**Effect of substituents on the 13C - NMR chemical shifts of substituted 5-benzylidene barbituric acids**

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**ABSTRACT**

Substituted 5-benzylidene barbituric acids have been prepared and characterized by 1H and 13C NMR spectral analysis. Investigation of substituents effect and mode of transmission of electronic effects have been carried out by 13C NMR chemical shifts measurement, correlated it with LFER parameters in substituted 5-benzylidene barbituric acids.

**Key words:** 1H, 13C NMR,substituted 5-benzylidene barbituric acids, substituent effects.

**INTRODUCTION**

**EXPERIMENTAL**

All chemicals used were purchased from Sigma Aldrich. Purity of the compounds was checked by TLC on silica gel G plate. 1H and 13C spectra were obtained on a BRUKER AMX 400 MHz spectrometer. Chemical shift of 1H were measured with the peak of DMSO at δ 2.51 as the internal reference, while those of 13C were recorded with the central peak of DMSO at δ 39.90 as the internal reference.

**General procedure for the synthesis of 5-benzylidenebarbituric acids (1 to 7)**

5-benzylidenebarbituric acid and its substituted compounds (1 to 7) were prepared by the modified procedure of Branko Jursic(2001) [12].

To the calculated amount of the pure benzaldehyde (2 g, 0.015 mol) and barbituric acid (1.55g, 0.015 mol) in warm ethyl alcohol was added a 10% solution of sodium hydroxide (catalytic amount) and the reaction mixture stirred for 2 hours. After completion of the reaction as indicated by TLC, the reaction mixture was left overnight (scheme I). Solid product was separated by filtration and washed several times with cold methanol.



Scheme I: Synthesis of 5-benzylidenebarbituric acids.

Spectral analysis of compounds (1 to 7)



Compound 1*: 5-(4’-methoxybenzylidene)barbituric acid*

1H NMR: δ 3.877 (s,3H), 7.065 (d,2H), 8.252(s,1H), 8.369 (d,2H), 11.175 (s,1H), 11.302 (s,1H);13C NMR: δ 56.22,114.41,116.00,125.62,137.96,150.67,155.46,162.64,163.92,164.39.

Compound 2: *5-(4’-hydroxybenzylidene)barbituric acid*

1H NMR: δ 6.878 (d,2H), 8.213 (s,1H), 8.320 (d,2H), 10.851 (s,1H), 11.117(s,1H), 11.249 (s,1H);

13C NMR: δ 114.61, 115.97, 124.24, 138.77, 150.70, 156.05,162.75,163.48,164.59.

Compound 3: *5-(4’-methylbenzylidene)barbituric acid*

1H NMR: δ 2.385 (s,3H), 7.304 (d,2H), 8.094 (d,2H), 8.255 (s,1H), 11.218 (s,1H), 11.365 (s,1H);

13C NMR: δ 118.30, 129.33, 130.31, 134043, 143.96, 150.68, 155.46, 162.26, 164.08.

Compound 4: *5-benzylidenebarbituric acid*

1H NMR: δ 7.485 (m,3H), 8.073 (d,2H), 8.285 (s,1H), 11.238 (s,1H), 11.397 (s,1H);

13C NMR: δ 119.55, 128.52, 132.69, 133.11, 133.54, 150.69, 155.20, 162.03, 163.87.

Compound 5: *5-(4’-chlorobenzylidene)barbituric acid*

1H NMR: δ 7.518 (d,2H), 8.069 (d,2H), 8.243 (s,1H), 11.275 (s,1H), 11.425 (s,1H);

13C NMR: δ 120.09, 128.55, 132.01, 135.15, 137.21, 150.65, 153.52, 162.04, 163.67.

Compound 6: *5-(4’-bromobenzylidene)barbituric acid*

1H NMR: δ 7.670 (d,2H), 7.979 (d,2H), 8.223 (s,1H), 11.272 (s,1H), 11.421 (s,1H);

13C NMR: δ 120.24, 126.29, 131.51, 132.40, 135.15, 150.65, 153.56, 162.04, 163.67.

Compound 7: *5-(4’-nitrobenzylidene)barbituric acid*

1H NMR: δ 8.017 (d,2H), 8.245 (d,2H), 8.324 (s,1H), 11.329 (s,1H), 1.504 (s,1H);

13C NMR: δ 123.15, 123.37, 132.69, 140.48, 148.49, 150.68, 151.63, 161.62, 163.13.

