Reaction of 1-Phenyl-2-indanone with Oxygen in Methanolic Sodium Methoxide

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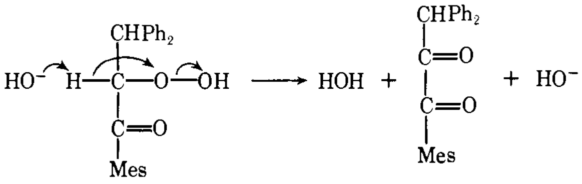
Abstract: In 0.05 *M* methanolic sodium methoxide solution 1-phenyl-2-indanone (**7**) is converted almost quantitatively to its enolate ion **7a** which has a high intensity maximum at 300 nm. The rate of reaction of **7a** with oxygen was measured by following the decrease in absorbance and also by following the increase in absorbance at 257 nm, which is characteristic of the ultimate product, methyl *o*-benzoylphenylacetate (**9**). The reaction **7a** → **9** was found to be first order, *i.e.*, independent of base concentration. It is concluded that the rate-limiting step is cleavage of an intermediate α-keto hydroperoxide, **8**, initiated by addition of methoxide ion to the carbonyl group. A pK_a of 15.7 is estimated for **7** from the kinetic results, and a value of 14.9 was obtained by observing changes in absorbance on addition of increments of methoxide to a solution of **7** in methanol.

In strongly basic media, such as *tert*-BuOK–*tert*-BuOH, ketones react rapidly with molecular oxygen to form α-hydroperoxides and products derived therefrom.[1] In particular systems[2] or at low temperatures[3] the hydroperoxides can be isolated.

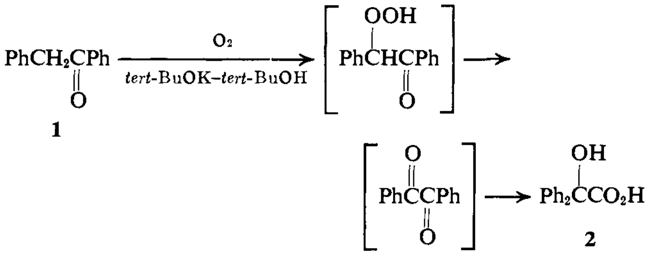
If the α-hydroperoxide bears an α-hydrogen atom, base-catalyzed elimination may give rise to α-diketones, which in some instances may be isolated.[2] An early example of a base-catalyzed conversion of a hydroperoxide to an α-diketone was supplied by Kohler and Thompson.[4]



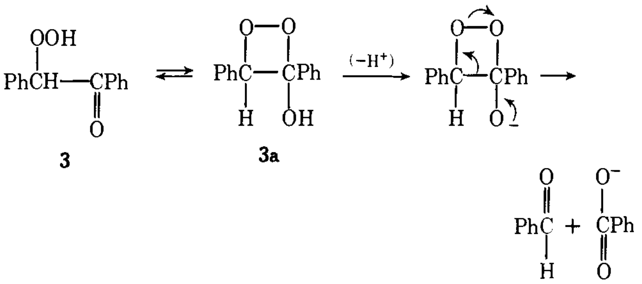
Mes = mesityl

The formation of radical anions of α-diketones from the reaction of a variety of ketones, including desoxybenzoin, propiophenone, and butyrophenone, when exposed to traces of oxygen in basic solution has been demonstrated by esr spectroscopy.[5]

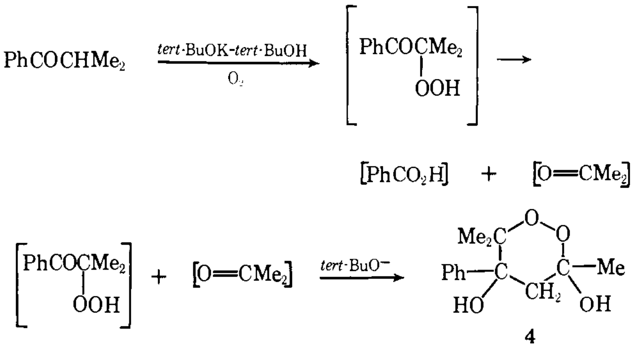
If a phenyl group is attached to the carbonyl group the initially formed α-diketone may undergo a benzilic acid rearrangement. For example, benzylacetophenone with *tert*-BuOK–*tert*-BuOH and oxygen gives 13% phenylbenzylglycolic acid,[1] and benzilic acid (**2**) is formed in 60% yield when oxygen is bubbled into a solution of desoxybenzoin (**1**) in *tert*-BuOK–*tert*-BuOH.[1]



