the position of one sulphamate group was located on the mirror plane at $Z = 1/4$ with the reliability factor $R = 21\%$. In the subsequent Fourier synthesis, while all other atoms have the mirror plane symmetry, the sulphur atom alone was found to be away from the mirror plane by 0.4 Å. This automatically excludes the presence of the mirror and indicates the space group to be $Pna2_1$. One of these two positions was chosen as the position of the sulphur atom and further refinement was done in the space group $Pna2_1$.

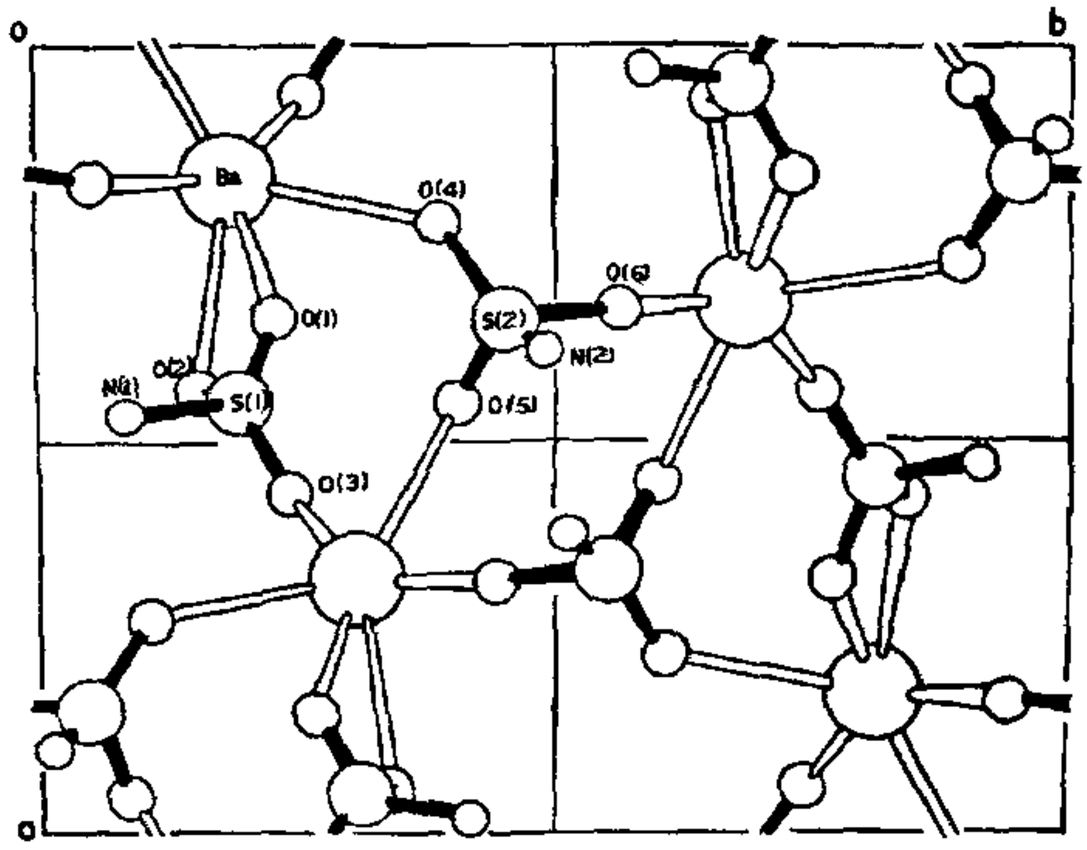

TABLE 2

Fractional Atomic Coordinates

Atom	X	Y	Z
Ba	0.1759	0.1849	0.0
S(1)	−0.0500	0.3172	0.4467
N(1)	−0.0278	0.4187	0.6902
O(1)	−0.1632	0.2720	0.4421
O(2)	−0.0710	0.3427	0.1849
O(3)	0.0641	0.2585	0.5340
S(2)	0.1683	−0.0502	0.5847
N(2)	0.1211	−0.0207	0.9027
O(4)	0.2758	−0.1098	0.5140
O(5)	0.0527	−0.0978	0.4727
O(6)	−0.3269	0.4456	−0.5181

