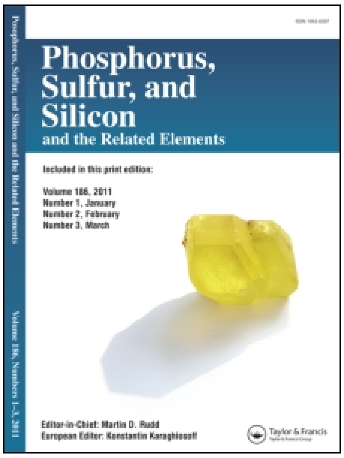

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ATTACK BY SULFUR NUCLEOPHILES ON CERTAIN 3-SUBSTITUTED OXINDOLE DERIVATIVES

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ATTACK BY SULFUR NUCLEOPHILES ON CERTAIN 3-SUBSTITUTED OXINDOLE DERIVATIVES

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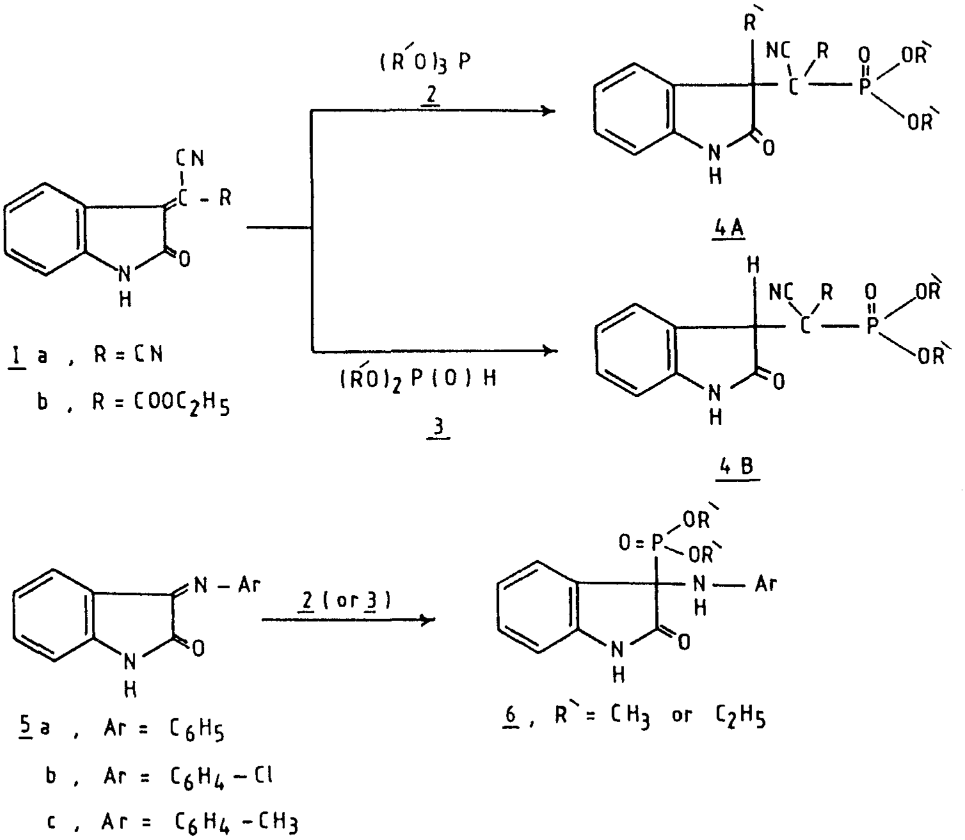
The behavior of 3-methylene oxindoles (1a,b), 3-arylimin-oxindoles (5a–c) and 2-methoxy-1-methyl-4-dicyanomethylene-1,4-dihydroquinoline (8) toward thiols (7a,b) has been studied. Structures of the new adducts were inferred from compatible elemental and spectroscopic measurements.

Key words: 3-Substituted oxindoles; sulfur nucleophiles; addition; demethylation.