On the other hand, when **1** was shaken with 2 atm of oxygen in *tert*-BuOK–*tert*-BuOH and the temperature allowed to rise, 74% of benzoic acid was formed in 2.5 min.[1] This and analogous cleavages of the α-C–C bond of ketones have been represented as involving a cyclic, tautomeric (3-hydroxy-1,2-dioxetane) form of the hydroperoxide (**3** ⇄ **3a**).[1]



This mechanism of cleavage can also be used to explain the formation of benzoic acid from ketones such as isobutyrophenone which cannot form α-diketones.[1] The formation of an α-hydroperoxide and acetone as intermediates in this reaction has been demonstrated by the isolation of a crystalline hydroperoxide, **4**, derived from a condensation of these two intermediates.[6]



The hypothesis that the base-catalyzed oxidative cleavage of ketones of this type occurs *via* hydroper-

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[1] W. E. Doering and R. M. Haines, *J. Amer. Chem. Soc.*, **76**, 482 (1954).

[2] E. J. Bailey, D. H. R. Barton, J. Elks, and J. F. Templeton, *J. Chem. Soc.*, 1578 (1962).

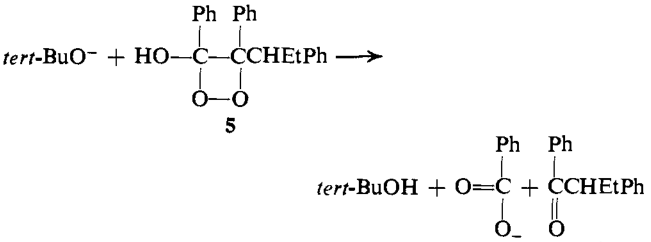
[3] H. R. Gersman and H. J. W. Nieuwenhuis, Netherlands Patent 111,310 (1965); *Chem. Abstr.*, **63**, 13081g (1965).

[4] E. P. Kohler and R. B. Thompson, *J. Amer. Chem. Soc.*, **59**, 887 (1937).

[5] (a) G. A. Russell and E. T. Strom, *ibid.*, **86**, 744 (1964); (b) G. A. Russell and E. R. Talaty, *ibid.*, **86**, 5345 (1964); (c) G. A. Russell, E. G. Janzen, A. G. Bemis, E. J. Geels, A. J. Moye, S. Mak, and E. T. Strom, *Advan. Chem. Ser.*, No. **51**, 112 (1965).

[6] J. E. Baldwin, D. H. R. Barton, D. J. Faulkner, and J. F. Templeton, *J. Chem. Soc.*, 4743 (1962).

oxide intermediates is given further credence by the observation that the hydroperoxide of α,β-diphenylvalerophenone (**5**) is cleaved by *tert*-BuOK to α-phenylbutyrophenone (**6**) and benzoic acid.[1,7]

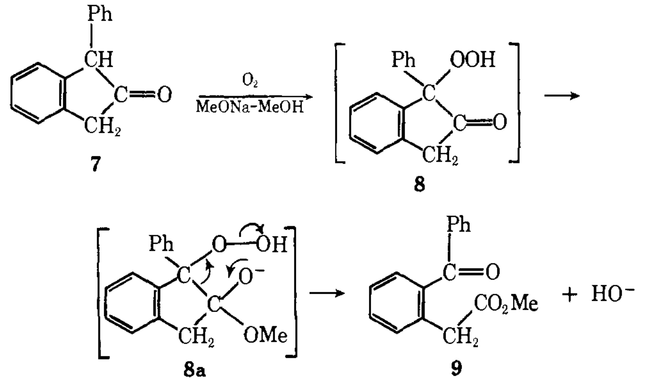


$$tert\text{-BuO}^- + \text{HO}-\overset{\text{Ph}}{\underset{\text{O—}}{\text{C}}}-\overset{\text{Ph}}{\underset{\text{O}}{\text{C}}}\text{CHEtPh} \longrightarrow tert\text{-BuOH} + \text{O}{=}\overset{\text{Ph}}{\underset{\text{O}^-}{\text{C}}} + \overset{\text{Ph}}{\underset{\text{O}}{\text{C}}}\text{CHEtPh}$$

