

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELHI]

**Acetylium Perchlorate-catalyzed Preparation of Ketones. The Use of Sodium Perchlorate-Acetyl Chloride Mixture in the Ring Acetylation of Phenol Ethers**

BY K. B. L. MATHUR, J. N. SHARMA, K. VENKATARAMANAN AND H. G. KRISHNAMURTY

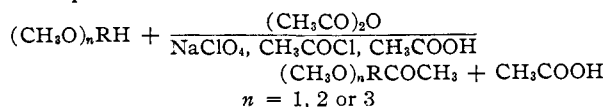
RECEIVED NOVEMBER 23, 1956

Sodium perchlorate and acetyl chloride taken in glacial acetic acid together work as satisfactorily as acetylium perchlorate or perchloric acid for ring acetylations. In the presence of acetic anhydride and using the above mixture certain monohydric, dihydric and trihydric phenol ethers have been found to undergo catalytic ring acetylations. A 30–50% conversion of the ethers into the acetophenones can generally be brought about at 40–60° in 4–6 hr., depending on the reactivity of the ethers. The acetyl group enters a position *para* to the ether grouping and, when this is not free, *ortho* substitution also can occur. Except for anisole, the perchlorate-catalyzed acetylations with various phenol ethers have been studied for the first time.

Several workers have studied the ring acetylations of aromatic hydrocarbons and phenol ethers in the presence of catalysts, *e.g.*, trifluoroacetic acid<sup>1a</sup> or its anhydride<sup>1b</sup>, chloroacetic acid at high temperatures,<sup>1c</sup> phosphorus pentoxide,<sup>1d</sup> polyphosphoric acid,<sup>1e</sup> sulfuric acid<sup>1f,10b</sup> and sundry other inorganic substances<sup>1g,3a</sup> all of which are different from the usual catalysts of the Friedel and Crafts type.<sup>2a–c,8a</sup> In this connection the use by Burton and Prail<sup>3a</sup> of perchloric acid or of acetylium perchlorate seems to be of greater practical importance.<sup>3b</sup> Thus, acetylium perchlorate, acetic acid, anisole and acetic anhydride when used in the molecular proportion 1:2:4:3 or 1:8:4:3 easily give 1.46 and 1.02 moles of *p*-methoxyacetophenone,<sup>3c</sup> respectively. It is, however, found that solvation with larger proportions of acetic acid or using larger proportions of acetic anhydride seriously lowers the yield of the ketone. The above workers minimized the side reactions, *e.g.*, formation of a certain amount of phenol, diketones, colored pyrrilium salts and tar by keeping the temperature low (0–5°) and limiting the reaction time to 45 minutes. Remarkably *p*-methoxyacetophenone is said to be obtainable in identical yields<sup>4</sup> whether acetylium

perchlorate or perchloric acid be used as the catalyst. No systematic study, however, has so far been made of the perchlorate-catalyzed acetylations of phenol ethers other than anisole. Even in the latter case Burton and Prail's own work<sup>3a</sup> was directed more to the elucidation of reaction mechanism. In the present investigation the acetylations of the above type of some monohydric, dihydric and trihydric phenol ethers have been undertaken from a preparatory point of view and by a modified technique.

The modification relates to the use of an equivalent amount of anhydrous sodium perchlorate and acetyl chloride in glacial acetic acid solution, and this solution has been found to work as satisfactorily as acetylium perchlorate or perchloric acid. The amount of acetic acid used as the solvent is limited to what will not cause much of its harmful effect on the yield of the ketones. In the first instance four acetylation mixtures containing sodium perchlorate, acetyl chloride, acetic acid, the phenol ether and acetic anhydride in the mol. proportion 1:1:8:*x*:3 (*x* = 1, 2, 3 or 4) have been examined with anisole. It is seen (*vide* Table III) that a greater conversion of the ether to the ketone takes place when only one or two (*x* = 1, 2) mol. proportions of it are used. But in these cases losses—mechanical, as well as those due to side reactions<sup>3a</sup>—are proportionately greater than when acetylation is done with a mixture of composition 1:1:8:4:3. The latter has, therefore, been chosen for acetylation because in most cases it is easy to remove the unchanged ether by vacuum distillation at low temperatures. However, in those cases where the separation is not so easy and the ethers are reactive, acetylation with a 1:1:8:2:3 or even 1:1:8:1:3 mixture may be done. Using the acetylation mixtures (*x* = 4 or 2), the ethers listed in Table I have been successfully acetylated to give in each case an acetophenone



in which the acetyl group is found to be present in a position *para* to the ether grouping. When the *para* position is not free, the acetyl group enters the *ortho* position but the yields then are poor.

When perchloric acid is the catalyst, the hydrogen ion available from this strong acid is supposed to initiate the reaction iv after which reactions iii and iv occur in sequence as above.

