SYNTHESIS OF tert-BUTYL- AND TRIFLUOROACETYL-SUBSTITUTED CARBAZOLES

N. V. Moskalev

UDC 547.759.32

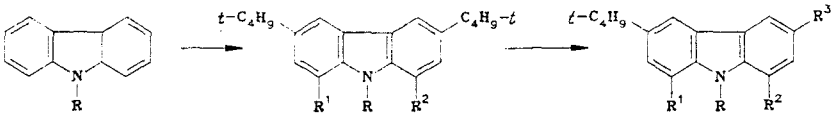
It has been shown that carbazole and its N-alkyl substituted derivatives are readily alkylated by a mixture of t-BuOH–CF_3COOH to form 1,3,6,8-tetra- and 3,6-di(tert-butyl)-substituted carbazoles, respectively. Trifluoroacetylation of these compounds leads to 1-trifluoroacetylated compounds but 1,3,6,8-tetra(tert-butyl)carbazole undergoes ipso- substitution to form the 3-trifluoroacetyl derivative.

1,3,6,8-Tetra(tert-butyl)carbazole (IId) is of interest in the chemistry of stable radicals [1, 2]. It is obtained by a Friedel-Crafts reaction which gives a mixture of alkyl substituted products from which the desired compound can be obtained in 68% yield [2].

We have found that the mixture of t-C_4H_9OH–CF_3COOH used for alkylation of anthracene [3] also proves effective for carbazole. Refluxing the 9-H carbazole Id with this mixture gives IId in quantitative yield. 9-Methyl- (Ia), 9-isopropyl- (Ib), and 9-allyl-carbazole (Ic) form only the corresponding 3,6-dialkyl derivatives IIa-c but 9-methyl-3-trifluoroacetylcarbazole (IV) is readily alkylated to give 9-methyl-3-trifluoroacetyl-6-tert-butylcarbazole (V).

It is known that carbazole itself is exclusively alkylated at the nitrogen atom [4] using trifluoroacetic anhydride but for 9-alkyl-carbazoles this occurs at ring positions 3 and 6 [5].

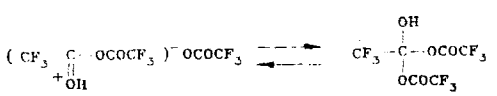
Introduction of an acyl fragment into carbazole substituted both at the nitrogen atom and at positions 3 and 6 which are most sensitive to electrophilic attack can easily be investigated in the case of the trifluoroacetyl compounds IIa-d.



Ia-d IIa-d IIIa-d,e

a R=CH_3, b R=i-C_3H_7, c R=$CH_2CH{=}CH_2$; Id, IId, IIId, e R=H; IIa–c $R^1{=}R^2{=}H$; IId, IIId $R^1{=}R^2{=}t$-C_4H_9; IIIa-c,e $R^1{=}H$, $R^2{=}COCF_3$, $R^3{=}t$-C_4H_9, d $R^3{=}COCF_3$

It was found that reaction of IIa-d with trifluoroacetic anhydride occurs only under forcing conditions. The NH group of IId remains free but substitution occurs at the 3(6)-tert-butyl group. This reaction course is in agreement with data concerning the greater reactivity of the 3(6) position when compared with the 1(8) position in carbazoles. In contrast to ipso- substitution in nitration [2] it probably occurs via nitronium cations, introduction of CF_3CO preceding protodealkylation of IId with CF_3COOH. In line with data in [6], trifluoroacetylation of heteroaromatics in analogous conditions is brought about not by the CF_3CO^+ cation but by the comparatively bulky and weakly electrophilic ion paired molecular form.



In our view, this direct ipso- substitution of a tert-butyl group involving overcoming considerable steric strain in the corresponding transition state is less preferred than proto-

S. M. Kirov Polytechnic Institute, Tomsk 634004. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 187-189, February, 1990. Original article submitted October 13, 1987; revision submitted June 12, 1989.