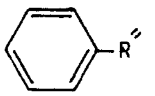
INTRODUCTION

Recently[1,2] we have shown that phosphorus nucleophiles, namely, trialkyl phosphites (2) and dialkyl phosphites (3) attack the exocyclic ethylenic carbon atom in



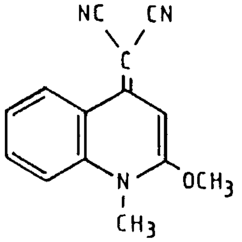
SCHEME I

3-cyanomethylene oxindoles (1a,b) to give phosphonate structures of type 4. On the other hand, ring attack by the same phosphorus reagents has been recorded[2] in their reactions with 3-aryliminoxindoles (5a–c) which produced phosphonate adducts of type (6) (Scheme I). This disparity in behavior toward phosphorus nucleophiles has prompted us now to study the mode of attack by sulfur nucleophiles (7) on the α,β-unsaturated carbonyl systems in 1a,b and 5a–c. A comparative study on the reaction of 7 with 2-methoxy-1-methyl-4-dicyanomethylene-1,4-dihydroquinoline (8) is also undertaken. Compound 8 is the ring-enlargement reaction product of 1a with diazomethane.[3]



7 a , $R'' = SH$

b , $R'' = CH_2SH$



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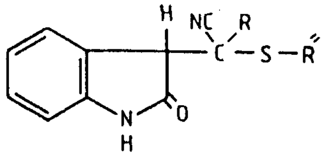
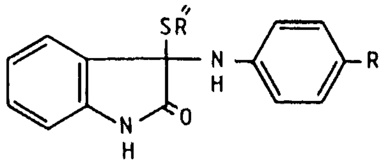
RESULTS AND DISCUSSION

It has been now found that compounds 1a,b react with thiols 7a,b in absence of solvent at ambient temperature to give 1:1 adducts for which structure 9 was assigned for the following reasons: (a) Adducts 9a–d regenerated the starting materials (1 + 7) upon heating above their mps., under reduced pressure. (b) Correct elemental analyses and molecular weight determination (MS) were obtained for all adducts. (c) The strong amidic carbonyl band present in the IR-spectra of 1a,b at *ca.* 1720 cm^{-1} was also recorded in the IR-spectra of 9a–c. The IR-spectrum of 9a, for example, showed this band at 1695 cm^{-1}. The carbonyl-carbon atom of the same group appeared at δ 175.6 ppm in its ^{13}C NMR spectrum. This spectrum also showed a signal at δ 35.2 ppm which coincides with a chemical shift expected for a ring sp^3-carbon atom bearing a methine proton.[4] Moreover, the PMR spectrum of 9a showed such ring methine proton as a singlet at δ 4.76 ppm. Based upon these arguments, alternative structures like 13 and 14 for the reaction products of 1a with 7a,b, can be excluded. (Scheme III)

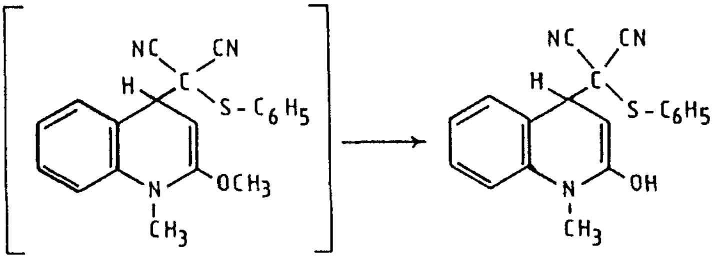
Compounds 5a–c also reacted with thiols 7a,b in absence of solvent at ambient temperature to give crystalline 1:1 adducts for which structure 10 was assigned. Compounds 10a–f regenerated the appropriate starting materials (5 + 7) upon thermolysis under reduced pressure. Structural reasonings for 10 are: (a) Elemental analyses and molecular weight determination (MS) for 10a, taken as an example, corresponded to $C_{20}H_{16}N_2OS$. (b) Its IR-spectrum (in KBr) showed strong absorption bands at 3230 cm^{-1} (NH), 1710 cm^{-1} (CO, amidic), 1620–1500 cm^{-1} (C=C, aromatic). The strong $>$C=N band present in the spectrum of 5a at 1650 cm^{-1} was absent in the spectrum of 10a. (c) The PMR spectrum of 10a was devoid



9 a , R = CN , $R'' = C_6H_5$
b , R = CN $R'' = CH_2C_6H_5$
c , R = $COOC_2H_5$, $R'' = C_6H_5$
d , R = $COOC_2H_5$, $R'' = CH_2C_6H_5$