(1) (a) M. S. Newman, *THIS JOURNAL*, **67**, 345 (1945); (b) E. J. Bourne, M. Stacey, J. C. Tatlow and J. M. Tedder, *J. Chem. Soc.*, 718 (1951); (c) F. Unger, *Ann.*, **504**, 267 (1933); (d) G. M. Kosolapoff, *THIS JOURNAL*, **69**, 1651 (1947); (e) P. D. Gardner, *et al.*, *ibid.*, **76**, 4550 (1954); **78**, 2541 (1956); *cf.* also W. J. Horton, *et al.*, *ibid.*, **77**, 2894 (1955), and K. Nakazawa, *et al.*, *J. Pharm. Soc. Japan*, **74**, 495, 1254 (1954); further parts I, III, VII and VIII of the series; (f) J. G. Belton, N. V. Nowlan and T. S. Wheeler, *Sci. Proc. Roy. Dublin Soc.*, **25**, 19 (1949); (g) A. I. Kozak and H. B. Hartough, *THIS JOURNAL*, **69**, 3144 (1947).

(2) (a) *Cf.* C. A. Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1941, Chapter VI and pp. 302–341; (b) C. R. Noller and R. Adams, *THIS JOURNAL*, **46**, 1889 (1924); (c) N. M. Cullinane, S. J. Chord and D. M. Layshon, *J. Chem. Soc.*, 376 (1952).

(3) (a) H. Burton and P. F. S. Prail, *J. Chem. Soc.*, 2036 (1950), and earlier and later papers; (b) *cf.* also R. E. Foster, U. S. Patent 2,496,786; *C. A.*, **44**, 4930c (1950); (c) it is, however, also reported<sup>3b</sup> that the perchloric acid-catalyzed acetylation of anisole results in the formation of both *o*- and *p*-methoxyacetophenone, the yield of the *o*-isomer being half as much (7.3%) as that of the *p*-isomer (14.7%).

(4) It is suggested<sup>1b</sup> that in these reactions, acetylium ions  $\text{CH}_3\text{CO}^+$ , or their solvated form  $(\text{CH}_3\text{CO})_2\text{OH}^+$ , are mainly concerned in bringing about acetylation. The reaction becomes catalytic if acetic anhydride is also present, the whole mechanism in the case, *e.g.*, of acetylium perchlorate and anisole is then represented thus:

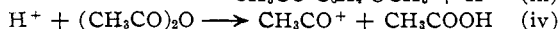
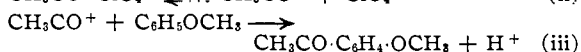
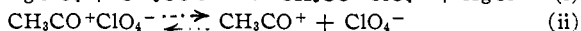


TABLE I  
YIELDS OF THE KETONES UNDER OPTIMUM CONDITIONS

Phenol ether	Moles	No.	Ketone <sup>c</sup> formed	Yield.	
				Mol. <sup>a</sup> prop.	Per cent. <sup>b</sup>
Anisole	4	1	4-Methoxyacetophenone	2.0	50
<i>o</i> -Cresol methyl ether	4	2	3-Methyl-4-methoxyacetophenone	1.8	45
<i>m</i> -Cresol methyl ether	4	3	2-Methyl-4-methoxyacetophenone	2.2	55
<i>p</i> -Cresol methyl ether	4	4	3-Methyl-6-methoxyacetophenone	0.68	17
Phenetole	4	5	4-Ethoxyacetophenone	1.83	45.8
1-Naphthol methyl ether	4	6	1-Acetyl-4-methoxynaphthalene	1.76	44
2-Naphthol methyl ether	4	7	1-Acetyl-2-methoxynaphthalene	1.48	37
Methylenedioxybenzene	4	8	3,4-Methylenedioxyacetophenone	1.2	30
Pyrogallol trimethyl ether	4	9	2,3,4-Trimethoxyacetophenone	0.67	16.8
Phloroglucinol trimethyl ether	2	10	2,4,6-Trimethoxyacetophenone	0.68	34
Phloroglucinol dimethyl ether	4	11	2-Hydroxy-4,6-dimethoxyacetophenone	0.64	16
Catechol dimethyl ether	2	12	3,4-Dimethoxyacetophenone	1.02	50.6
Resorcinol dimethyl ether	2	13	2,4-Dimethoxyacetophenone	1.23	62
Hydroquinone dimethyl ether	2	14	2,5-Dimethoxyacetophenone	0.58	30

<sup>a</sup> Moles of ketone formed per 4 or 2 moles of the ether. <sup>b</sup> Calculated on the ether used. <sup>c</sup> Obtainable in a fair degree of purity even by the first distillation; the ketones 1, 5-8 and 10-13 also have been obtained in the pure solidified forms, in spite of the low m.p. of some of them.

