# Restricted Rotation. Part 2.[1] Further Studies of Barriers to Rotation in Some 3-Arycyclohexenone Derivatives: Effect of Substituents on the Free Energy of Activation

By Dhanonjoy Nasipuri *and Pranab K. Bhattacharya, Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India

George T. Furst, Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514, U.S.A.

The free energy of activation for internal rotation about the aryl–cyclohexenone bond in a number of 2-aryl-6-oxo-cyclohex-1-enylacetic acid derivatives has been determined by dynamic n.m.r. from the coalescence temperature of the AB quartet of the side chain methylene protons. The results are discussed in terms of steric and electronic factors. Chemical shifts of some characteristic groups are correlated with the ground state conformations of the molecules.

IN Part 1,[1] we observed that the side chain methylene protons of some 2-aryl-6-oxocyclohex-1-enylacetic acid derivatives (I) (as acid), (II), and (VII) showed an AB quartet in the n.m.r. spectra due to restricted rotation about the aryl–cyclohexenone bond. The free energies of activation as determined by dynamic n.m.r. (d.n.m.r.)[2] from coalescence temperatures were quite high (16—22 kcal mol⁻¹), perhaps marginal for resolution into stable
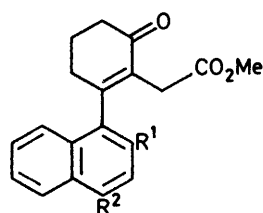
(I) R¹ = R² = H
(II) R¹ = OMe, R² = H
(III) R¹ = H, R² = OMe
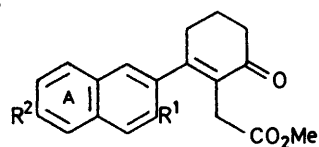
(IV) R¹ = R² = H
(V) R¹ = H, R² = OMe
(VI) R¹ = OMe, R² = H
(VII) R¹ = OMe, ring A reduced
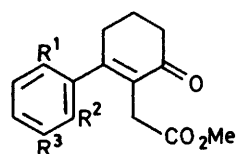
(VIII) R¹ = R² = R³ = H
(IX) R¹ = R³ = H, R² = OMe
(X) R¹ = R³ = H, R² = Me
(XI) R¹ = R³ = Me, R² = H
(XII) R¹ = Me, R² = H, R³ = Prⁱ

enantiomers but admirably suited for study by d.n.m.r. In the past, attempts have been made to examine the effect of substituents on the barrier to rotation about single bonds both qualitatively[3,4] and quantitatively[5,6] but such studies have been confined mainly to biphenyl systems. The arylcyclohexenones are easy to prepare, offer a reasonable variation of substitution patterns in

the aromatic ring, and are thus convenient for such an investigation. About a dozen of these compounds have now been studied by d.n.m.r. and the free energy of activation of internal rotation has been determined in appropriate cases. The significance of steric and electronic factors on the energy of activation is discussed and an attempt is made to explain the anomalous behaviour of the 2-methoxy-1-naphthyl derivative (II) in which the barrier height appeared to be considerably reduced in spite of additional steric hindrance.

RESULTS AND DISCUSSION

Methyl 2-aryl-6-oxocyclohex-1-enylacetates were prepared essentially by the method discussed earlier[1,7] from the respective aryl methyl ketones by first converting them into Mannich bases and then condensing the derived methiodide with ethyl β-oxoadipate in the presence of base followed by hydrolysis and esterification. Some of these compounds [(I), (II), (IV), (V), and (VIII)] have previously been reported by us.[1,7-9] 1-Acetyl-4-methoxynaphthalene, 1-acetyl-2,5-dimethylbenzene, and 1-acetyl-5-isopropyl-2-methylbenzene required for the synthesis of the arylcyclohexenones (III), (XI), and (XII) were obtained from 1-methoxynaphthalene, p-xylene, and p-cymene respectively by Friedel–Crafts reaction. 2-Acetyl-3-methoxy-5,6,7,8-tetrahydronaphthalene[8] was aromatised to 2-acetyl-3-methoxynaphthalene which was used for the synthesis of methyl 2-(3-methoxy-2-naphthyl)-6-oxocyclohex-1-enylacetate (VI). The purity of the starting ketones was checked by g.l.c. and the structures of the arylcyclohexenones were confirmed by spectral data (i.r. and n.m.r.). The synthesis of methyl 2-(2-methoxy-1-naphthyl)-6-oxocyclohex-1-enylacetate (II) was repeated[1] starting from 1-acetyl-2-methoxynaphthalene, which in turn was obtained from Fries rearrangement of 2-naphthyl acetate[10] followed by methylation. To

[1] Part 1, D. Nasipuri and P. R. Mukherjee, J.C.S. Perkin II, 1975, 464.

