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SYNTHESIS AND SOME REACTIONS OF 2 (α -PHENYLIMIDO-*p*-CHLORO)-STYRYL-3, 1-BENZOXAZIN-4 (H) ONE

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2-(α -phenylimido-*p*-chloro)-styryl-3, 1-benzoxazin-4(H)-one 1 has been prepared. 1 reacts with different nitrogen nucleophiles under different reaction conditions to give compounds 2- 5 while its thionation with P_2S_5 gives the corresponding benzothiazin-4-thione 6. Arylation of 1 under Friedel-Crafts condition afforded the corresponding *o*-arylamino-carbinol 9, while its reaction with Grignard reagents gave the *o*-amidophenyl alkyl ketone 10.

Key words: Benzoxazin-4-ones, Nucleophilic and electrophilic reactions.

Introduction

In continuation of our work on the reactions of heterocyclic compounds [1-4], in addition to what has been reported earlier [5-8] concerning the biological importances of benzoxazinones and quinazolones, we report herein the synthesis and reactions of 2(α -phenylimido-*p*-chloro)-styryl-3, 1-benzoxazin-4 (H) one 1 in order to study the steric and polar factors of α -phenylimido-*p*-chlorostyryl moiety as a bulky substituent in position-2 on the reactivity of the benzoxazinone nucleus towards some nitrogen and carbon nucleophiles.

Results and Discussion

Compound 1 was prepared via interaction of anthranilic acid with 2-phenyl-4(*p*-chlorobenzylidene)-5(4)-oxazolone. The IR spectrum of 1 showed bands at 1795, 1745, 1640 and 3300-3230 cm^{-1} due to CO, C=N, C=C and NH functions and its PMR spectrum (DMSO- d_6) showed signals at δ 7.5-8.2 (*m*, 13H, ArH and 1H olefinic) and at 10.4 (*s*, br, 1H, NH).

Recently [9-12], it was reported that 2-substituted 3, 1-benzoxazin-4 (H) ones underwent hetero-ring opening on reaction with nitrogen nucleophiles and afforded cinnamide derivatives. By analogy, aminolysis of 1 with amines such as aniline, glycine and/or piperidine in boiling ethanol gave 2-(substituted) carbamoyl phenyl acetanilides 2a-c, while on hydrazinolysis with hydrazine hydrate, phenylhydrazine or 2, 4-dinitrophenyl-hydrazine yielded N (substituted) anthranilic acid hydrazide derivatives 2 $_{d-f}$. The IR spectra of 2 exhibited bands at 3310-3220 and 1730-1700 cm^{-1} due to CO and NH functions and PMR spectrum of 2b (DMSO - d_6) showed signals at δ 4.4 (*d*, br 2H, NH CH_2 COOH), 7.1-8.6 (*m*, 13H of Ar H and 1H olefinic), 10.1, 11.2 (2 x br., 2H, NH disappeared by adding D_2O) and 11.8 (br., 1H, COOH) while 2c (DMSO- d_6) showed signals at 6.6 δ (*s*, 1H, olefinic), 7.3-8.7 (*m*, 18H, Ar H) and broadened centred at 10.7 (4H of NH disappeared by adding D_2O).