 0009-3122/90/2602-0158$12.50

dealkylation. The following facts support this hypothesis: a) even at room temperature IId in CF_3COOH in dichloroethane slowly forms a tert-butyl substituted mixture; b) 9-methylcarbazole is demethylated [7] whereas 9-methyl-3-halocarbazoles are dehalogenated [8] by CF_3COOH.

Compounds IIa-c are converted to the corresponding 1-trifluoroacetyl derivatives IIIa-c. Trifluoroacetylation of IIb forms both the expected IIIb and significant amounts of 3,6-di-(tert-butyl)-1-trifluoroacetylcarbazole IIIe (the product of dealkylation of IIIb).

The results obtained point to the preferred attack by the electrophile at the free position 1 of the ring when compared with ipso-substitution of the alkyl group at position 3(6). The trifluoroacetylated derivatives IIIa-e can be converted by means of dealkylation using known methods [9] or via fluoroform decomposition of the $COCF_3$ group in the corresponding carboxylic acids [10]. Thus tert-butylation of N-alkyl-substituted carbazoles by a mixture of $t\text{-}C_4H_9OH$–CF_3COOH followed by treatment with an electrophilic reagent can be used as a reliable method of introducing substituents into the 1- position of the carbazole ring.

EXPERIMENTAL

IR Spectra were recorded on a UR-20 instrument as KBr tablets (IIa, IIIa, IV), as thin layers (IIIb-d), or in nujol (remaining compounds). PMR Spectra were recorded on a Tesla BS-487C instrument (100 MHz) in CCl_4 (IIa-d and IV in $CDCl_3$) with HMDS as internal standard.

The reaction course was monitored by TLC on Silufol plates eluting with toluene-heptane (1:3). Reaction mixtures were separated by column chromatography on grade II Al_2O_3. Compounds were recrystallized from isopropanol. Elemental analytical data for C, H, N, and F agreed with those calculated.

9-Methyl-3,6-di(tert-butyl)carbazole (IIa, $C_{21}H_{27}N$). A mixture of Ia (1.8 g, 10 mmole), $t\text{-}C_4H_9OH$ (9 ml, 100 mmole), and CF_3COOH (14 ml, 200 mmole) were refluxed for 40 min, evaporated to half volume, and cooled to 0°C. The crystalline precipitate was filtered off, washed with water (2 × 10 ml), $NaHCO_3$ solution, again with water, and dried in air to give IIa (2.8 g, 96%) with mp 101-102°C. IR spectrum: 810, 750 cm^{-1} (C–H). PMR spectrum: 1.45 (18H, s, 3,6-t-C_4H_9); 3.50 (3H, s, N–CH_3); 6.95 (2H, d, J_{12} = 9 Hz, 1-H, 8-H); 7.30 (2H, dd, J_{21} = 9 Hz, J_{24} = 2 Hz, 2-H, 7-H); 7.95 ppm (2H, d, J_{57} = 2 Hz, 4-H, 5-H).

9-Isopropyl-3,6-di(tert-butyl)carbazole (IIb, $C_{23}H_{31}N$). Prepared similarly to the above from Ib (2.1 g, 10 mmole) to give IIb (3.0 g, 95%) with mp 185-186°C. IR spectrum: 810, 750 cm^{-1} (C–H). PMR Spectrum: 1.43 (18H, s, 3,6-t-C_4H_9); 1.65 (6H, d, J = 7 Hz, i-C_3H_7); 4.86 (1H, m, i-C_3H_7); 7.40 (4H, m, 1-H, 2-H, 7-H, 8-H); 8.05 ppm (2H, m, 4-H, 5-H).