In separating the ketones no earlier<sup>3b,3c</sup> or later ketonic fraction containing the acetyl group in a position different from the above has been obtained. Considering the purity of the ketones and the homogeneity of their derivatives, there does not seem to be any possibility of isomeric ketones present in the recovered ketone fractions either. As regards the yields, it will be noted from Table I that any one of the two acetylation mixtures chosen, a 30-50% conversion of the ether to the ketone generally occurs under optimum conditions, though it may be less in an ether of low reactivity. An idea about the reactivities of the ethers can be obtained from Table II in which results for the ex-

TABLE II  
EXTENT OF KETONE FORMATION AT 40° IN 2 HOURS

Ether	Ketone formed mol. proportion	
<i>m</i> -Cresol methyl ether	1.88	} Very reactive
1-Naphthol methyl ether	1.76	
Phenetole	1.05	
<i>o</i> -Cresol methyl ether	0.83	} Reactive
Anisole	0.44	
Pyrogallol trimethyl ether	0.67 (4 hr.)	} Less reactive
<i>p</i> -Cresol methyl ether	0.40	
Methylenedioxybenzene	0.20 (4 hr.)	
2-Naphthol methyl ether	Traces	
<i>o</i> -Bromoanisole	Nil	

tent of acetylation undergone by some of the representative phenol ethers at 40° in 2 hr. are compiled together. *m*-Cresol methyl ether, 1-naphthol methyl ether can thus be considered to be very reactive; phenetole, *o*-cresol methyl ether, anisole fairly reactive and pyrogallol trimethyl ether, *p*-cresol methyl ether, methylenedioxybenzene, 2-naphthol methyl ether less reactive. In the case of the reactive ethers the maximum yield of the ketones (*vide* Tables IV and V) can be obtained by heating at 40-45° for 4 hr. and in those of medium or low reactivity by heating at 60° for 4-6 hr. Higher temperatures (*cf.* expt. on *p*-cresol methyl ether at 70°) or a longer time of reaction (*cf.* expt. on 2-naphthol methyl ether for 8 hr.) either produce more residue or because of side reactions do

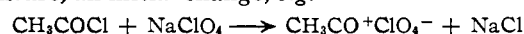
not improve the yield of the ketone materially.

At low temperatures (0-5°) very little acetylation is found to occur in the case of anisole. With ethers more reactive than anisole, yields comparable to those obtained by heating at 40-60° are had by keeping the reaction mixture at room temperature (15-22°) for 24 hr. or more. In fact, acetylation in the cold is the better procedure for the preparation of 3,4-dimethoxy- and 2,4-dimethoxyacetophenones from catechol and resorcinol dimethyl ethers. Remarkably for a 50% conversion to the ketones, resorcinol dimethyl ether requires only 0.75 hr., whereas catechol dimethyl ether takes 24 hr. at room temperature.

Partial methyl ethers of polyhydric phenols can be acetylated too. Phloroglucinol dimethyl ether gives 2-hydroxy-4,6-dimethoxyacetophenone. But resorcinol monomethyl ether gives a mixture of 2-hydroxy-4-methoxyacetophenone and 2-methoxy-4-hydroxyacetophenone. Here acetylation seems to have occurred both *para* and *ortho* to the methoxy group. This is rather unusual as in all other cases only one product has been isolated, *i.e.*, the one in which the acetyl group comes *para* or *ortho* to the ether group.

In connection with the identification of the various ketones, 2,3,4-trimethoxyacetophenone (galacetophenone trimethyl ether) has also been characterized by its oxidation to 2,3,4-trimethoxybenzoic acid by the iodoform reaction. The semicarbazone and picrate of 1-acetyl-2-methoxynaphthalene have been described for the first time. The m.p. of the picrate of 1-acetyl-4-methoxynaphthalene has been corrected.

As for the mode of working of the acetylation mixture, an initial change, *e.g.*



can be visualized to occur first in the acetic acid solution<sup>5a,b</sup> after which through the suggested se-

(5) (a) Potassium perchlorate does not work for acetylations, and its inability to do so has been traced to its insolubility in acetic acid. (b) We have tried a different modification also, *vis.*, using perchloric acid liberated *in situ* by mild heating of equivalent amount of sodium perchlorate and concd. sulfuric acid together. This modification, as far as acetylations are concerned, does not seem to be as expedient and efficient as using the sodium perchlorate-acetyl chloride mixture.

quence of changes involving acetylum ion,<sup>4</sup> the ketone formation would occur. However, it is found that by using lesser proportions of the catalyst mixture, proportionately lesser yields of 4-methoxyacetophenone are obtained. The catalyst mixture therefore acts like acetylum perchlorate or perchloric acid only in the sense that a given amount of the mixture can enable the acetylation of more phenol ether than is stoichiometrically possible on the amount of the perchlorate used.