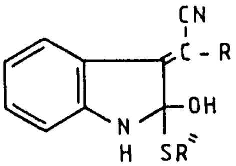
10 a , R = H ; $R'' = C_6H_5$
b , R = H ; $R'' = CH_2C_6H_5$
c , R = Cl ; $R'' = C_6H_5$
d , R = Cl ; $R'' = CH_2C_6H_5$
e , R = CH_3 ; $R'' = C_6H_5$
f , R = CH_3 ; $R'' = CH_2C_6H_5$



11 12

SCHEME II

of the signals due a ring-methine proton in the δ 4–5 ppm region. On these grounds, alternative structures like 15 and 16 for the reaction products of 5a–c with 7a,b, can be ruled out. When compound 8 was allowed to react with thiophenol (7a), in absence of solvent at 90°C, a pale yellow crystalline 1:1 adduct was produced and assigned structure 12, (Scheme II), for the following evidences: (a) Its elemental



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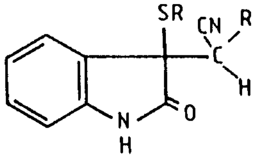

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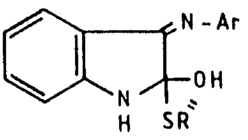

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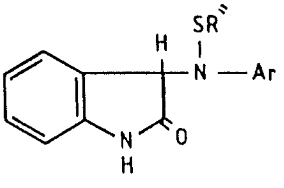

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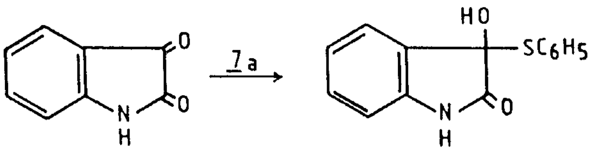
13-16, R as in 1a, b

Ar as in 5a-c

R* as in 7



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18

SCHEME III

analysis and molecular weight determination (MS) corresponded to $C_{19}H_{15}N_3OS$. (b) The IR spectrum of 12 (in KBr) showed a strong OH band at 3420 cm^{-1}. In the PMR spectrum of 12 (In DMSO), the same group gave rise to a broad singlet (exchangeable with D_2O) at 6.83 ppm. Moreover, the PMR spectrum showed a multiplet due to the aromatics (9H) in the δ 7.23–7.70 ppm region and a singlet (3H) at δ 3.60 ppm due to the N—CH_3 protons. The spectrum also showed two singlets at δ 4.82 and δ 6.56 ppm which are respectively assigned to the methine and vinyl protons of the heterocyclic ring.

CONCLUSION

Apparently, compounds 1a,b behave toward thiols 7a,b in a manner different from the behavior of 5a–c toward the same reagents. Thus, thiols 7a,b attack 1a,b preferentially at the exocyclic ethylenic part of the α,β-unsaturated carbonyl system in 1a,b to yield 9a–d. On the other hand, nucleophilic attack by thiols 7 on 5a–c occurs on the imine-carbon to afford 10a–f. In this sense, the effect of the sulfur nucleophiles 7 simulates phosphorus nucleophiles which attack 1a,b and 5a–c at similar centres.