**RESULTS AND DISCUSSION**

**Correlations with Lynch-Equation**

The SCS of monosubstituted benzenes have been very useful in signal assignment of polysubstituted compounds70-73 . However, in many published studies summarized by Craik74 it has been apparent that the SCS values of X and Y at positions 4’ and 1’ in disubstituted benzenes Fig. (25) are non-additive. Lynch75 has proposed that the non-additivity of the chemical shifts of C-1’ and C-4’ is reflected in the relationship Eq. (25) where SCSX(Y) is the substituent chemical shift of the 

Fig. (25)

SCSX (Y) = a + b [ SCSX (H)] ( 25)

carbon *para-*to X in the series of 1’,4’-disubstituted benzenes (Fig. 25, X, Y ≠ H), SCSX(H) is the corresponding substituent chemical shift of the carbon *para* to X in monosubstituted benzenes (Fig. 25, Y=H), ‘b’ is the slope parameter and ‘a’ is the shift calculated for the parent spices with X=Y. A wide range of successful correlations (using Lynch equation) have been established for the SCS of carbons bearing Y in Fig. (25) with the value of ‘b’ ranging from 0.6 to 1.542. When the slope is close to unity, experimental results could be reproduced by additivity relationship and when b ≠ 1, the Lynch equation can be used to predict the SCS values through proportionality relationships. The slope b of the Lynch equation Eq. (25) is less than one, then the fixed substituent at C-1’ Fig (25) diminishes the substituent effect. When slope b is larger than one, showing that the fixed substituent undergoes an amplification of the substituent effect.

In case of C1 there is satisfactory correlation with (r=0.988) appropriate SCS (Si) values, slope b is 0.97, which reveals that the fixed substituent Y=-CH-C-C3H2N2O3, has little effect on the additivity of this shifts42.

A satisfactory correlation exists between SCS of C22’ and So with correlation coefficient (r=0.828) and the slope value (b=0.84), indicating that the fixed substituent Y, significantly diminishes the substituent effect42.

A poor correlation exists between SCS of C33’ and Sm with correlation coefficient (r=0.113) and the slope value (b=0.71) which reveals that the fixed substituent Y diminishes the substituent effect42.

The C4 carbon afford a good correlation with Sp with correlation coefficient r=0.993 and the slope value b=0.94 demonstrates that the fixed substituent Y has little effect on the additivity of these shifts42. The results of Lynch correlations are given in table (6) and the plots of Lynch correlations shown in fig. (26) and ((27)

**Table ( 6 ) : Results of Lynch correlationsa of 13C chemical shifts of compound fig ( ) with SCS values for mono substituted benzenes.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| S.No. | Carbons | Benzene  SCS  (Sb) | Slope  (b) | Intercept  (a) | rc | nd | Se |
| 1. | C1 | Si | 0.97 | 132.23 | 0.988 | 6 | 2.17 |
|  |  |  |  |  |  |  |  |
| 2. | C22’ | SO | 0.84 | 129.73 | 0.828 | 6 | 4.14 |
|  |  |  |  |  |  |  |  |
| 3. | C33’ | Sm | 0.71 | 132.69 | 0.113 | 6 | 5.63 |
|  |  |  |  |  |  |  |  |
| 4. | C4 | Sp | 0.94 | -126.43 | 0.993 | 6 | 0.61 |

1. SCSX (Y) = a + b SCSX (H)
2. SCS values in Appendix (I)
3. Correlation coefficient
4. Number of data points
5. Standard deviations



**Fig. (26 ).** Lynch plot of SCS of C1 vs Si



**Fig. (27 ).** Lynch plot of SCS of C4 vs Sp

**Table (5): 13C NMR chemical shifts of substituted 5-benzylidenebarbituric acids**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S.No.** | **GROUP** | **C1** | **C22’** | **C33’** | **C4** | **C5** | **C6** | **C7** | **C9** | **C11** |
|  |  |  |  |  |  |  |  |  |  |  |
| 1 | -OCH3 | 162.64 | 114.41 | 137.96 | 125.62 | 155.46 | 116 | 163.92 | 150.67 | 164.39 |
|  |  |  |  |  |  |  |  |  |  |  |
| 2 | -OH | 163.48 | 115.97 | 138.77 | 124.24 | 156.05 | 114.61 | 162.75 | 150.7 | 164.59 |
|  |  |  |  |  |  |  |  |  |  |  |
| 3 | -CH3 | 143.96 | 129.33 | 134.43 | 130.31 | 155.46 | 118.3 | 162.26 | 150.68 | 164.08 |
|  |  |  |  |  |  |  |  |  |  |  |
| 4 | -H | 133.11 | 128.52 | 133.54 | 132.69 | 155.2 | 119.55 | 162.03 | 150.69 | 163.87 |
|  |  |  |  |  |  |  |  |  |  |  |
| 5 | -Cl | 137.21 | 128.55 | 135.15 | 132.01 | 153.52 | 120.09 | 162.04 | 150.65 | 163.67 |
|  |  |  |  |  |  |  |  |  |  |  |
| 6 | -Br | 126.29 | 131.51 | 135.15 | 132.4 | 153.56 | 120.24 | 162.04 | 150.65 | 163.67 |
|  |  |  |  |  |  |  |  |  |  |  |
| 7 | -NO2 | 148.49 | 132.69 | 123.37 | 140.48 | 151.63 | 123.15 | 161.62 | 150.68 | 163.13 |