Compared to the Friedel and Crafts reactions, where possibilities of side reactions and dealkylations in the ketone formed are greater,<sup>2a,b,12b,13a,13b</sup> acetylations of phenol ethers have been found to go smoothly by the use of sodium perchlorate-acetyl chloride mixture as the catalyst. The latter technique is also superior to the use of perchloric acid or acetylum perchlorate—obtainable from the hygroscopic silver perchlorate, in that the sodium salt is convenient to handle and its purity can be depended upon. A further advantage is that the reaction conditions do not require excessive cooling or heating. The sodium perchlorate-acetyl chloride mixture can be used successfully for the ring acetylation of phenol ethers.

### Experimental

Anhydrous sodium perchlorate was obtained by heating the monohydrate at 135–140° for 4 hr. It was found to be appreciably soluble in warm acetic acid (24 g. in 100 g. of acetic acid at 60°). Potassium perchlorate, however, was insoluble even in hot acetic acid and was ineffective as a catalyst.

Acetic acid, acetyl chloride and acetic anhydride were Merck pure reagents. Anisole, *p*-cresol methyl ether, *m*-cresol methyl ether, *p*-cresol methyl ether and phenetole were used from stock. 2-Naphthol methyl ether, methylenedioxybenzene, pyrogallol trimethyl ether, catechol dimethyl ether, resorcinol dimethyl ether, hydroquinone dimethyl ether and phloroglucinol trimethyl ether were prepared by standard methods described in literature. Phloroglucinol dimethyl ether, b.p. 185° (16 mm.), and resorcinol monomethyl ether, b.p. 240–242°, were obtained as reported by Robinson, *et al.*<sup>5</sup> The m.p. or b.p. of the ethers stated in Tables IV and V are those recorded in literature and were also checked. 2-Naphthol methyl ether was found to have b.p. 132–134° (10 mm.). 1-Naphthol methyl ether could be obtained better by methylation of 1-naphthol with dimethyl sulfate and alkali.

The following account is given as typical of the process of acetylation, being done with anisole under optimum conditions.

**Acetylation of Anisole, Taking Sodium Perchlorate, Acetyl Chloride, Acetic Acid, Anisole and Acetic Anhydride in the Molecular Proportion 1:1:8:4:3.**—Anhydrous sodium perchlorate (3.1 g., 0.025 mole) was dissolved at 60° in acetic acid (12 g., 0.2 mole) and, when cold, acetyl chloride (2.0 g., 0.025 mole) was added. Slight turbidity was produced. Anisole (10.8 g., 0.1 mole) and acetic anhydride (7.7 g., 0.75 mole) were then added and the reaction mixture warmed under reflux at 60° for 4 hr. There was gradual development of color which became deep brown toward the end. The reaction mixture was then poured over crushed ice. The aqueous liquor which contained the oily reaction product was extracted with ether (50 ml., thrice). The ether layer, separated from the aqueous layer,<sup>7a</sup> still contained a suspension of an orange-red solid and was therefore filtered. The filtered ether extract was washed suc-

cessively with aq. sodium carbonate, 2 *N* caustic soda solution and finally with water. The residue from the dried (Na<sub>2</sub>SO<sub>4</sub>) ether extract was fractionally distilled. Unchanged anisole (3.5 g.) admixed with little of the ketone came over at 45–47° (6–8 mm.). The ketone fraction came over at 119–120° (6–8 mm.) and solidified upon refrigeration giving m.p. 37° (4-methoxyacetophenone is reported<sup>3b</sup> to have b.p. 117° (6 mm.) and m.p. 37°); 2,4-dinitrophenylhydrazones, m.p. and mixed m.p. 221°<sup>7b</sup>; oxime,<sup>8a</sup> m.p. and mixed m.p. 88°; yield 7.5 g. (moles of ketone formed per 4 moles of the ether, *i.e.*, mol. prop. = 2); non-volatile residue, 1.7 g. The amount of the ketone formed corresponds to 50% conversion of the ether into 4-methoxyacetophenone. The latter could be obtained in equivalent yields by using hydrated sodium perchlorate NaClO<sub>4</sub>·H<sub>2</sub>O; the proportion of the sodium perchlorate, acetyl chloride, acetic acid, anisole and acetic anhydride then was 1:1:6:4:4.

When in these experiments acetyl chloride was not included in the acetylation mixture no acetylation took place, but when the acetic anhydride was omitted, there was some acetylation—4-methoxyacetophenone being obtained in poor yields (1.7 g. at 40° in 4 hr.). The results of acetylation of anisole, using different amounts at 60° in 4 hr., as well as those for the yield of the ketone at different temperature and time and with decreasing amount of the catalyst are incorporated in Table III.