TABLE I

Physical and analytical data for compounds 9 and 10

		mp.	Mol. Form.	Anal.		(Calcd./Found)			M⁺	IR (cm⁻¹)			
Cpd.	%[a]	°C	(M. Wt.)	C	H	Cl	N	S	(m/z)	OH	NH	CN	C=O
9a	90	173[b]	$C_{17}H_{11}N_3OS$ 305.362	66.86 66.83	3.63 3.59		13.76 13.71	10.50 10.10	305		3310	2180	1695
b	85	180[c]	$C_{18}H_{13}N_3OS$ 319.392	67.69 67.53	4.10 3.97		13.15 13.07	10.04 10.02	319		3420	2190	1690
c	88	105[d]	$C_{19}H_{16}N_2O_3S$ 352.417	64.76 64.23	4.58 4.52		7.95 7.79	9.10 9.08	352		3180	2250	1740 & 1705
d	80	128[d]	$C_{20}H_{18}N_2O_3S$ 366.444	65.55 65.34	4.95 4.92		7.65 7.63	8.75 8.72	366		3280	2250	1740 & 1720
10a	80	205[c]	$C_{20}H_{16}N_2OS$ 332.428	72.26 72.24	4.85 4.82		8.43 8.29	9.65 9.62	332		3230 & 3140		1710
b	75	86[e]	$C_{21}H_{18}N_2OS$ 346.455	72.80 72.76	5.24 5.21		8.09 7.97	9.26 9.23	346		3410 & 3170		1720
c	82	80[e]	$C_{20}H_{15}ClN_2OS$ 366.920	65.47 65.43	4.12 4.09	9.68 9.30	7.63 7.59	8.74 8.71	366		3280 & 3150		1710
d	78	86[e]	$C_{21}H_{17}ClN_2OS$ 380.747	66.25 66.21	4.47 4.44	9.32 9.30	7.36 7.33	8.42 8.39	380		3400 & 3180		1710
e	78	195[c]	$C_{21}H_{18}N_2OS$ 346.455	72.80 72.76	5.24 5.19		8.09 8.07	9.26 9.23	346		3240 & 3140		1710
f	72	142[b]	$C_{22}H_{20}N_2OS$ 360.482	73.30 73.29	5.59 5.56		7.77 7.75	8.90 8.87	360		3340 & 3140		1715
12	65	252[b]	$C_{19}H_{15}N_3OS$ 333.413	68.45 68.42	4.53 4.49		12.60 12.58	9.62 9.59	333	3420		2195	

[a] Yields are approximated; [b] solvent of crystallization is ethyl-acetate; [c] solvent of crystallization is alcohol; [d] solvent of crystallization is benzene; [e] solvent of crystallization is $CHCl_3$/n-pentane.

Like the case with 1a,b, thiophenol (7a) attacks 8 at the exocyclic ethylenic linkage of the molecule to give 11 which yields then 12 under the influence of the dealkylation properties of thiophenol.[5]

The non-formation of structures like 13–16 may be attributed to a reduced electron attracting capacity of the corresponding centers e.g. in 13, 15 and 16, or to thermodynamically reasons as for 14, which in a reversible reaction is completely suppressed in favour of its regioisomer 9.[1,6] Such state of affairs is also recorded in the reaction of isatin (17) with 7a which produces adduct 18 without affecting the amidic carbonyl group.[7] (Scheme III).

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded, in KBr, with Perkin-Elmer Infracord, 157 G. The PMR spectra were run on Varian Spectrometer at 60 MHz and/or 90 MHz, using TMS as

TABLE II

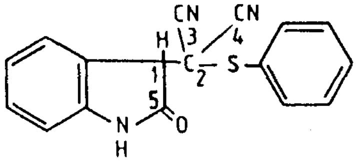
^{1}H NMR spectral data (δ scale ppm)

Cpd.*				^{1}H NMR			
9a				4.76(s) 1H CH	7.28(m) 9H Aryl-H		10.36(s) 1H NH
b			4.26(s) 2H S-CH$_2$	4.46(s) 1H CH	7.28(m) 9H Aryl-H		10.36(s) 1H NH
c	0.94(t) J_{HH} = 4.5 3H OOCH$_2$CH$_3$	3.77(q) J_{HH} = 4.5 2H OOCH$_2$		5.08(s) — 1H CH	7.35(m) — 9H Aryl-H		10.74(s) — 1H NH
d	0.96(t) J_{HH} = 4.5 3H OOCH$_2$CH$_3$	3.96(q) J_{HH} = 6 2H OOCH$_2$	4.05(s) — 2H S-CH$_2$	5.16(s) — 1H CH	7.16(m) — 9H Aryl-H		10.70(s) — 1H NH
10b		4.09 & 4.20 (d.d) J_{HH} = 2.5 2H S-CH$_2$			6.85(m) — 14H Aryl-H	9.10(s) — 1H NH	9.72 — 1H NH
d		3.85 & 3.96 (d.d) J_{HH} = 2.5 2H S-CH$_2$			6.74(m) — 13H Aryl-H	9.03(s) — 1H NH	9.66(s) — 1H NH
e	2.19(s) 3H Ar-CH$_3$				7.05(m) 13H Aryl-H	8.90(s) 1H NH	9.73(s) 1H NH
12	3.56(s) 1H N-CH$_3$	4.82(s) 1H methine-H	6.56 1H vinyl-H	6.83(s) 1H OH	7.46(m) 9H Aryl-H		

* The ^{1}H NMR spectra of cpds. 9c, d & 10b–d were run in CDCl$_3$ and those of cpds. 9a, b & 10a, e, f were run in DMSO.

an internal reference. ^{13}C NMR spectrum was recorded with a Varian FT-80 Spectrometer using TMS as an internal reference. The MS spectra were run at 70 eV on Kratos MS-50 equipment provided with data system. Solvents were dried by standard techniques.