9-Allyl-3,6-di(tert-butyl)carbazole (IIc, $C_{23}H_{29}N$). Prepared similarly by alkylation of Ic (2.1 g, 10 mmole) for 3 h. The reaction mixture was worked up as for IIa to give IIc (1.65 g, 80%) with mp 133-134°C. IR Spectrum: 890, 810, 750 cm^{-1} (C–H). PMR Spectrum: 1.45 (18H, s, 3,6-t-C_4H_9); 5.0 (4H, m, $-CH_2CH{=}CH_2$); 5.90 (1H, m, $-CH_2-CH_2{=}CH_2$); 7.18 (2H, d, J_{12} = 8 Hz, 1-H, 8-H); 7.45 (2H, dd, J_{21} = 8 Hz, J_{24} = 2 Hz, 2-H, 7-H); 8.07 ppm (2H, d, J_{57} = 2 Hz, 4-H, 5-H).

1,3,6,8-Tetra(tert-butyl)carbazole (IId, $C_{28}H_{41}N$). Similarly to IIa from carbazole Id (1.67 g, 10 mmole) to give IId (3.9 g, 100%) with mp 191-192°C. IR Spectrum: 3535 (N–H), 3010-2880 cm^{-1} (C–H). PMR Spectrum: 1.42 (18H, s, 3,6-t-C_4H_9); 1.54 (18H, s, 1,8-t-C_4H_9); 7.35 (2H, s, 2-H, 7-H); 7.90 (2H, s, 4-H, 5-H); 8.08 ppm (1H, s, NH).

9-Methyl-3,6-di(tert-butyl)-1-trifluoroacetylcarbazole (IIIa, $C_{23}H_{26}F_3NO$). A mixture of IIa (0.29 g, 1 mmole), $(CF_3CO)_2O$ (0.4 ml, 3 mmole), and 1,2-dichloroethane (4 ml) were heated in a sealed ampul for 8 h at 130°C. After cooling, the ampul was opened, the contents washed with water, the ether layer separated, dried with $CaCl_2$ and chromatographed on a 1 × 20 cm column (eluent benzene–hexane 1:3) to give IIIa as a yellow oil (0.25 g, 63%). IR Spectrum: 3000-2880 (C–H), 1710 (C=O), 1200-1150 cm^{-1} (C–F). PMR Spectrum: 1.41 (9H, s, 6-t-C_4H_9); 1.51 (9H, s, 3-t-C_4H_9); 3.65 (3H, s, NCH_3); 7.20 (1H, d, J_{87} = 8 Hz, 8-H); 7.47 (1H, dd, J_{78} = 8 Hz, 7-H); 7.95 (2H, m, 4-H, 5-H); 8.30 ppm (1H, d, J_{24} = 2 Hz, 2-H).

9-Isopropyl-3,6-di(tert-butyl)-1-trifluoroacetylcarbazole (IIIb, $C_{25}H_{30}F_3NO$). Similarly, to IIIa by trifluoroacetylation of the tert-butyl substituted IIb (0.32 g, 1 mmole). Column chromatographic separation of the mixture (2 × 40 cm, eluent benzene–hexane 1:10) gave IIIb as a yellow oil (0.26 g, 63%) with R_f 0.43. IR Spectrum: 3000-2870 (C–H), 1700 (C=O), 1210,

1150 cm^{-1} (C–F). PMR Spectrum: 1.45 (9H, s, 6-t-C_4H_9); 4.55 (1H, m, i-C_3H_7); 7.30 (1H, m, 8-H); 7.45 (1H, m, 7-H); 7.94 (2H, m, 4-H, 5-H); 8.25 ppm (1H, d, J_{24} = 2 Hz, 2-H).

9-Allyl-3,6-di(tert-butyl)-1-trifluoroacetylcarbazole (IIIc, $C_{25}H_{28}F_3NO$). Synthesis similarly to IIIa from IIc (0.32 g, 1 mmole) gave ketone IIIc (0.34 g, 82%) as a yellow oil. IR Spectrum: 3000-2870 (C–H), 1710 (C=O), 1210,1150 cm^{-1} (C–F). PMR Spectrum: 1.42 (9H, s, 6-t-C_4H_9); 1.47 (9H, s, 3-t-C_4H_9); 4.80 (4H, m, $-CH_2-CH=CH_2$); 5.45 (1H, m, 2-$CH_2-CH=CH_2$); 7.20 (2H, m, 4-H, 5-H); 8.30 ppm (1H, d, J_{24} = 2 Hz, 2-H).