On the other hand, aminolysis or hydrazinolysis of 1 in boiling acetic acid or in ethanol and fused sodium acetate gives 2-(α -phenylimido-*p*-chloro) styryl-3-alkyl and/or aralkyl-4(3H) quinazolinones 3a-j. The structure of compound 3a-j was confirmed by ring closure of 2a and 2 $_{d-f}$ with acetic anhydride to give the corresponding 3c and 3g-i respectively. Acylation of 3j with acetic anhydride or benzoyl yielded 3k and 3l. The structures were also confirmed spectroscopically; the IR spectra of 3 exhibited absorption bands at 3180-3290, 1685-1700 and 1660-1680 cm^{-1} due to NH and CO functions and the PMR spectrum of 3c (DMSO - d_6) showed signals at δ 6.8 (*s*, 1H, olefinic), 7.3-8.8 (*m*, 18H, ArH) and 11.4 (*s*, br, 1H, NH disappeared by adding D_2O) while the PMR spectrum of 3h (CDCl $_3$) showed signals at δ 6.6 (*s*, 1H, olefinic), 7.2-8.3 (*m*, 18H, ArH) and 11.7 (*s*, br., 1H, NH) and the PMR spectrum of 3j (CDCl $_3$) showed signals at δ 6.5 (*s*, 1H, olefinic), 7.1-8.6 (*m*, 13H, ArH) and 10.1 (*b*, *s*, 1H, NH). It was reported earlier [10-12], that benzoxazinone derivatives underwent the hetero-ring opening on reaction with sodium azide and phosphorus pentasulphide and afforded tetrazole and thione derivatives. In the present work, when the benzoxazinone 1 was submitted to react with sodium azide in boiling acetic acid, thiosemicarbazide in boiling pyridine, or phosphorus pentasulphide in xylene yielded the 1-1-[(2'-carboxyphenyl)-2-benzamido-(*p*-chloro) styryl]-tetrazole 4, the 3,5-disubstituted-s-triazolo [3, 4-c] quinazoline 5, or the 2-substituted 3, 1-benzothiazine-4(H)-thione 6, respectively. The IR spectrum of compound 4 exhibits strong absorption bands at 3325, 3100, 1660, and 1100 cm^{-1} attributable to ν OH, ν NH, ν CO and the tetrazole nucleus. The IR spectrum of compound 5 exhibits absorption bands at 3270, 1690, 1620 and 1320 cm^{-1} due to ν NH, ν CO, ν C=N and ν C=S respectively. The IR spectrum of compound 6 exhibits absorption bands at 1680, 1640, 1330 and 3230 cm^{-1} due to CO, C=N, C=S and NH functions respectively.

Amination of 6 with aniline or anisidine in boiling acid containing fused sodium acetate gave the corre

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2-(substituted)-quinazolin-4-thiones 7a,b. The IR spectra showed bands at 1700–1600, 1630, 1350 and 3260 cm^{-1} due to CO, C=N, C=S and NH functions respectively.

Benzoxazinone derivatives react with aromatic hydrocarbons with hetero-ring fission [10,11,13,14]. Thus, arylation of compound 1 with aromatic hydrocarbons such as benzene, toluene, anisole or *m*-xylene under Friedel-Crafts conditions gave *o*-(Substituted)-phenyl ketones 8_{a-d}. The IR spectra of 8 showed absorption bands at 1660–1680 and 3240–3300 cm^{-1} attributable to ketonic, amido CO and NH functions. The PMR spectrum of 8a (DMSO- d_6) showed signals at δ 6.7–8.6 (m, 19H, ArH and olefinic) and 11.8 (br, s, 2H, NH).

It was reported that [14], 2-isopropyl 4(H), 3-1-benzoxazin-4-one reacted with alkyl and/or aryl halides and yielded carbinols. Compound 1 reacted with Grignard reagents to give 2-(substituted amido) phenyl disubstituted carbinols, while the reaction of 1 with phenyl magnesium iodide gave *o*-aroylaminocarbinol 9. The IR spectrum of 9 showed bands at 3450, 3100 and 1670 cm^{-1} due to OH, NH and CO functions respectively and the PMR spectrum (DMSO- d_6) showed signals at δ 4.6 (s, br, 1H, OH), 6.8–8.4 (m, 24H, ArH and olefinic) and 11.3 (s, br., 1H-NH-). Furthermore, 1 reacted with benzyl magnesium chloride to give *o*-amidophenyl alkyl ketone 10. The IR spectrum of 10 showed bands at 3200, 1670, 1610 and 1580 cm^{-1} due to NH, CO, C=N and C=C functions.

Experimental

Melting points are uncorrected and were determined using a Gallenkamp melting point apparatus. IR spectra were recorded in KBr using an Unicam SP 1200 spectrophotometer and PMR spectra on a varian Em-390, 90 MHz instrument using TMS as an internal standard. The physical data of the various compounds prepared are given in Table I.

Preparation of compound 1. A mixture of 2-phenyl-4-(*o*-chloro) benzylidene-5(4)-oxazolone (0.05 mol) and anthranilic acid (0.035 mol) in boiling *n*-butanol (100 mL) was refluxed for 10 hrs. The solid product was crystallised from acetic acid to give 1.

