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CYCLOHEXADIENONES. 5. REACTION OF 4-HALO-2,4,6-TRI-t-BUTYL-2,5-CYCLOHEXADIEN-1-ONES WITH IMIDAZOLES[1]

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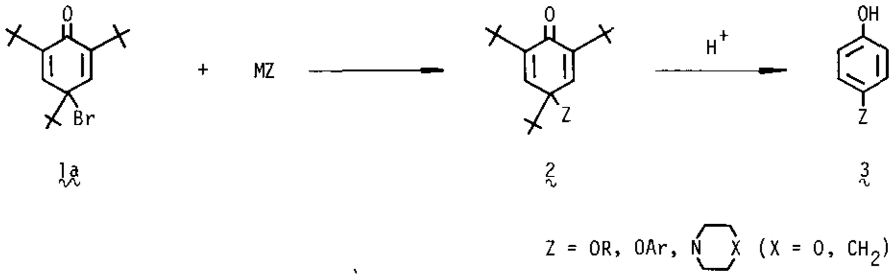
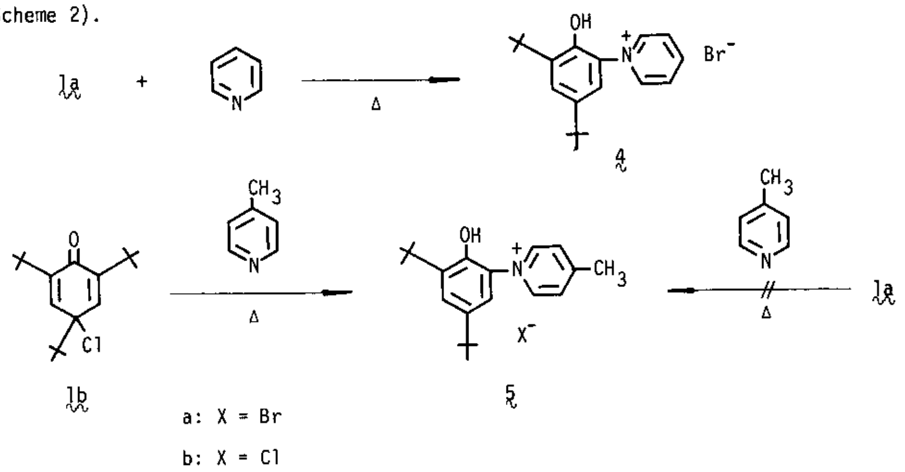
Abstract —— Reactions of 4-bromo-(1a) and 4-chloro-2,4,6-tri-t-butyl-2,5-cyclohexadien-1-one (1b) with imidazole (6b), 1-methyl-(6a), 2-methyl-(6c), 4-methylimidazole (6d), benzimidazole (6e), and 2-methylbenzimidazole (6f) were carried out under various conditions. It was found in these reactions that many products such as the 1-(4-oxo-2,5-cyclohexadienyl)-, 1-(2-hydroxyphenyl)- and 1-(4-hydroxyphenyl)imidazoles were formed and that the type of the products depended upon the structures of imidazoles 6.

It has been previously reported that 4-bromo-2,4,6-tri-t-butyl-2,5-cyclohexadien-1-one (1a) reacted with alcohols,[2] sodium phenolates,[3] amines such as piperidine and morpholine,[4] and sodium azide[5] to give the corresponding 4-substituted 2,4,6-tri-t-butyl-2,5-cyclohexadien-1-ones (2) which were easily leaded to 4-substituted phenols (3) except 4-azidophenol by the acid-catalyzed trans- or dealkylation.