Action of thiols on 3-substituted oxindoles. General Procedure. A mixture of the 3-substituted oxindol (1a,b)^{8,9} or (5a–c)$^{10-12}$ (0.01 mol) and thiols (7a,b) (2 ml) was left at ambient temperature for 6 hr. After the reaction was completed (TLC), excess thiol was evaporated *in vacuo*. The residue was washed several times with light petroleum ether. The residual substance was recrystallized from the appropriate solvent to give adducts (9a–d) or (10a–f), respectively. Percentage yields, physical and analytical data for compounds 9 and 10 are given in Tables I and II. ^{13}C-NMR spectrum of 9a (δ ppm in DMSO-d$_6$): 35.2 (C$_1$), 39.4 (C$_2$), 109.2 (C$_{3,4}$), 120.4–130.0 (C aromatic), 175.6 (C$_5$).



9a

Thermal decomposition of the adducts 9 and 10. Adduct 9a (or 10a) (1 g) was heated above its mp. (*cf.* Table I) for 1 hr under reduced pressure (5 mm/Hg) in a cold finger sublimator. The reaction vessel was left to cool and ethyl alcohol (5 ml) was added. The crystals which separated were recrystallized from ethanol to give 1 (or 5) and identified by mp., mixed mps., and comparative IR spectra with those of the corresponding reference samples.^{8,10} Thiophenol was detected in the receiver by the conventional procedure as the corresponding benzoate.^{5}

Action of thiophenol on 8. A mixture of 8 (0.01 mol) and 7a (2 ml) was allowed to react at 90°C for 10 hr. After the reaction was completed (TLC), the excess of thiol was evaporated *in vacuo*. The residue was washed several times with light petroleum ether. The residual material was recrystallized from ethyl-acetate to give adduct 12 as pale yellow crystals, mp. 252°C (dec.) (for percentage yields, physical and analytical data *cf.* Tables I and II).

REFERENCES

1. M. R. Mahran, W. M. Abdou, N. M. Abd El-Rahman and M. M. Sidky, *Phosphorus and Sulfur*, **45**, 47 (1989).
2. W. M. Abdou, N. M. Abd El-Rahman and M. R. Mahran, *J. fur Prakt. Chem.*, **331**, 906 (1989).
3. L. Capuano, V. Diehl and W. Ebner, *Chem. Ber.*, **105**, 3407 (1972).
4. M. Hesse, H. Meier and B. Zeeh, "Spektroskopische Methoden in der Organishen Chemie," G. Thieme-Verlag (Stuttgart), 1979.
5. W. Asker, A. F. A. M. Shalaby and S. M. A. D. Zayed, *J. Org. Chem.*, **23**, 1781 (1958); A. Mustafa, M. M. Sidky, S. M. A. D. Zayed and W. M. Abdou, *Monatsh. Chem.*, **98**, 310 (1967).
6. A. Mustafa, M. M. Sidky and F. M. Soliman, *Tetrahedron*, **22**, 393 (1966).
7. E. Baumann, *Chem. Ber.*, **18**, 890 (1885); A. Schönberg and O. Schutz, *Chem. Ber.*, **60**, 2344 (1927).
8. W. Walter, *Chem. Ber.*, **28**, 2251 (1951).
9. F. J. Ingleby, *J. Chem. Soc.*, 3639 (1958).
10. H. Schiff, *Justus Liebigs Ann. Chem.*, **144**, 51 (1867).
11. E. Hardt, *J. Prakt. Chem.*, **65**, 267 (1881).
12. R. Pummerer and N. Goettler, *Chem. Ber.*, **43**, 1381 (1910).
13. L. Capuano, V. Diehl and W. Ebner, *Chem. Ber.*, **105**, 3411 (1972).