TABLE III  
ACETYLATION OF ANISOLE UNDER DIFFERENT CONDITIONS

Temp., 60° NaClO <sub>4</sub> :AcCl:AcOH:Ani- sole:Ac <sub>2</sub> O Mol. proportion	Anisole used, g.	Time, 4 hours Yield <sup>a</sup> 4-methoxy- aceto- phenone, %	Ether recovd., g.
1:1:8:1:3	2.7	60	0.25
1:1:8:2:3	5.4	58	0.75
1:1:8:3:3	8.1	52	1.90
1:1:8:4:3	10.8	52 <sup>b,c</sup>	3.50
1:1:8:4:4	10.8	48 <sup>d</sup>	3.40

<sup>a</sup> Calculated on the anisole used. <sup>b</sup> At other temperatures and time the amount of the ketone formed was: 0–5°/72 hr. or 45°/4 hr., 3 g.; at 40°/2 hr., 1.7 g. (mol. prop. with anisole, 0.44). <sup>c</sup> AcOH, anisole and Ac<sub>2</sub>O remaining the same (8:4:3), at diminished mol. concentration of the catalyst mixture (NaClO<sub>4</sub> + AcCl), the amount of the ketone was: 0.25 mole/1.9 g., 0.5 mole/3.4 g., 0.75 mole/5.0 g., the first figures being those for the catalyst mixture. <sup>d</sup> With concentrations greater than 3 moles, Ac<sub>2</sub>O is utilized more in promoting side reactions (ref. 3a).

**Acetylation of Various Phenol Ethers.**—Further experiments were conducted with other ethers at different temperature and time in the manner described for anisole. The results are listed in Tables IV and V. Experiments relating to the ketones a–f in Table IV and c and d in Table V were conducted with an acetylation mixture of composition 1:1:8:4:3 and those for e–h in Table V with one of composition approximating 1:1:8:2:3. The actual amount of the ether is mentioned in the first column, the amount of the other constituents being adjusted accordingly. Distillation of the final reaction products under reduced pressure (as indicated) gave a forerun composed of the unchanged ether and containing also, in some cases, a little of the ketone fraction. After a sudden rise of 40–65°, the main ketone fraction came later at temperatures stated in the tables. Only in a few cases was a second distillation necessary to improve the purity of the ketones. The latter have been characterized through suitable derivatives (*vide* literature cited, Tables IV and V). In the case of 1-acetyl-4-methoxy- and 1-acetyl-2-methoxynaphthalene, their identity has been further confirmed by comparison with authentic samples of the ketones and of their derivatives. The purification of 2,4,6-trimethoxyacetophenone (phloracetophenone trimethyl ether) was done by crystallization. In all cases, losses entailed during the working of the reaction mixture as well as those due to side reactions were inevitable, but considering together the weights of the ketone fraction, forerun and residue (*cf.*

(6) R. Robinson, *et al.*, *J. Chem. Soc.*, **125**, 193 (1924); **127**, 945 (1926).

(7) (a) The filtered aqueous layer after repeated evaporation on the water-bath left a residue which did not contain an appreciable amount of the chloride. (b) Burton and Prail (ref. 3a) obtained m.p. 223°. Vogel ("Practical Organic Chemistry," Longmans, Green & Co., London, 1956, p. 743) gives m.p. 220°. However, W. Borsche and J. Barthenheier, *Ann.*, **553**, 250 (1942), report the m.p. to be 232–234°.

(8) (a) K. v. Auwers, M. Lechner and H. Bundesmann, *Ber.*, **58**, 41–44 (1925); (b) G. Stadnikoff and A. Baryschewa, *ibid.*, **61**, 1997 (1928).

TABLE IV  
 ACETYLATION OF MONOHYDRIC PHENOL ETHERS

Phenol ether	Reaction		Ketone fraction		Forerun Temp., °C. (6-8 mm.)	G.	Residue, g.
	Temp., °C.	Time, hr.	B.p., °C. (6-8 mm.)	Yield, %			
3-Methyl-4-methoxyacetophenone <sup>a</sup>							
<i>o</i> -Cresol methyl ether, b.p. 55.5° (9 mm.), 12.2 g., 0.1 mole	15	24	132-134	15	78-80	..	..
	40	2		20.8		6.5	2.1
	60	4		45		1.6	2.0
2-Methyl-4-methoxyacetophenone <sup>b</sup>							
<i>m</i> -Cresol methyl ether, b.p. 56.5° (9 mm.), 12.2 g., 0.1 mole	15	24	133-135	30	80-82	6.0	..
	40	2		47		3.4	0.7
	45	4		55		2.3	1.2
3-Methyl-6-methoxyacetophenone <sup>c</sup>							
<i>p</i> -Cresol methyl ether, b.p. 56.2° (9 mm.), 12.2 g., 0.1 mole	20	24	120-122	5	75-78	..	..
	40	2		10		9.8	1.0
	60	4		17		8.7	0.6
	70	2		23		6.7	2.3
4-Ethoxyacetophenone <sup>d</sup>							
Phenetole, b.p. 60° (9 mm.), 12.2 g., 0.1 mole	15	24	124-125	20.8	55-60	7.5	..
	40	2		26.3		6.6	0.6
	50	4		45.8		3.6	1.8
1-Acetyl-4-methoxynaphthalene <sup>e</sup>							
1-Naphthol methyl ether, <sup>g</sup> b.p. 134-135° (9.5 mm.), 7.9 g., 0.05 mole	25	24	192-195	44	136-140	2.9	..
	40	2		44		2.4	..
1-Acetyl-2-methoxynaphthalene <sup>f</sup>							
2-Naphthol methyl ether, <sup>g</sup> b.p. 132-134° (10 mm.), 7.9 g., 0.05 mole	28	70	174-178	Nil	132-134	7.5	..
	40	4		Traces		7.5	..
	60	6		37		4.0	..
	60	8		35		4.5	..