A few cycles of least squares refinement reduced the R factor to 11.3%. The positional parameters are presented in table 2 and a view of the structure down c axis is shown in the figure. The barium atom is coordinated by six oxygen atoms, belonging to five sulphamate groups exhibiting a distorted octahedral coordination. The distortion is mainly due to the fact that two oxygen atoms O(1) and O(2) of one sulphamate group coordinate to the same barium atom. Further refinement is under progress.

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ISOLATION AND REACTIONS OF A NEW STABLE PHOSPHONIUM YLIO: 10-ANTHRONYLIDENETRIPHENYL-PHOSPHORANE

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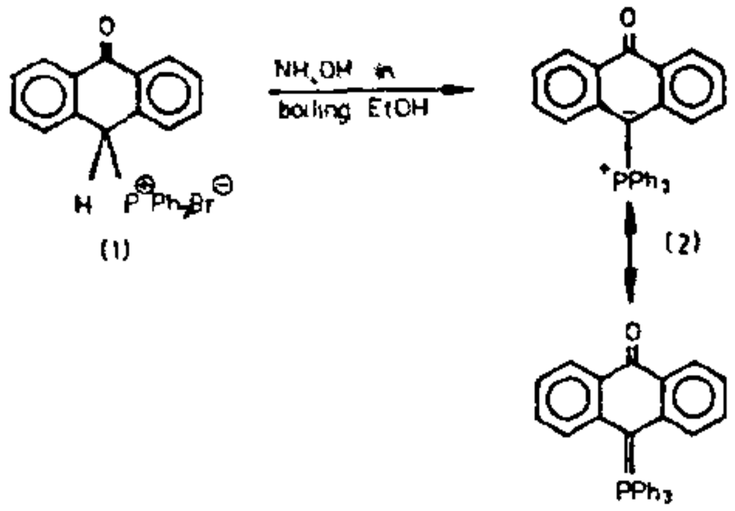
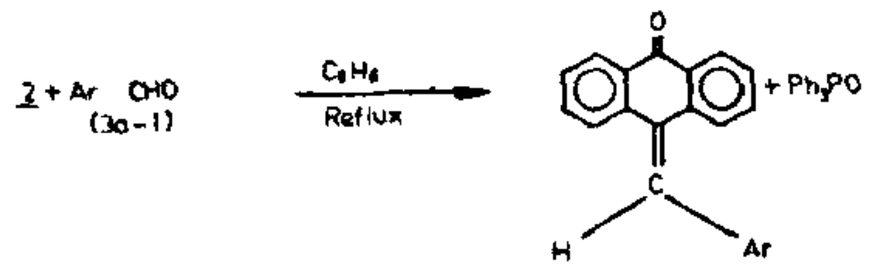
THE reaction of phosphonium ylids with carbonyl compounds has gained wide application in the synthesis of unsaturated compounds because of their specificity and mild reaction conditions[1-4]. Noteworthy in this regard are the reactions of ylids having two reactive centres to afford polymeric products or macrocyclic products via intermolecular or intramolecular condensation[5,6]. Prompted from this, following our previous studies on reactivity of various ylids[7-10], we have now synthesized a new bifunctional phosphonium ylid having ylid and carbonyl functions, 10-anthronylidenetriphenyl-phosphorane with a view to examining its reactivity in the condensation with carbonyl compounds.