**Hammett and dual-substituent parameter correlations**

The 13C chemical shifts of the carbon atoms of the 5-benzylidene barbituric acid series afford several reasonable correlations using Hammett substituent parameters Eqn (2) and the data are given in Table ().

*δ = ρσ + δo* (2)

The results of the correlations of 13C SCS values of 5-benzylidene barbituric acid series with *σI* and *σR* constants according to equation

*δ = ρIσI + ρRσR +δo* (3)

are presented in Table ()

**Table ( 7): Results of statistical treatment of 13C – Chemical shift with σp, σpo ,σp+, σp+/ σp, σp+/ σp-,σp+/ σp/ σp-substituent constants using single parameter equation**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S.No.** | **Carbons** | **Scale** | **ρ** | **r** | **s** | **F** | **log δo** | **n** |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| 1 | C4 | *σp* | 0.04±0.006 | 0.949 | 0.006 | 43.33 | 2.11±0.002 | 7 |
|  | *σpO* | 0.038±0.01 | 0.882 | 0.008 | 13.99 | 2.11±0.004 | 6 |
|  | *σp+* | 0.0320.002 | 0.986 | 0.003 | 179.37 | 2.12±0.001 | 7 |
|  | *σp+/ σp* | 0.03±0.006 | 0.924 | 0.007 | 29.11 | 2.12±0.003 | 7 |
|  | *σp+/ σp-* | 0.024±0.002 | 0.989 | 0.003 | 226.34 | 2.12±0.001 | 7 |
|  | *σp+/ σp/ σp-* | 0.026±0.004 | 0.938 | 0.006 | 37.12 | 2.12±0.002 | 7 |
|  |  |  |  |  |  |  |  |  |
| 2 | C5 | *σp* | -0.01±0.001 | 0.984 | 0.001 | 152.18 | 2.19±0.0003 | 7 |
|  | *σpO* | -0.01±0.001 | 0.988 | 0.001 | 163.39 | 2.19±0.0003 | 6 |
|  | *σp+* | -0.007±0.001 | 0.916 | 0.002 | 25.94 | 2.19±0.001 | 7 |
|  | *σp+/ σp* | -0.008±0.002 | 0.887 | 0.002 | 18.40 | 2.19±0.001 | 7 |
|  | *σp+/ σp-* | -0.006±0.001 | 0.938 | 0.002 | 36.47 | 2.18±0.001 | 7 |
|  | *σp+/ σp/ σp-* | -0.006±0.001 | 0.917 | 0.002 | 26.68 | 2.19±0.001 | 7 |
|  |  |  |  |  |  |  |  |  |
| 3 | C6 | *σp* | 0.03±0.004 | 0.950 | 0.004 | 45.95 | 2.07±0.001 | 7 |
|  | *σpO* | 0.02±0.005 | 0.900 | 0.004 | 17.16 | 2.07±0.002 | 6 |
|  | *σp+* | 0.018±0.001 | 0.995 | 0.001 | 508.52 | 2.08±0.0004 | 7 |
|  | *σp+/ σp* | 0.02±0.004 | 0.917 | 0.005 | 26.46 | 2.07±0.002 | 7 |
|  | *σp+/ σp-* | 0.014±0.002 | 0.970 | 0.003 | 80.18 | 2.07±0.001 | 7 |
|  | *σp+/ σp/ σp-* | 0.015±0.003 | 0.902 | 0.005 | 21.75 | 2.07±0.002 | 7 |
|  |  |  |  |  |  |  |  |  |
| 4 | C7 | *σp* | -0.004±0.002 | 0.722 | 0.001 | 5.43 | 2.21±0.001 | 7 |
|  | *σpO* | -0.004±0.002 | 0.620 | 0.002 | 2.51 | 2.21±0.001 | 6 |
|  | *σp+* | -0.003±0.0008 | 0.820 | 0.001 | 10.24 | 2.21±0.0004 | 7 |
|  | *σp+/ σp* | -0.004±0.0007 | 0.917 | 0.001 | 26.41 | 2.21±0.003 | 7 |
|  | *σp+/ σp-* | -0.002±0.001 | 0.775 | 0.001 | 7.51 | 2.21±0.0005 | 7 |
|  | *σp+/ σp/ σp-* | -0.003±0.001 | 0.836 | 0.001 | 11.63 | 2.21±0.0005 | 7 |
|  |  |  |  |  |  |  |  |  |
| 5 | C11 | *σp* | -0.003±0.0003 | 0.979 | 0.0003 | 116.72 | 2.21±0.0001 | 7 |
|  | *σpO* | -0.003±0.0005 | 0.945 | 0.0004 | 33.30 | 2.21±0.0002 | 6 |
|  | *σp+* | -0.002±0.0001 | 0.996 | 0.0001 | 640.41 | 2.21±0.0004 | 7 |
|  | *σp+/ σp* | -0.002±0.0004 | 0.935 | 0.0005 | 34.80 | 2.21±0.002 | 7 |
|  | *σp+/ σp-* | -0.002±0.0001 | 0.983 | 0.0003 | 145.26 | 2.21±.0001 | 7 |
|  | *σp+/ σp/ σp-* | -0.002±0.0003 | 0.930 | 0.0005 | 32.23 | 2.21±0.0002 | 7 |
|  |  |  |  |  |  |  |  |  |
| 6 | C22’ | *σo* | 0.044±0.02 | 0.632 | 0.02 | 3.33 | 2.09±0.008 | 7 |
|  | *σo\** | 0.038±0.02 | 0.691 | 0.02 | 3.66 | 2.09±0.01 | 6 |
|  | *Es* | -0.04±0.013 | 0.825 | 0.016 | 10.69 | 2.13±0.006 | 7 |