Scheme 1

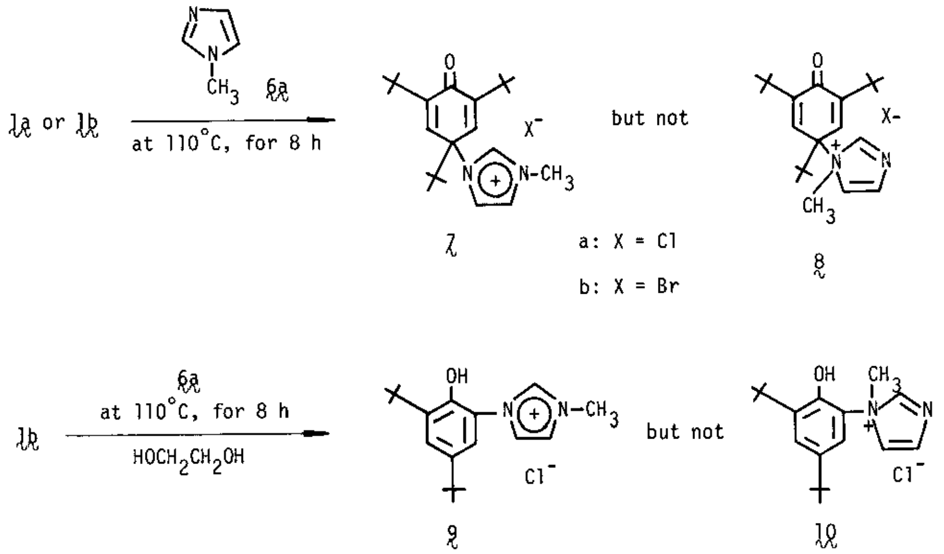
On the other hand, the reaction of 1a with pyridine afforded 1-(3,5-di-t-butyl-2-hydroxyphenyl)-pyridinium bromide.[6] It was also found in this reaction that addition of ethylene glycol increased the yield of 4. However, the reaction of 1a with γ-picoline did not give the expected 5a in the presence or absence of ethylene glycol. In contrast 1a, 4-chloro-2,4,6-tri-t-butyl-2,5-cyclohexadien-1-one (1b) reacted with γ-picoline in the presence of ethylene glycol to afford the expected 5b[7] (Scheme 2).



Scheme 2

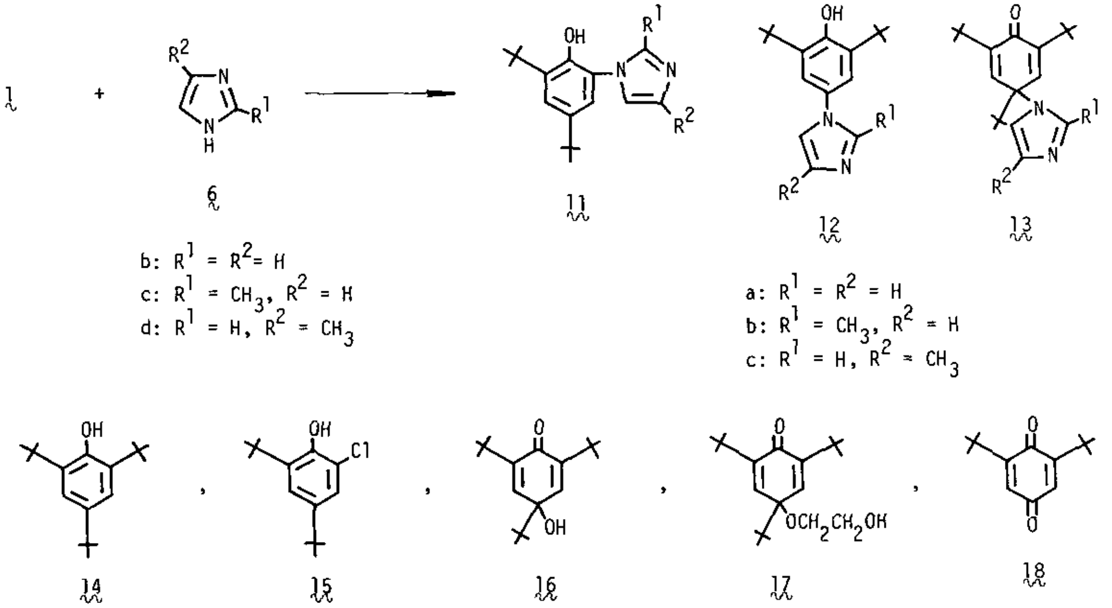
In the present work, the reactions of 1a and 1b with imidazoles 6 were investigated to see what products were formed.

When 1a and 1b were heated with 1-methylimidazole (6a) at 110°C (temperature of oil bath) for 8 h in the absence of ethylene glycol, compounds 7 were obtained in 52% and 57% yields, respectively. The structure of 7 was proposed by elemental analysis as well as spectral data[8] as 1-(1,3,5-tri-t-butyl-4-oxo-2,5-cyclohexadienyl)-3-methylimidazolinium halides (Scheme 3).