Treatment of triphenylphosphine with 10-bromoanthrone at reflux temperature in benzene gave 10-anthronyltriphenylphosphonium bromide (1) in 65% yield. The salt (1) on dehydrohalogenation with iodium ethoxide or 30% ammonium hydroxide, in boiling ethanol gave a yellow precipitate due to the formation of a stable ylid, 10-anthronylidene-triphenylphosphorane (2) which was hygroscopic in nature (Scheme 1). The structures of salt (1) and ylid (2) were confirmed by their IR and NMR spectral data. The IR spectrum of salt (1) showed a strong band at 1658 cm^{-1} of carbonyl group. The NMR spectrum, a proton attached to C_{10} of anthrone ring which is directly linked to P Ph_3 group, was absorbed as a doublet centered at δ 6.37 (J PCH = 12 Cps) and aromatic protons were exhibited in the range δ 7.33-8.53 IR Spectrum of ylid (2) showed a band at 1650 cm^{-1} due to stretching vibration of carbonyl group.

Scheme 1





In order to test the reactivity of ylid(2) towards carbonyl compounds, ylid(2) was allowed to react with mono, di-and trisubstituted benzaldehydes[3a-j] at reflux temperatures for 10–20 hr. to afford substituted 10-benzylideneanthrones (4a-j) in 40–75% yields. Similarly ylid(2) also energetically reacted with furfural (3k) and cinnamaldehyde (3l) to give 10-furfurylideneanthrone (4k) and 10-cinnamylideneanthrone (4l) respectively (Scheme 1).

It was noted that ylid(2) failed to react with ketones such as acetophenone, benzophenone, fluorenone and xanthone, probably due to decreased nucleophilicity of ylid (2) caused by extensive delocalization of electrons of the ylid (2) through anthrone ring and carbonyl group.

Attempts were also made to prepare polymeric ylid by intermolecular carbonyl olefination. But the ylid (2) failed to react intermolecularly with carbonyl group of another molecule of same ylid (2).

All the products (4a-l) synthesized in the present study gave satisfactory elemental analysis and most of the them were new. The melting points for known compounds were in accordance with those reported in literature[11-13]. The IR spectra of these compounds in general showed two characterstic absorption bands at 1610–1595 cm^{-1} (ν)C=C) and 1705–1680 cm^{-1} (γ) C=0). The absorption bands in region 960–937 cm^{-1} were associated with out of plane deformations of hydrogen attached to exocyclic carbon carbon double bond. The NMR spectra exhibited olefinic protons in the range of δ6 60–7.22 and aromatic protons in the region δ6.70–8.45 (Table 1).

Melting points reported were determined on a Gallenkamp apparatus and were uncorrected. A Perkin Elmer infracord spectrophotometer was used to record the IR spectra in KBr phase. The NMR spectra ($CDCl_3$) were run on varian A-60 spectrometer using tetramethylsilane (TMS) as an internal standard. The column chromatography was done over neutral alumina to purify the products. For thin layer chromatography, glass microscope slides coated with silica gel G were used. The spots on these slides were detected by iodine.

Preparation of 10-anthronyltriphenyl phosphonium bromide (1)

A solution of 10.48 g (0.04 mole) of triphenylphosphine and 10.92 g (0.04 mole) of 10-bromoanthrone in 250 ml of anhydrous benzene was refluxed under the atmosphere of nitrogen on a steam bath for 8 hr. The mixture was cooled at room temperature to give yellow crystalline solid which was separated by filtration and recrystallized from chloroform-ehtylacetate (1.2) to give microcrystals of new 10-anthronyltriphenylphosphonium bromide (1) in 65% yield, m.p. 250–52° C, hygroscopic in nature (Anal. data. Found: C, 71.72; H, 4.50% calcd. for $C_{32}H_{24}BrOP$, C, 71.77; H, 4.48%).

IR spectrum (KBr): 1658 cm^{-1} (γC=0)

NMR spectrum ($CDCl_3$): δ6.37 (d, J=12 cps, 1H, C_9—H of anthrone ring); δ7.33–8.53 (m, 23H, aromatic).