**Table (8 ): DSP analysis of chemical shift data with dual parameter equations (16 ) and (17 ).**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S.No** | **Carbons** | **Scale** | ***ρI*** | ***ρR*** | **R** | **SE** | **F** | **log δo** | **n** | **λ=*ρR*/*ρI*** |
|
| 1 | C4 | *σI ,σR* | 0.02±0.003 | 0.005±0.003 | 0.995 | 0.002 | 154.44 | 2.12±0.001 | 6 | 0.25 |
|  |  | *σI ,σRo* | 0.03±0.017 | 0.04±0.016 | 0.849 | 0.01 | 3.89 | 2.12±0.007 | 6 | 1.33 |
|  |  | *σI ,σR+* | 0.01±0.03 | 0.018±0.016 | 0.640 | 0.016 | 1.39 | 2.12±0.015 | 7 | 1.8 |
|  |  | *σI ,σR-* | 0.02±0.01 | 0.04±0.009 | 0.943 | 0.007 | 12.10 | 2.12±0.005 | 6 | 2.0 |
|  |  | *F,R* | 0.025±0.003 | 0.05±0.002 | 0.996 | 0.002 | 279.61 | 2.12±0.001 | 7 | 2.0 |
|  |  |  |  |  |  |  |  |  |  |  |
| 2 | C5 | *σI ,σR* | -0.01±0.001 | -0.007±0.001 | 0.998 | 0.0003 | 349.25 | 2.19±0.003 | 6 | 0.7 |
|  |  | *σI ,σRo* | -0.014±0.003 | -0.005±0.002 | 0.956 | 0.002 | 16.09 | 2.19±0.001 | 6 | 0.36 |
|  |  | *σI ,σR+* | -0.01±0.006 | -0.002±0.003 | 0.838 | 0.003 | 4.74 | 2.19±0.003 | 7 | 0.2 |
|  |  | *σI ,σR-* | -0.012±0.002 | -0.005±0.001 | 0.980 | 0.001 | 36.20 | 2.19±0.001 | 6 | 0.42 |
|  |  | *F,R* | -0.014±0.001 | -0.01±0.001 | 0.993 | 0.001 | 146.55 | 2.19±0.005 | 7 | 0.71 |
|  |  |  |  |  |  |  |  |  |  |  |
| 3 | C6 | *σI ,σR* | 0.016±0.002 | 0.026±0.002 | 0.996 | 0.001 | 176.46 | 2.08±0.001 | 6 | 1.63 |
|  |  | *σI ,σRo* | 0.02±0.01 | 0.016±0.01 | 0.810 | 0.006 | 2.86 | 2.07±0.004 | 6 | 0.8 |
|  |  | *σI ,σR+* | 0.008±0.019 | 0.01±0.01 | 0.636 | 0.01 | 1.36 | 2.07±0.009 | 7 | 1.25 |
|  |  | *σI ,σR-* | 0.014±0.008 | 0.017±0.007 | 0.885 | 0.005 | 5.43 | 2.07±0.003 | 6 | 1.21 |
|  |  | *F,R* | 0.015±0.003 | 0.032±0.002 | 0.990 | 0.002 | 105.40 | 2.08±0.001 | 7 | 2.13 |
|  |  |  |  |  |  |  |  |  |  |  |
| 4 | C7 | *σI ,σR* | -0.001±0.002 | -0.008±0.002 | 0.928 | 0.001 | 9.34 | 2.21±0.0018 | 6 | 2.0 |