Scheme 3

On the contrary, the reaction of 1b with 6a in the presence of ethylene glycol gave in 35% yield a different product 9 which was confirmed by its elemental analysis and spectral data[9] as 1-(3,5-di-t-butyl-2-hydroxyphenyl)-3-methylimidazolinium chloride. However, it is not clear why such different results are obtained. Although there are the other possible structures, 8 and 10, for the products, 7 and 9, respectively, they should be omitted by the following considerations: i) the formers must be less stable than that of the latters since 8 and 10 could not be stabilized by resonance; ii) the formers might be more sterically hinder than the latters, respectively.



b: $R^1 = R^2 = H$
c: $R^1 = CH_3$, $R^2 = H$
d: $R^1 = H$, $R^2 = CH_3$

a: $R^1 = R^2 = H$
b: $R^1 = CH_3$, $R^2 = H$
c: $R^1 = H$, $R^2 = CH_3$

Scheme 4

Table 1. Reaction of 1 with Imidazoles (6b-6d).[a)]

Run	1	Imidazole	Time (h)	Product (%)[c)]
1	1a	6b	6	11a (24), 13a (18), 14 (40), 18 (5)
2	1b	6b	9	11a (15), 13a (43), 14 (1), 15 (6), 16 (2)
3[b)]	1b	6b	8.5	11a (7), 13a (22), 14 (1), 15 (6), 16 (2), 17 (17)
4	1b	6c	6.5	11b (3), 12b (49), 13b (5), 14 (4), 15 (15), 16 (1)
5[b)]	1b	6c	3.0	11b (13), 12b (7), 13b (16), 14 (7), 15 (10), 17 (21)
6	1b	6d	6.0	11c (28), 13c (27), 14 (6), 15 (5), 16 (19)

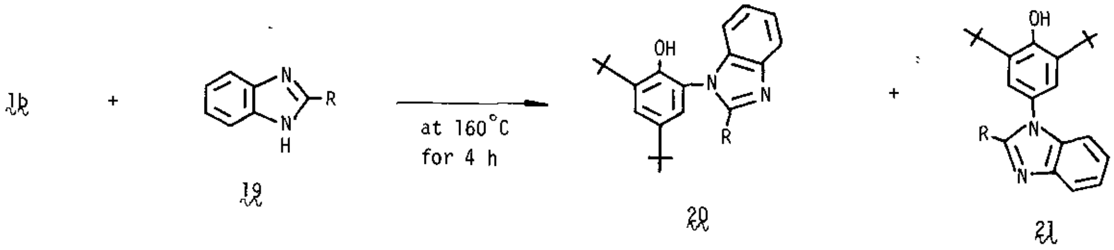
a) A mixture of 1 and 6 was heated without solvent at 110°C unless otherwise indicated.

b) Ethylene glycol (one mole per one mole of 1) was added. c) The isolated yields are shown.

The results of the reactions of 1 with the other imidazoles 6b-6d are summarized in Table 1 and Scheme 4.

The data of Table I show that the reactions of 1a and 1b with imidazole (6b) itself afforded 1-(1,3,5-tri-t-butyl-4-oxo-2,5-cyclohexadienyl)-(13a)[10] and 1-(3,5-di-t-butyl-2-hydroxyphenyl)imidazole (11a)[11,19] together with by-procuts such as 14, 15,[12] 16,[6] 17,[1,2] and 18[6] which are known compounds. However, in the reaction of 1b with 6c, 1-(3,5-di-t-butyl-4-hydroxyphenyl)-2-methylimidazole (12b)[13] was obtained in 49% yield as a main product. In the above reactions, addition of ethylene glycol decreased the yields of the main products such as 11, 12, and 13. The reaction with 6d gave 11c[14] and 13c[15] but not 12c.