Aminolysis and hydrazinolysis of 1 in boiling ethanol: Formation of 2a-f. A solution of 1 (0.01 mol) and aniline, glycine, piperidine (0.01 mol) or a hydrazine, namely hydrazine hydrate, phenylhydrazine and 2,4-dinitrophenylhydrazine (0.03 mol) in ethanol (50 mL) was refluxed for 4–8 hrs. The solid product obtained on cooling was crystallised from ethanol to give 2 a-f respectively.

Aminolysis and hydrazinolysis of 1 in boiling acetic acid: Formation of 3a-i. A mixture of 1 (0.01 mol) and a primary amine such as methylamine, benzylamine, aniline, *m*-anisidine, 2-aminothiazole, 4-aminophenol (0.01 mol), or hydrazines, namely hydrazine hydrate, phenylhydrazine or 2,4-dinitrophenylhydrazine, (0.03 mol) in acetic acid (50 mL) was refluxed for 6–8 hrs. The solid which separated was

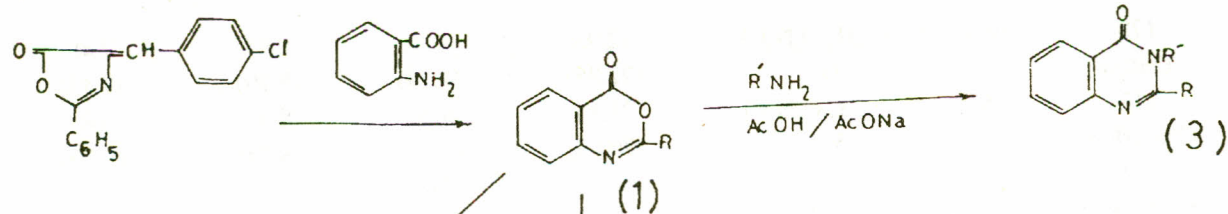
TABLE I. PHYSICAL DATA OF THE VARIOUS COMPOUNDS PREPARED.

| Compd. | M.P. °C Colour | Yield % | Formula Mol. wt. | Analysis | | | |
|----------------|--------------------|------------|---|------------------|----------------|------------------|----------------|
| | | | | Found (%) | | (Calc.) | |
| | | | | C | H | N | Cl |
| 1 | 166 Yellow | 85 | C ₂₃ H ₁₅ O ₃ N ₂ Cl 402.5 | 68.75 (68.57) | 3.76 (3.72) | 6.90 (6.95) | 8.90 (8.82) |
| 2 _a | 234 Colourless | 70 | C ₂₉ H ₂₂ O ₃ N ₃ Cl 495.5 | 70.4 (70.23) | 4.55 (4.44) | 8.30 (8.47) | 7.25 (7.16) |
| 2 _b | 250 Colourless | 75 | C ₂₅ H ₂₀ O ₅ N ₃ Cl 477.5 | 62.95 (62.83) | 4.10 (4.18) | 8.92 (8.79) | 7.5 (7.43) |
| 2 _c | 138 Pale Yellow | 65 | C ₂₈ H ₂₆ O ₃ N ₃ Cl 487.5 | 68.85 (68.92) | 5.21 (5.33) | 8.70 (8.61) | 7.40 (7.28) |
| 2 _d | 118 Pale Yellow | 77 | C ₂₃ H ₁₉ O ₃ N ₄ Cl 434.5 | 63.40 (63.52) | 4.40 (4.37) | 13.00 (12.88) | 8.30 (8.17) |
| 2 _e | 217 Pale Yellow | 65 | C ₂₉ H ₂₃ O ₃ N ₄ Cl 510.5 | 68.30 (68.16) | 4.40 (4.51) | 10.80 (10.96) | 7.10 (6.95) |
| 2 _f | 214 Colourless | 70 | C ₂₉ H ₂₁ O ₇ N ₆ Cl 600.5 | 57.80 (57.95) | 3.60 (3.49) | 13.85 (13.98) | 6.00 (5.91) |
| 3 _a | 148 Pale Yellow | 70 | C ₂₄ H ₁₈ O ₂ N ₃ Cl 415.5 | 69.50 (69.31) | 4.20 (4.33) | 10.20 (10.11) | 8.60 (8.54) |
| 3 _b | 122 Pale Yellow | 65 | C ₃₀ H ₂₂ O ₂ N ₃ Cl 491.5 | 73.45 (73.24) | 4.52 (4.47) | 8.60 (8.54) | 7.30 (7.22) |