5

6

The cleavage of 1-phenyl-2-indanone (**7**) to methyl *o*-benzoylphenylacetate (**9**)[8] cannot be accounted for by the mechanism invoking decomposition of an α-hydroxy four-membered ring peroxide since this would lead to *o*-benzoylphenylacetic acid, rather than the ester. It is necessary, instead, to assume that methoxide ion adds to the carbonyl group of the hydroperoxide, and that the resulting adduct **8a** undergoes a fragmentation reaction involving the cleavage of both the C–C and O–O bonds (not necessarily at the same time).[8]



7 **8** **8a** **9**

This reaction has now been examined further.

Results

A 5×10^{-5} *M* solution of **7** in methanol has a broad uv maximum centered near 265 nm (ϵ_{max} 1800). Addition of a solution of sodium methoxide (0.006 *M*) caused the immediate development of a high intensity maximum near 300 nm characteristic of enolate ion **7a** derived from **7**. On standing, the absorption due to **7a** gradually decreased and was replaced by a new maximum at 257 nm characteristic of methyl *o*-benzoylphenylacetate (**9**).

At low temperature (6.45°) the rate of oxidation of **7a** was sufficiently slow to allow an estimate of the pK_a of **7** from the change in absorbance with a change in methoxide ion concentration. The average of two runs gave pK_a = 14.9.[9]

Rates of reaction of **7** with oxygen at 25° using concentrations of sodium methoxide of 0.0015–0.076 *M* were followed by observation of (a) the rate of decrease in absorbance at 300 nm (disappearance of **7a**) and (b) the rate of increase in absorbance at 250 nm (appearance of **9**). At a given (excess) base concentration each of these changes followed excellent pseudo-first-order plots; the rate constants are designated as k_a and k_b, respectively (Table I).

Table I. Rate of Methoxide-Catalyzed Reaction of 1-Phenyl-2-indanone (**7**)[a] with Oxygen in Methanol at 25°

[MeO$^-$], *M*	k_a,[b] sec^{-1}	k_b,[b] sec^{-1}	[MeO$^-$]/k_b
0.00152	4.32×10^{-4}	3.13×10^{-4}	4.86
0.00152[c]	3.28×10^{-4}	2.94×10^{-4}	
0.00303	6.04×10^{-4}	4.15×10^{-4}	7.30
0.00604	7.16×10^{-4}	6.06×10^{-4}	9.97
0.00604[c]	3.07×10^{-4}	4.07×10^{-4}	
0.00754	7.68×10^{-4}	6.21×10^{-4}	12.14
0.0117		6.9×10^{-4}	16.96
0.01495	8.99×10^{-4}	6.74×10^{-4}	22.18
0.0222		7.27×10^{-4}	30.54
0.0294		7.98×10^{-4}	36.84
0.070		9.67×10^{-4}	72.39
0.070		9.08×10^{-4}	77.09
0.070[d]		1.30×10^{-3}	
0.070[d]		1.54×10^{-3}	

[a] The indanone concentration was *ca.* 5×10^{-5} *M*. [b] Correlation coefficients were better than 0.999 for most runs. [c] Methanol saturated with nitrogen. [d] Methanol saturated with oxygen.

If the assumption is made that the rate of formation of **9** from enolate ion **7a** is a pseudo-first-order process, then the kinetic expression may be derived as follows. Assuming

$$\text{I} + \text{MeO}^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{MeOH} + \text{I}^- \xrightarrow{k_2} \text{P}$$

where I = 1-phenyl-2-indanone (**7**), I$^-$ = enolate ion **7a**, and P = methyl *o*-benzoylphenylacetate (**9**)

$$d[\text{P}]/dt = k_2[\text{I}^-]_t = k_2K[\text{I}]_t[\text{MeO}^-]$$

where $K = [\text{I}^-]/[\text{I}][\text{MeO}^-]$. Since $[\text{P}]_\infty = [\text{I}^-]_t + [\text{I}]_t + [\text{P}]_t$

$$[\text{I}]_t(1 + K[\text{MeO}^-]) = P_\infty - P_t$$

and

$$d[\text{P}]/dt = k_2K[\text{MeO}^-]\left(\frac{P_\infty - P_t}{1 + K[\text{MeO}^-]}\right)$$