[2] G. Binsch, Topics Stereochem., 1968, 3, 97.

[3] F. H. Westheimer, 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, New York, 1956, p. 542.

[4] M. M. Harris and C. Cheung King Ling, J. Chem. Soc., 1964, 1825.

[5] M. Oki, H. Iwamura, and G. Yamamoto, Bull. Chem. Soc. Japan, 1971, 44, 262.

[6] M. Oki and G. Yamamoto, Bull. Chem. Soc. Japan, 1971, 44, 266.

[7] D. Nasipuri, A. C. Choudhuri, and J. Roy, J. Chem. Soc., 1958, 2734; D. Nasipuri and J. Roy, ibid., 1960, 1571.

[8] D. Nasipuri and A. Bhattacharya, Indian J. Chem., 1972, 10, 799.

[9] M. Guha, U. Rakshit, and D. Nasipuri, J. Indian Chem. Soc., 1960, 37, 267.

[10] K. Fries, Ber., 1921, 54B, 709.

remove any element of uncertainty in the structure of the ketone, it was carefully compared with the isomeric 2-acetyl-3-methoxy- and 2-acetyl-6-methoxy-naphth-

fast inversion on the n.m.r. time scale. Introduction of a methoxy-group adjacent to the pivotal bond raises the activation energy substantially. The values (15.95—

TABLE 1

N.m.r. parameters [a] and free energies [b] of activation of rotation about the aryl–cyclohexenone bond

No.	Compound	Frequency/ MHz	Solvent	$\Delta\nu_{AB}$/Hz	J_{AB}/Hz	T_c/°C	k_c	$\Delta G^{\ddagger}$/ kcal mol^{-1}
1	(I)	100	$C_6D_5NO_2$	23.0	16.5	183	103.5	22.80
2	(I) as acid	60	$C_6H_5NO_2$	17.0	17.0	165	100.0	21.90 [c]
3	(II)	60	$CDCl_3$	10.5	17.0	45	95.5	15.80 [c]
4	(III)	100	$C_6D_5NO_2$	22.3	17.0	170	105.0	22.15
5	(VI)	100	$C_6D_5NO_2$	23.5	17.0	65	106.3	16.70
6	(VII)	100	CCl_3CHCl_2	23.5	17.0	50	106.3	15.95
7	(IX)	100	C_6D_6	34.4	15.0	56	111.8	16.22
8	(IX)	100	$CDCl_3$	28.8	16.0	56	108.1	16.24
9	(IX) as acid	100	$C_6D_5NO_2$	26.0 [d]	17.0 [d]	20	109.0	14.40
10	(X)	100	$C_6D_5NO_2$	18.8	16.5	150	99.0	21.15
11	(XI)	100	$C_6D_5NO_2$	18.0	16.0	150	95.7	21.20
12	(XII)	100	$C_6D_5NO_2$	31.7	17.0	160	116.3	21.60

[a] The spectral changes are reversible with temperature. [b] The maximum errors are estimated to be ±0.2 kcal mol^{-1}. [c] Data are taken from ref. 1. [d] Values are calculated from a spectrum at −10°.

alene which were the only other possible products of Fries rearrangement. The three ketones were found to be different as were the three arylcyclohexenones (II), (VI), and (V) derived from them.

As expected, the methylene protons of the acetate side chain in compounds (IV), (V), and (VIII) appeared as a singlet at τ 6.80 and remained so down to −70°. Evidently, the energy barrier in these compounds is too