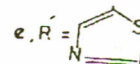
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(Table 1, continue)

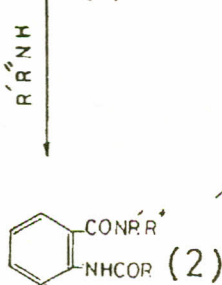
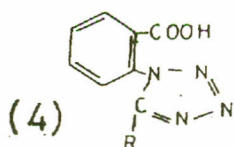
| | | | | | | | |
|----------------|--------------------|----|--|-------------------|----------------|------------------|----------------|
| 3 _c | 178 Yellow | 68 | C ₂₉ H ₂₀ O ₂ N ₃ Cl 477.5 | 72.95 (72.8%) | 4.30 (4.19) | 8.95 (8.79) | 7.48 (7.43) |
| 3 _d | 212 Colourless | 65 | C ₃₀ H ₂₂ O ₃ N ₂ Cl 507.5 | 71.15 (70.93) | 4.50 (4.33) | 8.32 (8.27) | 6.84 (6.99) |
| 3 _e | 153 Pale Orange | 55 | C ₂₆ H ₁₇ O ₂ N ₄ ClS 484.5 | 64.50 (64.39) | 3.40 (3.51) | 11.52 (11.56) | 7.52 (7.33) |
| | | | | S: 6.70, (6.60) | | | |
| 3 _f | 187 Pale Yellow | 70 | C ₂₉ H ₂₀ O ₃ N ₃ Cl 493.5 | 70.67 (70.51) | 4.13 (4.05) | 8.65 (8.51) | 7.32 (7.19) |
| 3 _g | 167 Pale Yellow | 65 | C ₂₃ H ₁₇ O ₂ N ₄ Cl 416.5 | 66.40 (66.26) | 4.15 (4.08) | 13.65 (13.44) | 8.57 (8.52) |
| 3 _h | 183 Yellow | 55 | C ₂₉ H ₂₁ O ₂ N ₄ Cl 492.5 | 70.75 (70.65) | 4.13 (4.26) | 11.28 (11.37) | 7.33 (7.21) |
| 3 _i | 193 Yellow | 70 | C ₂₉ H ₁₉ O ₆ N ₆ Cl 582.5 | 59.60 (59.74) | 3.32 (3.26) | 14.55 (14.42) | 6.16 (6.09) |
| 3 _j | 235 Colourless | 80 | C ₂₃ H ₁₆ O ₃ N ₃ Cl 417.5 | 66.00 (66.11) | 3.88 (3.83) | 9.82 (10.05) | 8.42 (8.50) |
| 3 _k | 195 Brown | 50 | C ₂₅ H ₁₈ O ₄ N ₃ Cl 459.5 | 65.42 (65.28) | 3.95 (3.91) | 9.35 (9.14) | 7.90 (7.72) |
| 3 _l | 173 Brown | 50 | C ₃₀ H ₂₀ O ₄ N ₃ Cl 521.5 | 68.90 (69.03) | 3.95 (3.83) | 8.22 (8.05) | 6.94 (6.81) |
| 4 | 132 Pale Yellow | 50 | C ₂₃ H ₁₆ O ₃ N ₅ Cl 445.5 | 61.72 (61.95) | 3.43 (3.59) | 15.65 (15.71) | 7.90 (7.96) |
| 5 | 135 Yellow | 40 | C ₂₄ H ₁₆ ON ₅ SCl 457.5 | 62.80 (62.95) | 3.55 (3.49) | 15.15 (15.30) | 7.60 (7.75) |
| | | | | S: 6.85, (7.00) | | | |
| 6 | 218 Yellow | 50 | C ₂₃ H ₁₅ ON ₂ ClS ₂ 434.5 | 63.40 (63.52) | 3.60 (3.45) | 6.60 (6.44) | 8.25 (8.17) |
| | | | | S: 14.55, (14.75) | | | |
| 7 _a | 118 Pale Yellow | 50 | C ₂₉ H ₂₀ ON ₃ SCl 493.5 | 70.72 (70.51) | 4.15 (4.05) | 8.42 (8.51) | 7.05 (7.19) |
| | | | | S: 6.52, (6.48) | | | |
| 7 _b | 133 Yellow | 55 | C ₃₀ H ₂₂ O ₂ N ₃ SCl 523.5 | 68.86 (68.76) | 4.30 (4.20) | 8.15 (8.0) | 6.60 (6.78) |
| | | | | S: 6.30, (6.43) | | | |
| 8 _a | 210 Colourless | 50 | C ₂₉ H ₂₁ O ₃ N ₂ Cl 480.5 | 72.65 (72.42) | 4.22 (4.37) | 5.68 (5.82) | 7.50 (7.40) |
| 8 _b | 240 Colourless | 45 | C ₃₀ H ₂₃ O ₃ N ₂ Cl 494.5 | 72.62 (72.80) | 4.55 (4.65) | 5.75 (5.65) | 7.35 (7.20) |
| 8 _c | 230 Colourless | 55 | C ₃₀ H ₂₃ O ₄ N ₂ Cl 510.5 | 70.70 (70.50) | 4.57 (4.50) | 5.27 (5.50) | 6.85 (6.95) |
| 8 _d | 225 Colourless | 40 | C ₃₁ H ₂₅ O ₃ N ₂ Cl 508.5 | 73.40 (73.15) | 5.05 (4.90) | 5.35 (5.50) | 6.78 (7.00) |
| 9 | 124 Orange | 60 | C ₃₅ H ₂₇ O ₃ N ₂ Cl 558.5 | 75.35 (75.20) | 4.95 (4.80) | 5.15 (5.00) | 6.30 (6.35) |
| 10 | 137 Orange | 55 | C ₃₀ H ₂₃ O ₃ N ₂ Cl 494.5 | 72.95 (72.80) | 4.72 (4.65) | 5.82 (5.65) | 7.05 (7.20) |