It was also found that the reaction of 1b with benzimidazole (19a) at 160°C for 4 h afforded 1-(3,5-



a: R = H
b: R = CH_3

Table 2. Melting points and Appearances of the products.[a)]

Compound	Mp.(°C)[b)]	Appearance (Solvent)	Compound	Mp.(°C)[b)]	Appearance (Solvent)
7a	ca.180 (d.)	colorless needles (benzene)	13a	120-123	colorless needles (hexane)
7b	ca.200 (d.)	colorless needles (benzene)	13b	115-116	colorless prisms (hexane)
9	> 290	colorless prisms (hexane)	13c	181-183	colorless plates (hexane)
11a	202-203	colorless needles (benzene/hexane)	20a	215-217	colorless prisms (methanol/water)
11b	206-208	colorless needles (methanol/water)	20b	244-245	colorless prisms (hexane)
11c	219-220	colorless prisms (hexane)	21a	169-171	colorless prisms (methanol/water)
12b	212-213	pale yellow prisms (methanol/water)			

a) The micro analyses for all products were in satisfactory agreement with the calculated values (C ± 0.30, H ± 0.30, N ± 0.30). b) Uncorrected.

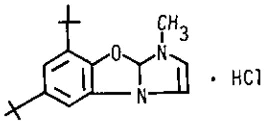
di-t-butyl-2-hydroxyphenyl)-(**20a**)[16,19] and 1-(3,5-di-t-butyl-4-hydroxyphenyl)benzimidazole (**21a**)[17] were obtained in 50% and 6% yields, respectively. The reaction with 2-methylbenzimidazole (**19b**) gave 1-(3,5-di-t-butyl-2-hydroxyphenyl)-2-methylbenzimidazole (**20b**)[18] in 23% yield but not the expected **21b**.

The structures of the products **11**, **12**, **13**, **20**, and **21** were confirmed by means of their elemental analyses and spectral data. The melting points and appearances of the main products obtained are summarized in Table 2.

As mentioned above, the different type of imidazoles sometimes gave different type of the products. Unfortunately, it is still obscure why such different results are obtained.

REFERENCES AND NOTES

1. Part 4. G. Fukata and M. Tashiro, submitted in *J. Org. Chem.*.
2. M. Tashiro, G. Fukata, and H. Yoshiya, *Synthesis*, 1979, 988.
3. M. Tashiro, H. Yoshiya, and T. Yamato, *Synthesis*, 1978, 399.
4. M. Tashiro and G. Fukata, *Synthesis*, 1979, 602.
5. G. Fukata, N. Sakamoto, and M. Tashiro, *Heterocycles*, **14**, 1259 (1980).
6. M. Tashiro and G. Fukata, *Heterocycles*, **12**, 1551 (1979).
7. M. Tashiro. G. Fukata, and T. Itoh, submitted in *J. Org. Chem.*, **5b**: mp. ca.240°C (d.), colorless prisms (benzene), ^{1}H-nmr (CDCl$_3$): δ 1.28, 1.44 (each 9H, s), 1.80 (1H, br: disappeared with D$_2$O), 2.68 (3H, s), 6.92, 7.48 (each 1H, d, J = 2 Hz), 7.96, 8.66 (each 2H, d, J = 7 Hz).
8. **7a**: IR (KBr): ν_{max} = 1670, 1645 cm^{-1}. ^{1}H-nmr (CDCl$_3$): δ 1.05 (9H, s), 1.30 (18H, s), 4.24 (3H, s), 7.08 (2H, s), 7.45 (1H, d.d, J = 1.8 and 2.2 Hz), 7.72 (1H, d.d, J = 1.0 and 2.2 Hz), 11.06 (1H, d.d, J = 1.0 and 1.8 Hz). ^{1}H-nmr (DMSO-d$_6$): δ 0.96 (9H, s), 1.25 (18H, s), 3.93 (3H, s), 7.20 (2H, s), 7.84-7.94 (1H, m), 8.32-8.42 (1H, m), 10.00 (1H, br.s).
   7b: IR (KBr): ν_{max} = 1670, 1645 cm^{-1}. ^{1}H-nmr (CDCl$_3$): δ 1.07 (9H, s), 1.31 (18H, s), 4.28 (3H, s), 7.08 (2H, s), 7.44 (1H, d.d, J = 1.8 and 2.2 Hz), 7.68 (1H, d.d, J = 1.0 and 2.2 Hz), 11.10 (1H, d.d, J = 1.0 and 1.8 Hz).
9. **9**: IR (KBr): ν_{max} = 2700, 2580 cm^{-1}. ^{1}H-nmr (CDCl$_3$): δ 1.27, 1.40 (each 9H, s), 4.05 (3H, s), 6.95 (1H, d, J = 2.5 Hz), 7.23 (1H, s), 7.27 (1H, d, J = 2 Hz), 7.40 (1H, d, J = 2.5 Hz), 7.50 (1H, d, J = 2 Hz), 9.50 (1H, br.s: disappeared with D$_2$O). ^{1}H-nmr (DMSO-d$_6$): δ 1.26, 1.40 (each 9H, s), 3.92 (3H, s), 7.22, 7.36 (each 1H, d, J = 2.5 Hz), 7.80-7.90 (2H, m), 9.32 (1H, br.s: disappeared with D$_2$O), 9.40-9.52 (1H, m).
   Structure **9**' might also be considered for the methyl imidazolinium chloride **9**. A clear distinction between structures **9** and **9**' is not possible on the basis of the presently available data.