<sup>a</sup> Reported<sup>8a</sup> b.p. 145-146° (14 mm.); oxime, m.p. 101-102°, reported<sup>8a</sup> 101-102.5°; semicarbazone, m.p. 206-207°, reported<sup>8b</sup> 206-207°. <sup>b</sup> Reported<sup>8a</sup> b.p. 140-141° (14 mm.); semicarbazone, m.p. 194-196°, reported<sup>8a</sup> 194-195°. <sup>c</sup> Reported<sup>8b</sup> b.p. 120.5° (7 mm.); oxime m.p. 89-91°, reported<sup>8a</sup> 89-90°; semicarbazone, m.p. 176-177°, reported<sup>8b</sup> 176-177°. <sup>d</sup> Reported<sup>1d</sup> b.p. 131° (6 mm.). After redistillation and refrigeration solidified, m.p.<sup>8a</sup> 36-37°. Upon oxidation<sup>8b</sup> (with KMnO<sub>4</sub> and aq. K<sub>2</sub>CO<sub>3</sub>) gave *p*-ethoxybenzoic acid, m.p. 195-196°. <sup>e</sup> Reported<sup>10a</sup> b.p. 224-225° (15 mm.). Solidified on keeping. Crystals (from alcohol and then petroleum ether) gave m.p. and mixed m.p. with authentic sample<sup>10b</sup> 70-71°. Semicarbazone, m.p. and mixed m.p. 221-222°. (*Anal.* Calcd. for C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>: N, 16.34. Found: N, 15.91.) Picrate, m.p. and mixed m.p. 129-130° (*Anal.* Calcd. for C<sub>19</sub>H<sub>15</sub>N<sub>3</sub>O<sub>7</sub>: C, 53.14; H, 3.49. Found: C, 53.2; H, 3.6.) Schneider and Kunau<sup>10b</sup> had reported m.p. of the picrate to be 119-121°. <sup>f</sup> Reported<sup>2b</sup> b.p. 158° (2 mm.). Solidified on keeping to give crystals m.p. and mixed m.p. with authentic sample<sup>2b</sup> 59-60°. Semicarbazone, m.p. and mixed m.p. 234-235°. (*Anal.* Calcd. for C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>: N, 16.34. Found: N, 16.64.) Picrate m.p. and mixed m.p. 134-135°. (*Anal.* Calcd. for C<sub>19</sub>H<sub>15</sub>N<sub>3</sub>O<sub>7</sub>: C, 53.1; H, 3.19. Found: C, 52.7; H, 3.57.) <sup>g</sup> Fractionation in the case of the reaction products from these two ethers was done under 8-10 mm. pressure.

Tables IV and V), these losses are not found to be more than 1.5-2.5 g. With 0.1-mole quantities of the ethers, this weight might account for the fate of 15-25% of the phenol ether used.

**Acetylation of Resorcinol Monomethyl and Phloroglucinol Dimethyl Ether.**—Resorcinol monomethyl ether (12.4 g., 0.1 mole) was acetylated at 60° for 4 hr. using the acetylation mixture of composition 1:1:8:4:3. The reaction mixture was made alkaline and refluxed for 1 hr. to hydrolyze the O-acetyl group if any. It was then acidified and extracted with ether. The ether layer was filtered from suspended matter (0.5 g.) and the ether removed. The residual liquid mass was steam distilled till no more emulsion came over. The steam distillate upon ether extraction yielded an oil (5 g.) which did not solidify but contained 2-hydroxy-4-methoxyacetophenone (peonol); semicarbazone, m.p. 219-221°, reported<sup>17a</sup> 221-222°. Four tenths gram of the oil gave 0.13 g. of semicarbazone, indicating it to contain 25-30% peonol (total ca. 1.3 g.), the rest being the unused ether. The colored solid left behind after steam distillation

was extracted with ether, the extract treated with animal charcoal and filtered. After removing the ether and crystallizing the residue (1 g., m.p., crude, 120-125°) from alcohol, pure 2-methoxy-4-hydroxyacetophenone (isopeonol) was obtained, m.p.<sup>17b</sup> 137-138°; 2,4-dinitrophenylhydrazones, m.p. 219-220°, reported<sup>17c</sup> 216-217°.