$$|1-3| = [\Delta\nu_{AB}{}^2 + J_{AB}{}^2]^{\frac{1}{2}} \qquad (1)$$

$$k_c = \pi[(\Delta\nu_{AB}{}^2 + 6J_{AB}{}^2)/2]^{\frac{1}{2}} \qquad (2)$$

$$\Delta G^{\ddagger} = 4.57\ T_c\ (10.32 + \log T_c/k_c) \qquad (3)$$

low to be studied by d.n.m.r. Compound (IX) (as acid) showed a singlet for these protons at ambient temperature which split into a quartet below 20°. The remaining compounds had n.m.r. spectra in which all the four peaks of the quartet were clearly seen at room temperature. The values for J_{AB} and $\Delta\nu_{AB}$ were calculated in the usual way from the positions of the first and second and first and third peaks [equation (1)] respectively.[11] The approximate exchange rate k_c and the free energy of configurational inversion $\Delta G^{\ddagger}$ at the coalescence temperature T_c were calculated as before [1] using equations (2) and (3). All these values and some other details of n.m.r. are given in Table 1 along with those reported earlier [1] for sake of comparison. For reasons mentioned in Part 1, the measurements are at present limited to the calculation of free energies to conformational inversion at T_c. The relevant portions of the n.m.r. spectra of the compound (III) at different temperatures are shown in Figure which is typical for all compounds in this series with restricted rotation.

The results of d.n.m.r. analysis present more or less a consistent pattern with only one exception to be discussed later. Thus compounds (IV), (V), and (VIII) having no *ortho*-substituent or *peri*-interaction undergo

16.70 kcal mol^{-1}) are comparable in the three related cases (VI), (VII), and (IX) (Table 1, entries 5—8).
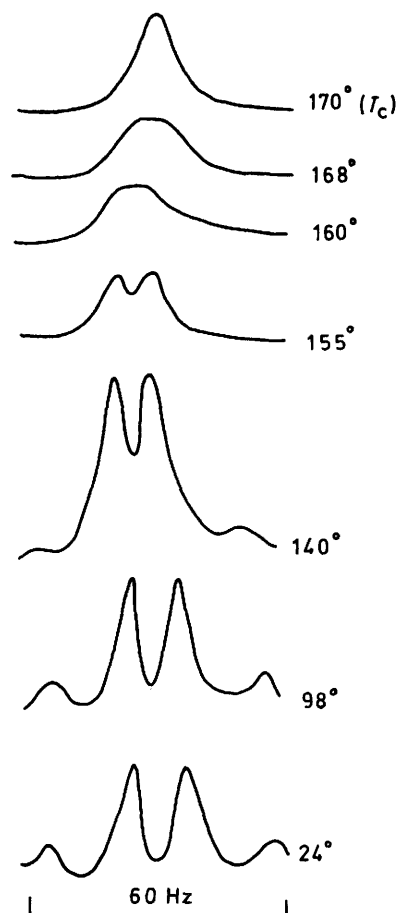
100 MHz Variable temperature n.m.r. spectra of the keto-ester (III) in $C_6D_5NO_2$

Replacement of methoxy by a bulkier [12] methyl group increases the energy barrier to a much higher level

[11] L. M. Jackman and S. Sternhell, 'Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 1969, p. 129.

[12] E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962, p. 163.

(21.15 kcal mol⁻¹) (Table 1, entry 10). The *peri*-interaction in the 1-naphthyl derivatives (I) and (III) (Table 1, entries 1 and 4) elevates the barrier still more to the highest value in the series (22.15—22.80 kcal mol⁻¹).

The barriers to rotation for the compounds (XI) and (XII) are very similar to (perhaps only marginally higher than) that of the simple *o*-methyl derivative (X) (Table 1, entries 10—12). Apparently, the buttressing of hydrogen by adjacent alkyl substituents does not contribute much toward raising the energy barrier. This is in line with similar observation in the biphenyl series.[12]

The lowering of the activation energy in the acids *vis-à-vis* the esters as (I) and (IX) (Table 1, entries 1, 2, 8, and 9) might be due to an intramolecular hydrogen bonding between the carbonyl and carboxy-groups in the former giving rise to a seven-membered cyclic chelate (XIII) thereby reducing the steric strain in the transition state. Spectral evidence for hydrogen bonded structure
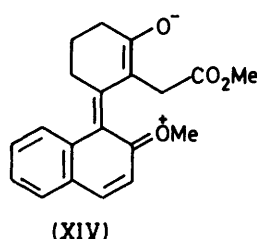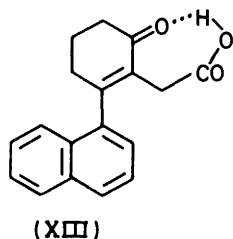
(XIII) of the acid [as (I)] in the ground state has already been adduced.[8]