9'

10. 13a: IR (KBr): ν_{max} = 1670, 1650 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 1.00 (9H, s), 1.28 (18H, s), 7.00 (2H, s), 7.09, 7.14 (each 1H, d, J = 1 Hz), 7.69 (1H, br.s). Mass: m/e 328 (M^+).

11. 11a: IR (KBr): ν_{max} = 2780, 2550 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 1.29, 1.48 (each 9H, s), 6.90 (1H, d, J = 2.5 Hz), 6.92, 7.03, 7.29 (each 1H, br.s), 7.37 (1H, d, J = 2.5 Hz). Mass: m/e 272 (M^+).

12. M. Tashiro, H. Yoshiya, and G. Fukata, submitted in *J. Org. Chem.*, 15: colorless oil, bp. 112.5-113°C/2 mm.

13. 12b: IR (KBr): ν_{max} = 3440, 2630, 2490 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 1.44 (18H, s), 2.31 (3H, s), 5.48 (1H, br.s: disappeared with D_2O), 6.94, 6.96 (each 1H, d, J = 1.5 Hz), 7.02 (2H, s). Mass: m/e 286 (M^+).

14. 11c: IR (KBr): ν_{max} = 2680, 2550 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 1.28, 1.49 (each 9H, s), 2.06 (3H, d, J = 0.8 Hz), 6.65 (1H, d.d, J = 0.8 and 1.2 Hz), 6.90 (1H, d, J = 2.5 Hz), 7.10 (1H, d, J = 0.8 Hz), 7.37 (1H, d, J = 2.5 Hz).

15. 13c: IR (KBr): ν_{max} = 1670, 1645 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 0.99 (9H, s), 1.27 (18H, s), 2.23 (3H, d, J = 0.8 Hz), 6.80 (1H, d.d, J = 0.8 and 1.2 Hz), 6.93 (2H, s), 7.52 (1H, d, J = 1.2 Hz). Mass: m/e 342 (M^+).

16. 20a: IR (KBr): ν_{max} = 2700, 2550 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 1.29, 1.37 (each 9H, s), 6.88, 7.47 (each 1H, d, J = 2.5 Hz), 7.09-7.27 (4H, m), 7.38-7.48 (1H, m). Mass: m/e 322 (M^+).

17. 21a: IR (KBr): ν_{max} = 3300 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 1.28 (18H, s), 5.44 (1H, br.s: disappeared with D_2O), 7.24 (2H, s), 7.22-7.30 (3H, m), 7.80-7.90 (1H, m), 8.04 (1H, s). Mass: m/e 322 (M^+).

18. 20b: IR (KBr): ν_{max} = 2670, 2550 cm^{-1}. ^{1}H-nmr ($CDCl_3$): δ 1.29, 1.52 (each 9H, s), 1.92 (3H, s), 6.80 (1H, d, J = 2.5 Hz), 7.02-7.29 (3H, m), 7.44 (1H, d, J = 2.5 Hz), 7.43-7.52 (1H, m). Mass: m/e 336 (M^+).

19. Although the hydroxy protons of 11a and 20a were not observed in the region of δ 0-15 ppm, their acetylations with acetic anhydride under mild conditions gave expected acetyl derivatives in quantitative yields, respectctively.

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