. J. *J. Am. Chem. Soc.* **81** (1959) 5991.
3. The addition of trifluoroiodomethane to unsaturated systems has been extensively investigated by Haszeldine. See, *e.g.*, Walling, C. *Free Radicals in Solution*, John Wiley & Sons, New York 1957, pp. 247–272.
4. Bowers, A., Ibàñez, L. C. and Ringold, H. J. *Tetrahedron* **7** (1959) 138.
5. Djerassi, C., Osiecki, J., Riniker, R. and Rinker, B. *J. Am. Chem. Soc.* **80** (1958) 1216.
6. Prepared from III by the dioxolane method: Dauben, H. J., Löken, B. and Ringold, H. J. *J. Am. Chem. Soc.* **76** (1954) 1359.

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