1,3,8-Tri(tert-butyl)-6-trifluoroacetylcarbazole (IIId). Similarly to IIIa from tert-butyl substituted IId (0.39 g, 1 mmole) to give ketone IIId (0.37 g, 87%) with mp 128-129°C. IR Spectrum: 3485 (N–H), 2980-2880 (C–H), 1680 (C=O), 1205-1160 (C–F); 725, 680 cm^{-1} (C–H). PMR Spectrum: 1.52 (9H, s, 1-t-C_4H_9); 1.57 (9H, s, 3-t-C_4H_9); 7.42 (1H, d, J_{24} = 2 Hz, 2-H) 7.87 (1H, J_{42} = 2 Hz, 4-H); 8.05 ppm (1H, m, 7-H).

3,6-Di(tert-butyl)-1-trifluoroacetylcarbazole (IIIe, $C_{22}H_{24}F_3NO$). Chromatographic separation of IIIb also gave IIIe (0.15 g, 40%) with mp 129-130°C and R_f 0.36. IR Spectrum: 3425 (N–H), 1670 (C=O), 1220-1155 (C–F), 830, 720 cm^{-1}. PMR Spectrum: 1.45 (9H, s, 6-t-C_4H_9); 1.50 (9H, s, 3-t-C_4H_9); 7.40 (2H, m, 7-H, 8-H); 8.02 (2H, m, 4-H, 5-H); 8.35 ppm (1H, d, J_{24} = 2 Hz, 2-H).

9-Methyl-3-trifluoroacetyl-6-tert-butylcarbazole (V). Alkylation of ketone IV (2.7 g, 10 mmole) under the same conditions as for IIa gave ketone V (3.1 g, 95%) with mp 164-165°C. IR Spectrum: 2900-2850 (C–H), 1700 (C=O), 1240-1100 cm^{-1} (C–F). PMR Spectrum: 1.45 (9H, s, 3-t-C_4H_9); 3.81 (3H, s, NCH_3); 7.32 (1H, d, J_{12} = 8.5 Hz, 8-H); 7.60 (1H, d, J_{21} = 8.5 Hz, J_{24} = 2 Hz, 2-H); 8.12 (1H, m, 7-H); 8.18 ppm (1H, m, 4-H).

LITERATURE CITED

1. A. L. Buchachenko and A. M. Vasserman, Stable Radicals, Electronic Structure, Reactivity and Uses [Russian translation], Khimiya, Moscow (1973), p. 209.
2. F. A. Neugebauer and H. Fisher, Chem. Ber., 105, 2686 (1972).
3. Yu. V. Pozdnyakovich, Zh. Org. Khim., 22, 590 (1986).
4. A. Cipiciani, S. Clementi, P. Linda, G. Savelli, and G. V. Sebastiani, Tetrahedron, 32, 2595 (1976).
5. E. E. Sirotkina, N. V. Moskalev, and I. G. Shabotkin, Khim. Geterotsikl. Soedin., No. 5, 640 (1984).
6. S. Alunni and S. Clementi, J. Chem. Soc., Perkin Trans. 2, No. 11, 1521 (1972).
7. N. V. Moskalev and E. E. Sirotkina, Khim. Geterotsikl. Soedin., No. 3, 329 (1987).
8. N. V. Moskalev and E. E. Sirotkina, Khim. Geterotsikl. Soedin., No. 11, 1492 (1987).
9. D. McOmie, Protective Groups in Organic Chemistry [Russian translation], Mir, Moscow (1976), p. 34.
10. R. K. Mackie, S. Mhatre, and J. M. Tedder, J. Fluor. Chem., No. 4, 437 (1977).