The pseudo-first-order rate constant, k_{app}, is then

$$k_{app} = \frac{k_2K[\text{MeO}^-]}{1 + K[\text{MeO}^-]}$$

This may be expressed in the form

$$[\text{MeO}^-]/k_{app} = [\text{MeO}^-]/k_2 + 1/k_2K$$

A plot of [MeO$^-$]/k_b (Table I) *vs.* [MeO$^-$] gave a line with slope = $1/k_2$ and intercept = $1/k_2K$. From this plot $k_2 = 8.6 \times 10^{-4}$ sec^{-1} and $K = 387$. The pK_a of indanone **1** can be evaluated since pK_a = $-\log K$ + pK_a^{MeOH} = $-2.59 + 18.3 = 15.7$, which is in fair agreement with the value determined directly (14.9). The difference in temperature (25 and 6.45°) may (or may not) account for some of the discrepancy. (The pK_a's

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(7) E. P. Kohler, *Amer. Chem. J.*, **36**, 177 (1906).

(8) F. G. Bordwell, R. G. Scamehorn, and A. C. Knipe, *J. Amer. Chem. Soc.*, **92**, 2172 (1970); F. G. Bordwell and R. G. Scamehorn, *ibid.*, **93**, 3410 (1971).

(9) The pK_a of 5-nitro-2-indanone is 8.94 in water.[10] Taking into account the differences in solvent (pK_a's in methanol are generally four-five units higher than those in water[11]) and the presence of the nitro group, the value of *ca.* 15 for the pK_a of 1-phenyl-2-indanone in methanol appears to be of the right order of magnitude.

(10) P. S. Tobias and F. J. Kézdy, *J. Amer. Chem. Soc.*, **91**, 5171 (1969).

(11) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 46.

for some acids decrease with decreased temperature whereas the pK_a's of others increase.)

Note that from $K = 387$ it follows that most of the indanone will be present in the form of its enolate ion in dilute methoxide ion solutions (95% with 0.05 *M* NaOMe). At base concentrations of this order of magnitude $k_b \cong k_2$. It will be observed that the values of k_b obtained for 0.07 *M* NaOMe do agree reasonably well with the graphically determined value for k_2.

Discussion

The reaction of oxygen with carbanions has been studied carefully by Russell and his students.[5,12] For the Ph_2CH^- and Ph_3C^- carbanions the rate of reaction with oxygen is extremely rapid (near diffusion control), and the rate-limiting step is generation of the carbanion from the hydrocarbon (*e.g.*, with *tert*-BuOK in *tert*-BuOH–DMSO).[12] On the other hand the more acidic hydrocarbon, fluorene (pK_a = 20.5 in DMSO or H_2O),[13] forms the carbanion rapidly and subsequent reactions are slow. A sequence of steps involving a radical-chain mechanism to form a hydroperoxide which undergoes elimination to form fluorenone has been suggested.[5c] The rate-limiting step was not specified. A similar mechanism has been suggested for the reaction of the enolate ions derived from ketones with oxygen, the final step being base-catalyzed elimination with the hydroperoxide to form the diketone (see above) or cleavage of the O–O bond to form the α-hydroxy ketone.[5c]

The earlier studies[1–3,5–7] provide ample precedent, therefore, for assuming that enolate ion **7a** reacts with oxygen to form a hydroperoxide **8** and that this undergoes a base-catalyzed fragmentation reaction in the manner outlined above. It is of interest that even in 50% MeOH–H_2O (70 mol % water) the product was ester **9** to the exclusion of the corresponding acid. A similar high selectivity for methoxide ion *vs.* hydroxide ion attack at a carbonyl group has been observed in the cleavage of esters.[14]