The case of the 2-methoxy-1-naphthyl derivative (II), however, remains difficult to explain. The previous suggestion [1] that the lowering of the barrier height might be due to an extended conjugation involving the methoxy and carbonyl groups in the planar transition state appears to be invalidated by the observation that the 4-methoxy-1-naphthyl derivative (III), capable of a similar resonance, has a $\Delta G^{\ddagger}$ value only 0.65 kcal mol⁻¹ lower than the 1-naphthyl analogue (I). This small difference is quite in order and compares well with that for related biphenyl systems reported by Oki *et al.*[6] who have attributed it to a joint effect of resonance stabilisation of the transition state and release of steric interaction by the out-of-plane bending of the pivotal bond. In the case of the 2-methoxy-derivative (II), however, the resonance contribution may be more important and the stabilisation of the planar transition state more appreciable due to a favourable electronic interaction between the two oppositely developing dipoles, namely, the methoxy-group and the cyclohexenone system, as shown in the canonical form (XIV). This could be a major factor for lowering the energy barrier and would necessitate that the acetate side chain slides past the methoxy-group in the transition state [as (XIV)] instead of moving over the *peri*-hydrogen. This seems to be logical since the *peri*-interaction in the compound (I) is quite large.

So far we have considered the effects of substituents on the transition states only. The preferred ground state conformation of the molecules [*e.g.* (I) and (II)] is presumably the one with the aromatic and cyclohexenone rings approximately perpendicular to each other. While this situation is quite satisfactory for (I), it may not be so for (II) in which, given free rotation for the O–CH₃ bond, the methoxy-hydrogens will interfere sterically with the methylene hydrogens of the side chain and also of the cyclohexenone ring. As a result, the acetate group will be pushed towards the centre of the naphthalene nucleus and steric strain is partly released at the expense of the *peri*-interaction thereby reducing the energy gap between the ground and transition states.

In Table 2, the peak positions of some characteristic

TABLE 2

Some characteristic peaks in n.m.r. spectra of compounds (I)—(XII)

Com-pound	Solvent	Chemical shift (τ) [a]		
		OCH₃	CO₂CH₃	CH₂CO₂Me [b]
(I)	C₈D₅NO₂		6.48	6.91
	CDCl₃		6.50	7.00
(II)	CDCl₃	6.15	6.50	7.00
(III)	C₈D₅NO₂	6.12	6.58	6.97
	CDCl₃	6.00	6.45	6.95
(IV)	CDCl₃		6.38	6.78
(V)	C₈D₅NO₂	6.06	6.38	6.80
(VI)	C₈D₅NO₂	6.05	6.34	6.90
	CDCl₃	6.02	6.33	6.85
(VII)	CDCl₃	6.20	6.38	6.90
(VIII)	CDCl₃		6.34	6.80
(IX)	CDCl₃	6.18	6.38	6.92
(X)	C₈D₅NO₂		6.46	6.95
(XI)	CDCl₃		6.42	6.97
(XII)	CDCl₃		6.41	6.99

[a] Me₄Si as internal standard. [b] Values refer to the midpoint of the AB quartet.

groups (OCH₃, CO₂CH₃, and C*H₂*CO₂Me) in compounds (I)—(XII) at ambient temperature are recorded. The signals due to OCH₃ in (II) and (III) have identical chemical shift suggesting that there is little or no distortion in the aromatic ring in the ground state of the more crowded molecule (II). The positions of the ester protons (CO₂CH₃) in the same series (naphthyl or phenyl), on the other hand, vary, although slightly but unmistakeably from the unhindered arylcyclohexenones to the hindered ones. Thus in the three crowded naphthylcyclohexenones (I)—(III), these protons appear at *ca.* 0.12 p.p.m. higher field than in the other naphthyl derivatives (IV)—(VI). A similar shielding is noted in the three hindered phenylcyclohexenones (X)—(XII) for the ester methyl as compared to the phenylcyclohexenone (VIII). The signals due to the side chain methylene protons are likewise affected appearing at τ 6.90—7.00 for the hindered ketones and at τ 6.80 for the unhindered ones (Table 2). Although the chemical shifts of these protons are controlled by the conformational mobility at various C–C and C–O bonds (in addition to the aryl–cyclohexenone bond), this change in chemical shift may be attributed to the fact that in the ground state conformation of the hindered molecules, the

acetate side chain is placed above the aromatic plane and therefore partly shielded by the aromatic ring current.