|  |  | *σI ,σRo* | -0.002±0.004 | -0.004±0.004 | 0.550 | 0.002 | 0.649 | 2.21±0.002 | 6 | 2.0 |
|  |  | *σI ,σR+* | 0.0014±0.002 | -0.003±0.002 | 0.669 | 0.002 | 1.618 | 2.21±0.002 | 7 | 0.21 |
|  |  | *σI ,σR-* | -0.001±0.003 | -0.004±0.003 | 0.648 | 0.002 | 1.087 | 2.21±0.01 | 6 | 4.0 |
|  |  | *F,R* | -0.001±0.003 | -0.005±0.002 | 0.806 | 0.001 | 3.719 | 2.21±0.001 | 7 | 5.0 |
|  |  |  |  |  |  |  |  |  |  |  |
| 5 | C11 | *σI ,σR* | -0.002±0.0002 | -0.003±0.0002 | 0.998 | 0.0001 | 341.86 | 2.21±0.0001 | 6 | 1.5 |
|  |  | *σI ,σRo* | -0.003±0.001 | -0.002±0.001 | 0.859 | 0.0007 | 4.22 | 2.21±0.0005 | 6 | 0.66 |
|  |  | *σI ,σR+* | -0.001±0.002 | -0.0012±0.001 | 0.699 | 0.001 | 1.91 | 2.21±0.001 | 7 | 1.2 |
|  |  | *σI ,σR-* | -0.0023±0.001 | -0.002±0.001 | 0.915 | 0.001 | 7.70 | 2.21±0.0004 | 6 | 0.87 |
|  |  | *F,R* | -0.002±0.0003 | -0.004±0.0002 | 0.993 | 0.002 | 152.18 | 2.21±0.001 | 7 | 2.0 |
|  |  |  |  |  |  |  |  |  |  |  |
| 6 | C22’ | *σI ,σR* | 0.01±0.02 | 0.08±0.02 | 0.891 | 0.01 | 5.81 | 2.11±0.01 | 6 | 8.0 |
|  |  | *σI ,σRo* | 0.02±0.01 | 0.03±0.04 | 0.438 | 0.03 | 0.35 | 2.10±0.02 | 6 | 1.5 |
|  |  | *σI ,σR+* | -0.01±0.05 | 0.02±0.02 | 0.475 | 0.03 | 0.58 | 2.11±0.03 | 7 | 2.0 |
|  |  | *σI ,σR-* | 0.008±0.04 | 0.04±0.03 | 0.595 | 0.02 | 0.82 | 2.10±0.02 | 6 | 5.0 |
|  |  | *F,R* | 0.006±0.02 | 0.008±0.02 | 0.903 | 0.01 | 8.85 | 2.12±0.01 | 7 | 1.33 |

**Table ( ): TSP analysis of SCS data of C22’ carbon atom of** **substituted**

**5-benzylidenebarbituric acids employing equations () and ().**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
| S.No. | Scale | α | β | φ | R | S | n | PR | PS |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| 1. | *σI ,σRo,ν* | -0.0077  (±0.09) | 0.0187  (±0.06) | 0.0215  (±0.06) | 0.492 | 0.03 | 6 | 17.00 | 44.89 |
|  |  |  |  |  |  |  |  |  |  |
| 2. | *F, R, ν* | -0.0009  (±0.05) | 0.078  (±0.027) | 0.005  (±0.03) | 0.904 | 0.016 | 7 | 93.19 | 5.97 |
|  |  |  |  |  |  |  |  |  |  |