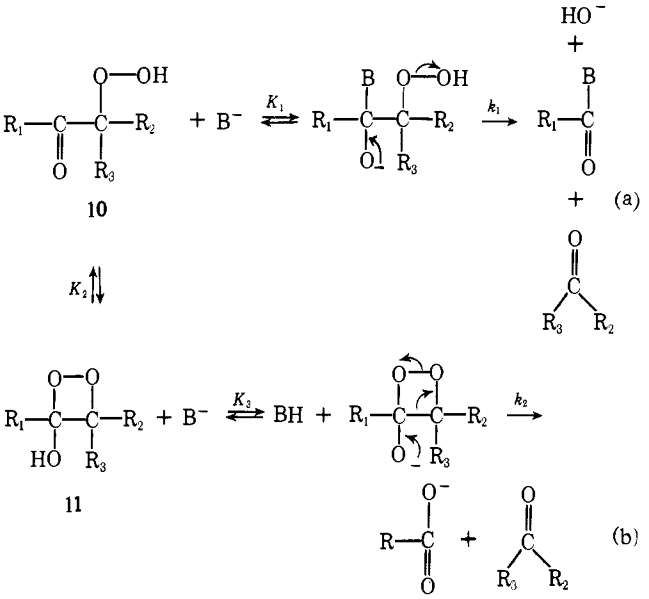
This scheme can accommodate the observed first-order kinetics and the relative insensitivity to methoxide ion concentration, if the reaction of **7a** with oxygen to form hydroperoxide **8** is assumed to be fast and reversible.[15] The slow, rate-limiting cleavage of the hydroperoxide is pseudo-zero-order in methoxide ion concentration because the hydroperoxide concentration is inversely proportional to the methoxide ion concentration.

$$ROO^- + MeOH \rightleftharpoons ROOH\ (\mathbf{8}) + MeO^-$$

$$MeO^- + ROOH\ (\mathbf{8}) \longrightarrow \mathbf{9} + HO^-$$

Because methoxide ion is present in excess and conversion of **7** to its anion **7a** is practically complete, the reaction is relatively insensitive to changes in methoxide ion concentration.

The present results show that α-keto hydroperoxides (**10**) can be cleaved by base attack at the carbonyl group and subsequent fragmentation (path a) as well as by cleavage of the tautomeric 3-hydroxy-1,2-dioxetane (**11**) by path b.



Recent work indicates that α-keto hydroperoxides exist as such, rather than in the 3-hydroxy-1,2-dioxetane form **11** assigned by Kohler.[7,16] On the surface this would appear to make path a the favored one for base-initiated decomposition of hydroperoxides. Actually, however, the reaction path chosen will depend not only on the value of the **10** ⇄ **11** equilibrium constant (K_2), but also on the equilibrium constants K_1 and K_3, and on the rate constants k_1 and k_2. For α-keto hydroperoxide **8**, formation of the tautomeric 3-hydroxy-1,2-dioxetane is made especially unfavorable because the dioxetane contains a strained 4–5 ring fusion. Reaction occurs, therefore, entirely by path a. On the other hand, for acyclic systems path b appears to be favored, at least for *tert*-BuOK–*tert*-BuOH, judging from the formation of acids rather than esters in the cleavage of ketones by oxygenation in this medium.[1]

Experimental Section

Evaluation of pK_a of 1-Phenyl-2-indanone (7) in Methanol at 6.45°. Methanol (3.0 ml) in a cuvette of path length 1 cm was allowed to attain thermal equilibrium at 6.45° in the cell compartment of a Cary 15 spectrophotometer. The solution was balanced optically against a methanol reference sample and 5 μl of a 0.03 *M* solution of **7** in methanol was added. The absorbance at 300 nm was recorded following incremental additions (2–220 μl) of 0.912 *M* sodium methoxide in methanol upon attainment of equilibrium (*ca.* 300 sec).

Using the symbols I for indanone **7** and I⁻ for its anion

$$[I^-] = \frac{Ac}{A_{max}}$$

$$I = \frac{(A_{max} - A)c}{A_{max}}$$

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(12) G. A. Russell, A. G. Bemis, E. J. Ceels, E. G. Janzen, and A. T. Moye, *Advan. Chem. Ser.*, No. **75**, 174 (1968).

(13) C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, **89**, 2752 (1967).

(14) W. P. Jencks and M. Gilchrist, *ibid.*, 90, 2622 (1968).