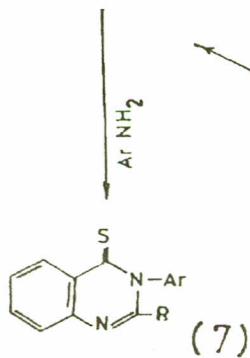
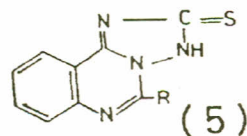
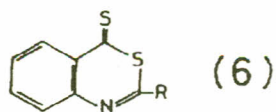
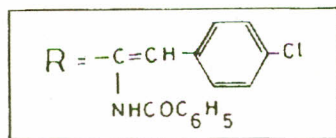
a, R' = CH₃
 b, R' = CH₂C₆H₅
 c, R' = C₆H₅
 d, R' = C₆H₄ · OCH₃-3



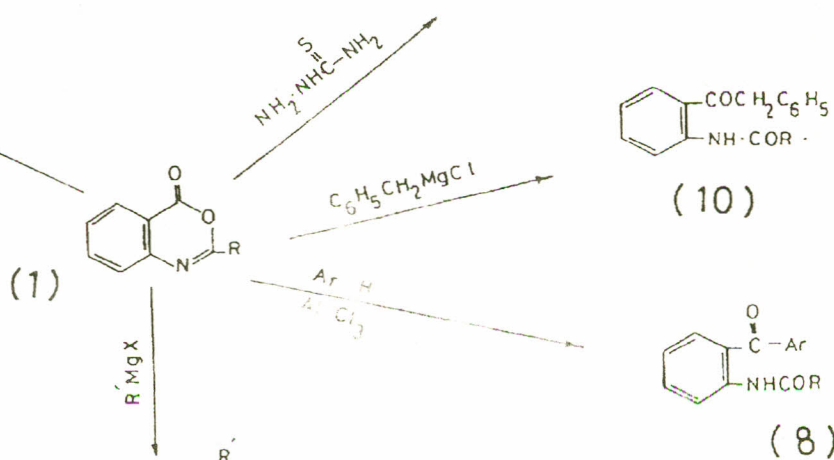
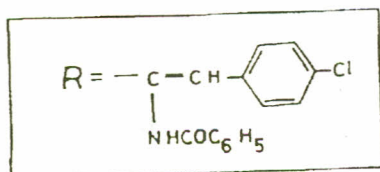
f, R' = C₆H₄ · OH-4
 g, R' = NH₂
 h, R' = NHC₆H₅
 i, R' = NHC₆H₃(NO₂)₂-2,4
 j, R' = OH
 k, R' = OCOCH₃
 l, R' = OCOC₆H₅