We record here an unusual feature of the n.m.r. spectra of the compound (III) at higher temperatures. The singlets due to the two methoxy-groups (OMe and CO_2Me) show signs of splitting into doublets above 155°, the separation growing with increase of temperature. The changes are, however, perfectly reversible with temperature.

EXPERIMENTAL

^{1}H N.m.r. spectra at different temperatures were taken on a Varian XL-100 100 MHz machine operating in the Fourier transform mode using 16 K data points. Temperature control was provided by a Varian variable temperature controller with an accuracy of ± 2 °C. The temperature was measured by inserting a calibrated 5 mm thermometer into the probe before and after each run. Temperatures above 160° were read using the shift difference of an ethylene glycol sample. A few spectra were also taken on Varian A-60, T-60, and HR-100 spectrophotometers for [²H]chloroform solutions unless otherwise stated; chemical shifts (τ) are reported relative to tetramethylsilane as internal standard. Petroleum refers to a fraction, b.p. 60—80°, and light petroleum to a fraction, b.p. 40—60°. Organic solutions were dried over anhydrous sodium sulphate.

1-*Acetyl-4-methoxynaphthalene*.—To a solution of anhydrous iron(III) chloride (32.4 g, 0.2 mol) in carbon disulphide (40 ml) cooled in ice was slowly added a mixture of 1-methoxynaphthalene (32.7 g, 0.2 mol) and acetyl chloride (15.6 g, 0.2 mol). After stirring for 2 h in the cold and 4 h at room temperature, the dark red mixture was decomposed with ice and concentrated hydrochloric acid and the product worked up in the usual way. 1-Acetyl-4-methoxynaphthalene, b.p. 175—180° at 2 mmHg, was obtained as a solid which recrystallised from petroleum as plates (25.5 g), m.p. 72° (lit.,[13] 72°) (Found: C, 77.9; H, 6.2. Calc. for $C_{13}H_{12}O_2$: C, 78.0; H, 6.0%).

2-*Acetyl-3-methoxynaphthalene*.— 2-Acetyl-3-methoxy-5,6,7,8-tetrahydronaphthalene[8,14] (2.0 g) was heated with powdered sulphur (0.7 g) at 220—250° for 2 h. The mixture was taken up in dry benzene and refluxed with freshly precipitated copper powder. 2-Acetyl-3-methoxynaphthalene, b.p. 140—145° at 0.2 mmHg, was obtained as plates (1.1 g) (from petroleum), m.p. 48° (lit.,[15] 48°) (Found: C, 77.8; H, 5.9%); τ (CCl$_4$, 60 MHz) 1.74 (1 H, s, 1-H), 2.00—2.65 (4 H, m, ArH), 2.80 (1 H, s, 4-H), 6.02 (3 H, s, OMe), and 7.40 (3 H, s, COMe); $\nu_{max.}$ (Nujol) 1 670, 1 630, and 1 600 cm^{-1}; oxime, m.p. 122° (lit.,[16] 121.5°).

1-*Acetyl-2,5-dimethylbenzene*.— 1-Acetyl-2,5-dimethylbenzene was prepared from acetylation of p-xylene in the presence of anhydrous aluminium chloride according to a known procedure.[17] It had b.p. 85° at 5 mmHg; τ (60 MHz) 2.50 (1 H, s, 6-H), 2.84 (2 H, m, ArH), 7.43 (3 H, s, COMe), and 7.53 and 7.63 (6 H, 2s, ArMe); $\nu_{max.}$ (neat) 1 690 and 1 585 cm^{-1}.

1-Acetyl-5-isopropyl-2-methylbenzene was prepared in a

similar fashion from p-cymene using anhydrous iron(III) chloride as condensing agent.[18] It had b.p. 114° at 5 mmHg; τ (60 MHz) 2.43 (1 H, s, 6-H), 2.80 (2 H, m, ArH), 7.10 (1 H, m, CHPr^i), 7.42 (3 H, s, COMe), 7.50 (3 H, s, ArMe), and 8.67 and 8.80 (6 H, d, CHMe$_2$); semicarbazone (from ethanol), m.p. 168° (lit.,[18] 168°).