The experiment with phloroglucinol dimethyl ether (7.7 g., 0.05 mole) was done in the same way. The steam distillate gave 2-hydroxy-4,6-dimethoxyacetophenone (1.6 g., mol. prop. 0.64); m.p. and mixed m.p. 84-85° with an authentic sample of m.p. 85°. The m.p.'s of this ketone are variously reported, e.g., 80°,<sup>18a</sup> 85-88°,<sup>18b</sup> 86-87°,<sup>18a</sup> etc. The sample gave with nitric acid<sup>12b</sup> a blue color turning green on making alkaline and an intense violet color with ferric chloride in alcoholic solution.<sup>18b</sup>

**Acetylations Using Perchloric Acid Liberated *in situ*.**—Anhydrous sodium perchlorate (1.54 g., 0.0125 mole) and concd. sulfuric acid (1.22 g., 0.0125 mole) were heated together at 100-110° for 0.5 hr. The heated mass was cooled and extracted with glacial acetic acid (2 g., 0.034 mole). The extract was filtered through glass wool which was pressed to squeeze out the extract. Acetic anhydride (4.1 g., 0.0 mole) and anisole (5.4 g., 0.05 mole) were then added. This mixture was maintained at 50° for 4 hr. The reaction

(9) (a) A. F. Hollemann, *Rec. trav. chim.*, **10**, 219 (1891); (b) *vide* L. Gattermann, R. Erhardt and H. Maisch, *Ber.*, **23**, 1205 (1890).

(10) (a) S. Ruheman and S. I. Levy, *ibid.*, **53**, 270 (1920); (b) *vide* W. Schneider and F. Kunau, *ibid.*, **54**, 2304 (1921).

(11) (a) G. Ciamician and P. Silber, *Ber.*, **24**, 2989 (1891); (b) F. Mauthner, *J. prakt. Chem.*, **116**, (ii) 324 (1927); (c) T. Posner, *Ann.*, **389**, 67 (1912).

(12) (a) C. Mannich and F. Hahn, *Ber.*, **44**, 1551 (1911); (b) W. H. Perkin and C. Weizmann, *J. Chem. Soc.*, **89**, 1654 (1906); (c) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds."

TABLE V  
 ACETYLATION OF DI- AND TRIHYDRIC PHENOL ETHERS

Phenol ether	Reaction		Ketone fraction		Forerun Temp., °C. (8-10 mm.)	G.	Residue, g.
	Temp., °C.	Time, hr.	B.p., °C. (8-10 mm.)	Yield, %			
3,4-Methylenedioxyacetophenone <sup>c</sup>							
Methylenedioxybenzene, <sup>a</sup> b.p. 55-56° (9 mm), 6.1 g., 0.05 mole	40	4	138-140	5	56-58	..	..
	70	4		30		1.0	1.0
2,3,4-Trimethoxyacetophenone <sup>d</sup>							
Pyrogallol trimethyl ether, <sup>a</sup> b.p. 241°, 8.4 g., 0.05 mole	20	24	156-158	Traces	116-118	..	..
	40	4		16.8		..	..
	50 <sup>b</sup>	4		16.8		5.0	..
2,4,6-Trimethoxyacetophenone <sup>e</sup>							
Phloroglucinol trimethyl ether, m.p. 52°, 7.5 g., 0.045 mole	22	24		34		..	..
3,4-Dimethoxyacetophenone <sup>f</sup>							
Catechol dimethyl ether, b.p. 205-206°, 6.5 g., 0.047 mole	15	24	160-161	46.1	93-94	..	..
	22	60		50.6		..	..
2,4-Dimethoxyacetophenone <sup>g</sup>							
Resorcinol dimethyl ether, <sup>i</sup> b.p. 207-208°, 6.5 g., 0.047 mole	15	0.5	165-167	27	96-98	..	..
	5-10	0.75		49.4		2.1	1.1
	22	0.75		62		1.4	0.7
2,5-Dimethoxyacetophenone <sup>h</sup>							
Hydroquinone dimethyl ether, <sup>i</sup> b.p. 109° (20 mm.), 6.5 g., 0.047 mole	50	4	156-158	22.4	120-121	..	..
	60	4		30		..	..