a, R' = H ; R'' = C₆H₅
 b, R' = H ; R'' = CH₂COOH
 c, R' + R'' = (-CH₂)₂
 d, R' = H ; R'' = NH₂
 e, R' = H ; R'' = NHC₆H₅
 f, R' = H ; R'' = NHC₆H₃(NO₂)₂-2,4



a, Ar = C₆H₅-
 b, Ar = C₆H₄ · OCH₃-4



a, Ar = C₆H₅-
 b, Ar = C₆H₄CH₃-4
 c, Ar = C₆H₄ · OCH₃-4
 d, Ar = C₆H₃(CH₃)₂-2,4

recrystallised from ethanol or methanol to give 3a-i.

Reaction of hydroxylamine hydrochloride with 1: Formation of 3j. A mixture of 1 (0.01 mol), hydroxylamine hydrochloride (0.03 mol) and sodium acetate (0.03 mol) in ethanol (50 mL) was refluxed for 8 hrs. The reaction mixture was filtered off while hot, left to cool and the solid that separated on cooling was recrystallised from ethanol to give 3_j.

Action of acetic anhydride and/or benzoyl chloride on 3_j: Formation of 3k and 3_l. A mixture of 3_j (0.01 mol) and 10 mL acetic anhydride or (0.01 mol) of 3_j and 5 mL of benzoyl chloride in pyridine (20 mL) was heated on a steam bath for 3 hrs. The solids that separated were washed with water and recrystallized from ethanol to give 3k and 3_l respectively.

Action of sodium azide on 1: Formation of 4. A mixture of 1 (0.01 mol) and sodium azide (0.015 mol) in boiling acetic acid (50 mL) was refluxed for 4 hrs and concentrated. The solid which separated was filtered, dried and recrystallised from methanol to give 4.

Action of thiosemicarbazide on 1: Formation of 5. A mixture of 1 (0.01 mol) and thiosemicarbazide (0.03 mol) in pyridine (30 mL) was refluxed for 6 hrs and the solid that separated upon cooling was filtered off, washed with light petroleum (b.p. 60–80°) and recrystallized from light petroleum to give 5.

Action of phosphorus pentasulphide on 1: Formation of 6. A suspension of 1 (0.01 mol) and phosphorus pentasulphide (0.02 mol) in dry xylene (100 mL) was refluxed for 8 hrs. The reaction mixture was filtered while hot, then concentrated, and the solid that separated on cooling was washed with light petroleum (b.p. 80–100°). Recrystallisation from ethanol gave 6.

Action of primary amines on 6: Formation of 7a,b. Equimolecular quantities (0.01 mol) of 6 and a primary amine such as aniline or *p*-anisidine was refluxed in acetic acid (50 mL) containing sodium acetate (0.01 mol) for 6 hrs and the solid that separated upon cooling was crystallised from ethanol to give 7a or 7b.

Friedel-Crafts reaction of 1: Formation of 8a-d. Anhydrous AlCl₃ (0.03 mol) was added portionwise with stirring for 30 mins to a solution of 1 (0.01 mol) in dry aromatic reactant such as benzene, toluene, anisole or *m*-xylene. Stiring was continued for an additional 8 hrs at room temperature. The reaction mixture was the poured into ice-cold HCl. The organic layer was separated, washed with water and the excess solvent

was distilled under reduced pressure. The solid obtained was crystallised from ethanol to give 8a-d.

Action of Grignard reagents on 1: Formation of 9 and 10. An ethereal solution of phenylmagnesium iodide or benzylmagnesium chloride (0.03 mol) was added in portions to a solution of 1 (0.01 mol) in dry ether. The reaction mixture was stirred for 4 hrs on a water bath then left overnight at room temperature. The reaction mixture was worked up as usual and the ethereal extract was distilled under reduced pressure to give a viscous oil, which was triturated with light petroleum to give a solid product, which was crystallised from petroleum ether to give 9 and 10 respectively.

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