Preparation of 10-anthronylidenetriphenylphosphorane (2).

To a stirred solution of 18.16 g (0.04 mole) of salt (1) m 200 ml of boiling ethanol, was added in an atmosphere of nitrogen, 25 ml of 30% ammonia solution and mixture was refluxed for additional 2 hr. On cooling yellow solid was separated which was crystallized from chloroform-benzene to give microcrystals of 10-anthronylidenetriphenylphosphorane (2) in 70% yield, m.p. 230–32° C, hygroscopic in nature.

(Anal. data: c, 84.51; H, 5–10%—calcd for $C_{32}H_{23}OP$; C, 84.58; H, 5.06%.)

Preparation of 10-arylideneanthrones (4a–l). General Procedure:

A mixture of ylid (2) and 0.004 mole of aromatic aldehyde (3a–l) in 100 ml anhydrous benzene was refluxed under nitrogen for 6–12 hr. The precipitate containing triphenylphosphineoxide was removed by filtration and filtrate was concentrated on a water bath under reduced pressure. The resulting oily mass was chromatographed using benzene: pet-ether (4:1) as eluent to afford 10-arylideneanthrones (4a–l) in 40–75% yields. The products were further recrystallized from suitable solvents given in table 1.

TABLE 1

Physical and spectral data of 10-arylideneanthrones (4a–l)

Compound*	Ar	Yield %	m.p. °C	Lit. m.p. °C	Recrystn. Solvent	IR (KBr) data cm^{-1} δC = O	δC = C	δC—H**	^{1}H-NMR ($CDCl_3$) data δ (ppm)
4a	C_6H_5	40	126–28	127[9]	EtOH	1665	1585	993	
b	4-ClC_6H_4	45	176–78	175–78[11]	EtOH	1689	1600	936	
c	3-$NO_2C_6H_4$	55	171–73	174–75[10]	$CHCl_3$	1695	1605	934	
d	4-$NO_2C_6H_4$	75	180–82	180–82[11]	EtOH	1670	1610	950 e	
e	3-$CH_3C_6H_4$	40	110–11	112–14[11]	—	—	—	—	AcOH 2.35 (s, 3H, CH_3); 7.05 (s, 1H, olefinic); 7.15–8.00 (m, 12H, ArH)
f	4-$CH_3C_6H_4$	35	178–79	180–82[11]	AcOH	1681	1600	935	2.42 (s, 3H, CH_3); 7.18 (s, 1H, Olefinic); 7.24–8.24 (m, 12H, ArH)
g	4-$CH_3OC_6H_4$	40	205–07	203–05[11]	EtOH	—	—	—	4.15 (s, 3H, OCH_3; 7.22 (s, 1H, olefinic); 7.30–8.45 (m, 12H, ArH)
h	3,4-diCH_3O-C_6H_3	25	180–82	182–83[11]	AcOH	—	—	—	3.86 (d, 6H, diOCH_3); 6.75 (s, 1H, olefinic); 6.80–7.90 (m, 11H, ArH)
i	3,4-diCH_3O-6-BrC_6H_2	30	138–40	140[11]	$CHCl_3$	—	—	—	3.75 (d, 6H, diOCH_3); 6.60 (s, 1H, olefinic); 6.70–7.90 (m, 10H, ArH)
j	3,4-$O_2CH_2C_6H_3$	40	210–12	210–12[11]	AcOH	1680	1595	935	5.90 (s, 2H, O_2CH_2); 6.66 (s, 1H, olefinic); 6.75–8.10 (m, 11H, ArH)
k	C_4H_3O	38	236–38	235–37[11]	$CHCl_3$	1700	1600	925	
l	C_6H_5OH=OH—	50	111–13	110–12[9]	AcOH	1705	1610	960	

*All compounds gave satisfactory C,H analysis; **Out of plane deformations of hydrogen attached to exocyclic C=C bond.
S=singlet; d=doublet; m=multiplet.