<sup>a</sup> Composition of the acetylation mixture was 1:1:8:4:3, in others it was 1:1:8:2:3. <sup>b</sup> Perchloric acid, from NaClO<sub>4</sub> + H<sub>2</sub>SO<sub>4</sub> (*v. infra*), was the catalyst. <sup>c</sup> Solidified upon refrigeration. After recrystallization from benzene, m.p.<sup>11a,b</sup> 87°; oxime, from hydroxylamine hydrochloride and sodium acetate, m.p. 155-156°, reported<sup>11c</sup> 156-157°; phenylhydrazine, m.p. 115°, reported<sup>11a</sup> 114°. Semicarbazone, m.p. 238-240°, reported<sup>11b</sup> 241-242°. <sup>d</sup> The ketone fraction did not solidify; reported<sup>12a</sup> m.p. 14-15°, b.p. 165° (12 mm.). Semicarbazone, m.p. 168-169°. (*Anal.* Calcd. for C<sub>12</sub>H<sub>17</sub>N<sub>3</sub>O<sub>4</sub>: N, 15.73. Found: N, 15.49.) Oxidation with iodine and alkali<sup>12b</sup> gave iodoform, m.p. 119°, and 2,3,4-trimethoxybenzoic acid, m.p. 98° (reported 100°). <sup>e</sup> The reaction product was first decolorized with animal charcoal in 20% alcohol (40 ml.) at 80° and the extract filtered. The residue was then further extracted with alcohol (10 ml. thrice). The combined extracts on concentration and cooling deposited the crude product (3.2 g.), representing a 34% conversion of the ether. The crude product upon recrystallization from alcohol gave crystals, m.p.<sup>13a,13b</sup> 99-100°. The latter gave a blue color with nitric acid.<sup>13b</sup> In a similar experiment, using 5.7 g. of ether and doing the acetylation at 70° for 4 hr., the yield of the crude ketone was 2.4 g., showing 33% conversion of the ether. <sup>f</sup> Reported<sup>14a</sup> b.p. 158° (9 mm.). After redistillation and refrigeration, m.p.<sup>14b</sup> 48-49°; oxime,<sup>14a</sup> m.p. 140°; semicarbazone,<sup>14a</sup> m.p. 211°. <sup>g</sup> Reported<sup>15b</sup> b.p. 157.5° (7 mm.) and<sup>15a</sup> 163-165° (12 mm.). After redistillation and refrigeration solidified to give m.p.<sup>15a</sup> 40°; oxime,<sup>15b</sup> m.p. 125°. At higher reaction temperature considerable colored and tarry material was also produced. <sup>h</sup> Reported<sup>16a</sup> b.p. 156-158° (11 mm.); semicarbazone,<sup>16b</sup> m.p. 181-182°. <sup>i</sup> Fractionation was done under 10-12 mm. pressure.

mixture was then worked as described before for anisole.

John Wiley and Sons, Inc., New York, N. Y., 1948, p. 138.

(13) (a) F. Tutin and F. W. Caton, *J. Chem. Soc.*, **97**, 2067 (1910); (b) E. H. Rennie, W. T. Cooke and R. H. Finlayson, *ibid.*, **117**, 345 (1920).

(14) (a) C. Mannich, *Arch. Pharm.*, **248**, 138 (1910); (b) E. Neitzel, *Ber.*, **24**, 2864 (1891).

(15) (a) F. Mauthner, *J. prakt. Chem.*, **119**, (ii) 314 (1928); (b) S. Sachs and V. Harold, *Ber.*, **40**, 2724 (1907).

(16) (a) A. Oliverio and E. Lugli, *Gazz. chim. ital.*, **78**, 16 (1948); (b) A. Klaiques, *Ber.*, **37**, 3996 (1904).

(17) (a) v. Auwers and P. Pohl, *Ann.*, **405**, 265 (1914); (b) K. Hoesch, *Ber.*, **48**, 1126 (1915); (c) B. Kamthung and A. Robertson, *J. Chem. Soc.*, 925 (1939).

(18) (a) Cf. R. F. Dean and M. Nierenstein, *THIS JOURNAL*, **47**, 1679 (1925); (b) F. Friedlander and L. C. Schnell, *Ber.*, **30**, 2152 (1897).

4-Methoxyacetophenone isolated weighed 2 g. The amount was 2.5 g. by the sodium perchlorate-acetyl chloride method. The yields of ketones obtained from *m*-cresol methyl ether and pyrogallol trimethyl ether when sodium perchlorate-sulfuric acid was used approached the yields obtained using the sodium perchlorate-acetyl chloride method (*cf.* Table V). In other cases (*e.g.*, phenetole, 1-naphthol methyl ether, phloroglucinol dimethyl ether) the yields were less. Similar results were obtained when the experiments were conducted at room temperatures.

The authors wish to thank Prof. T. R. Seshadri, Dean of the Science Faculty and Head of the Chemistry Department, University of Delhi, for his interest in this work and for facilities.

DELHI-8, INDIA