2-Methylacetophenone, b.p. 112° at 20 mmHg, was prepared from o-toluic acid by condensing the derived acid chloride with diethyl ethoxymagnesiomalonate followed by hydrolysis according to a known procedure.[19]

The purity of the above aryl methyl ketones was checked by g.l.c. carried out on a column (6 ft × ¼ in) of 10% poly(diethylene glycol adipate) on Gaschrom-Z (60—80 mesh) or alternatively on a column of Carbowax 20M on Chromasorb (60—80 mesh).

Methyl 2-Aryl-6-oxocyclohex-1-enylacetates.—The methyl esters of the new 2-aryl-6-oxocyclohex-1-enylacetic acids used in the d.n.m.r. experiments were all prepared by the general procedure described before.[7-9] 2-Dimethylaminoethyl 4-methoxy-1-naphthyl ketone (9.6 g) obtained from 1-acetyl-4-methoxynaphthalene condensed with ethyl β-oxoadipate[20] to afford *methyl 2-(4-methoxy-1-naphthyl)-6-oxocyclohex-1-enylacetate* (III) (5.1 g, 40%), b.p. 220—230° at 0.3 mmHg, which crystallised from ether–light petroleum as plates, m.p. 88° (Found: C, 74.0; H, 6.3. $C_{20}H_{20}O_4$ requires C, 74.1; H, 6.2%); τ (60 MHz) 1.70 (1 H, m, 8-H), 2.40 (3 H, m, 3ArH), 2.80 (1 H, d, J 8 Hz, 2-H), 3.20 (1 H, d, J 8 Hz, 3-H), 6.00 (3 H, s, OMe), 6.50 (3 H, s, CO$_2$Me), 6.98 (2 H, q, CH_2CO$_2$Me), 7.34 (4 H, m, 2CH$_2$), and 7.80 (2 H, m, CH$_2$); $\nu_{max.}$ (KBr) 1 730, 1 670, and 1 590 cm^{-1}.

The other arylcyclohexenones were obtained in 30—50% overall yield from the respective ketones: *methyl 2-(3-methoxy-2-naphthyl)-6-oxocyclohex-1-enylacetate* (VI), m.p. 136° (chloroform–petroleum) (Found: C, 74.2; H, 6.3%); methyl 2-(o-methoxyphenyl)-6-oxocyclohex-1-enylacetate (IX), m.p. 86° (ether–light petroleum) (lit.,[8] 80—81°); the derived *acid*, m.p. 142° (aqueous methanol) (Found: C, 69.5; H, 6.3. $C_{15}H_{16}O_4$ requires C, 69.2; H, 6.2%); *methyl 2-(o-methylphenyl)-6-oxocyclohex-1-enylacetate* (X), m.p. 64° (ether–light petroleum) (Found: C, 74.3; H, 7.0. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%); *methyl 2-(2,5-dimethylphenyl)-6-oxocyclohex-1-enylacetate* (XI), m.p. 89—90° (ether–petroleum) (Found: C, 75.1; H, 7.3. $C_{17}H_{20}O_3$ requires C, 75.0; H, 7.3%); *methyl 2-(5-isopropyl-2-methylphenyl)-6-oxocyclohex-1-enylacetate* (XII), m.p. 71—72° (petroleum) (Found: C, 76.2; H, 8.0. $C_{19}H_{24}O_3$ requires C, 76.0; H, 8.0%). All these compounds were characterised by i.r. and n.m.r. spectra, some features of which are shown in Table 2.

[13] W. Schneider and F. Kunau, *Ber.*, 1921, **54B**, 2302; M. Akram and R. D. Desai, *Proc. Indian Acad. Sci.*, 1940, **A11**, 149.
[14] I. M. Hunsberger, H. S. Gutosky, W. Powell, L. Morin, and V. Bandurco, *J. Amer. Chem. Soc.*, 1958, **80**, 3294.
[15] K. Fries and K. Schimmelschmidt, *Ber.*, 1925, **58B**, 2835.
[16] H. Wahl, *Compt. rend.*, 1938, **206**, 521.

[17] D. V. Nightingale and H. B. Hucker, *J. Org. Chem.*, 1953, **18**, 1529.
[18] D. V. Nightingale and J. M. Shackelford, *J. Amer. Chem. Soc.*, 1956, **78**, 133.
[19] G. A. Reynolds and C. R. Hauser, *Org. Synth.*, 1963, Coll. Vol. IV, p. 708.
[20] *Cf.* M. Guha and D. Nasipuri, *Org. Synth.*, 1962, **42**, 41.