(15) This conversion is believed to occur in the following steps[5c]

$$R^-\ (\mathbf{7a}) + O_2 \rightleftharpoons R\cdot + O_2\cdot^-$$

$$R\cdot + O_2 \rightleftharpoons RO_2\cdot$$

$$R^- + RO_2\cdot \rightleftharpoons R\cdot + RO_2^-$$

$$RO_2^- + MeOH \rightleftharpoons RO_2H\ (\mathbf{8}) + MeO^-$$

(16) W. H. Richardson and R. F. Steed, *J. Org. Chem.*, **32**, 771 (1967); A. G. Pinkus, M. Z. Haq, and J. G. Lindberg, *ibid.*, **35**, 2555 (1970).

Table II. Changes in Absorbance on Addition of Increments of 0.912 *M* Sodium Methoxide to 1-Phenyl-2-indanone (7)

Vol of base added[a]	$10^4[\mathrm{MeO^-}]$[b]	A_{obsd}[c]	A_{corr}[b]	$A(A_{\mathrm{corr}} - A_0)$	$1/A$	$1/[\mathrm{MeO}]^- \times 10^{-1}$
			Run 1			
0	0	0.048	0.048	0		
2	6.03	0.359	0.359	0.311	3.215	165.8
4	12.00	0.495	0.496	0.448	2.234	83.33
6	17.88	0.556	0.557	0.509	1.965	55.93
8	23.69	0.589	0.591	0.543	1.843	42.21
10	29.42	0.610	0.612	0.564	1.773	33.99
15	43.43	0.640	0.643	0.595	1.680	23.03
20	57.00	0.653	0.657	0.609	1.641	17.54
120	350.77	0.690	0.718	0.670	1.493	2.851
220	623.11	0.680	0.730	0.682	1.467	1.605
			Run 2			
0	0	0.027	0.027	0		
2	6.03	0.369	0.369	0.342	2.922	165.8
4	12.00	0.512	0.513	0.486	2.059	83.33
6	17.88	0.581	0.582	0.555	1.801	55.93
8	23.69	0.619	0.621	0.594	1.684	42.21
10	29.42	0.642	0.644	0.617	1.621	33.99
15	43.43	0.674	0.677	0.650	1.538	23.03
20	57.00	0.689	0.694	0.667	1.500	17.54
120	350.77	0.730	0.759	0.732	1.364	2.851
220	623.11	0.719	0.772	0.745	1.343	1.605

[a] Microliters of 0.912 *M* sodium methoxide in methanol. [b] Corrected for volume change on addition of the base solution. [c] At 300 nm.

where *c* is the initial indanone concentration corrected for dilution effects and the change in volume of methanol on cooling to 6.45°.

$$\mathrm{I} + \mathrm{MeO^-} \rightleftharpoons \mathrm{I^-} + \mathrm{MeOH}$$

$$K = \frac{[\mathrm{I^-}]}{[\mathrm{I}][\mathrm{MeO^-}]} = \frac{Ac/A_{\mathrm{max}}}{\dfrac{A_{\mathrm{max}} - A}{A_{\mathrm{max}}}c[\mathrm{MeO^-}]} = \frac{A}{(A_{\mathrm{max}} - A)[\mathrm{MeO^-}]}$$

By rearranging terms this equation can be written in the form

$$\frac{1}{A} = \frac{1}{K[\mathrm{MeO^-}]A_{\mathrm{max}}} + \frac{1}{A_{\mathrm{max}}}$$

A plot of $1/A$ against $1/[\mathrm{MeO^-}]$ will be linear with a slope of $1/KA_{\mathrm{max}}$ and an intercept of $1/A_{\mathrm{max}}$; K = intercept/slope.

The data for two runs are summarized in Table II. Values determined graphically for the two runs are: slope, 7.32×10^{-4} and 8.62×10^{-4}; intercept, 1.458 and 1.339; A_{max} 0.686 and 0.748; K, 1.537×10^3 and 1.526×10^3.

Using the mean value for K (1.531×10^3) and the relationship $\mathrm{p}K_\mathrm{a} = -\log K + \mathrm{p}K_\mathrm{a}^{\mathrm{MeOH}} + \log\,[\mathrm{MeOH}]$ gives: $\mathrm{p}K_\mathrm{a} = -3.185 + 16.7 + 1.391 = 14.9$.

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