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MUTAGENICITY STUDIES OF NITRAZEPAM AND ITS METABOLITE IN SALMONELLA/ MICROSOME TEST

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NITRAZEPAM and its metabolite 2-amino-5-nitrobenzophenone were tested for their possible mutagenic activity in Salmonella/microsome test developed recently[1] to detect the environmental mutagens *in vitro*. The test employs *Salmonella typhimurium* strains as the sensitive indicators for DNA damage and mammalian liver microsomal and cytosolic fractions (S-9 fraction) for metabolic conversion of the carcinogen to their mutagenic action. Many of the nitro derivatives have been found to be mutagenic[2] in this short-term technique. The demonstration of the carcinogenicity of nitrofuran[3,4] (furylfuramide, a food preservative), nitroimidazole[5,6] (niridazole, an anti-schistosomal drug and metronidazole, a trichomonacidal drug) led us to investigate nitrazepam, a frequently used anti-convulsant drug, and its metabolite for its mutagenic activity.

For the biological activity of nitroaromatic or heteroaromatic compounds reduction of nitro group by hepatic nitro reductases present in microsomes and cytosols[7,8] appears to be essential. The reduction pathway of nitro derivatives has been postulated as: $RNO_2 \xrightarrow{2e} RNO \xrightarrow{2e} RNHOH \xrightarrow{2e} RNH_2$. The intermediate metabolites nitroso and hydroxylamino[9-11] are considered highly toxic reacting with cellular macromolecules leading to necrosis and carcinogenesis.

Nitrazepam was kindly provided by the Industrical Chemical and Pharmaceutical Laboratories, Bombay. $NADP^+$ and glucose-6-phosphate were obtained from Sigma Chemicals, USA. Histidine and biotin of E. Merck (Germany) were used. Agar used was of Difco, USA. Histidine requiring strains of *Salmonella typhimurium* TA 100 and TA 98 were generously provided by Prof. B. N. Ames (Department of Biochemistry, University of Berkeley, USA). The metabolite 2-amino-5-nitrobenzophenone was prepared from nitrazepam (0.035 M) by refluxing for 3 hr in 250 ml ethanolic hydrochloric acid. The solvent was removed under reduced pressure and the reaction mixture cooled. The separated product was crystallized from methanol, m.p. 143–145° C lit[12]. The homogeniety of the product was established by its TLC studies, R_f 0.72 (chloroform-methanol 95:5) and R_f 0.62 (benzene-ethyl acetate 70:30). Its structure was further confirmed through spectral data. IR was characteristic for C = 0 (1639 cm^{-1}, low due to possible intramolecular hydrogen bonding), $-NO_2$ (1540 and 870 cm^{-1}), and —NH (3330 cm^{-1}). ^1H NMR indicated as expected eight aromatic H, δ8.55 (1 Hd, J = 2Hz), 8.35 (1H dd J = 9Hz and 2Hz), δ7.5–7.8 (5 Hm), δ6.85 (1 Hd, J = 9Hz), δ6.9 (NH_2, broad, disappeared after deuterium washing). MS gave molecular ion M^+ 242 and a characteristic fragment at m/e 214 (M-28).

The S-9 fraction routinely employed for microsomal activation was prepared from livers of male rats (Kasauli strain) weighing 200 ± 20 g which had been given an intraperitoneal injection of 500 mg/kg. Aroclor 1254 (Monsanto Co., St. Louis, USA) for the induction of hepatic mono-oxygenases. Five days later, the rats were sacrificed by cervical dislocation. The livers were removed, chopped in a beaker containing 0.15 M KCl, homogenized and centrifuged at 0–4° C in a refrigerated ultracentrifuge at 9000 g as described by Ames *et al.*[1] The supernatant, called S-9 fraction, containing about 40 mg/ml of protein concentration[13] was kept in 2 ml quantities at —80° C in a